Overview of Current Strategies for Diagnostic Imaging of Biliary Tract and Gallbladder Tumors

Heljä Oikarinen

Contents

Abstract

Early diagnosis of biliary cancers would be important to improve their prognosis, and accurate staging would help to choose the best possible treatment. However, biliary cancers present specific diagnostic challenges. Imaging modalities, imaging-guided fine-needle aspiration, and endoscopic brush samples play a crucial role in the diagnostic work-up. However, there is no single modality capable of reliably detecting and accurately staging biliary cancers; hence, complementary modalities are usually needed. Transabdominal ultrasound (US) is often the first imaging modality applied to patients with jaundice or nonspecific gastrointestinal complaints. US visualizes bile duct obstruction accurately and is a suitable method for assessing even mild symptoms, and it is noninvasive, nonradiative, and commonly available. If a biliary malignancy is suspected, further investigations are usually performed after US. Magnetic resonance imaging (MRI) and multidetector computed tomography (MDCT) may yield additional information of the tumor and/or its extent. Fast-imaging techniques have made MRI potentially more valuable, and magnetic resonance cholangiography (MRC) is the least invasive mode of cholangiography, which is useful with MRI in the case of biliary obstruction. MDCT can produce multiplanar reconstructions of good quality but it has exposed patients to relatively high dose of radiation. In ambiguous cases, both MRI and MDCT may be needed. Direct cholangiography may provide the most accurate anatomic information of the bile ducts. It is also needed for therapeutic purposes in the case of bile duct obstruction. Further, positron emission tomography (PET), PET/CT, and endoscopic or intraductal US may help in the diagnostic work-up, when available.

H. Oikarinen (✉)
Department of Diagnostic Radiology,
Oulu University Hospital (OYS),
POB 50FI-90029 Oulu, Finland
e-mail: helja.oikarinen@ppshp.fi

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1 Introduction

Carcinoma of the gallbladder is the most common biliary malignancy. Cancers of the bile ducts are less common, but their incidence has been increasing. Bile duct tumors can be classified as intrahepatic (or peripheral) cholangiocarcinoma (ICC), hilar (or Klatskin) tumors, and extrahepatic tumors. Klatskin tumors are the most common. Most biliary tumors (tumors of the gallbladder and the bile ducts) are malignant adenocarcinomas, the prognosis for which has been dismal. Early diagnosis of biliary tumors would be important to improve their prognosis, and accurate staging would help to choose the best possible treatment. However, biliary tumors present specific diagnostic challenges. Their symptoms may be mild or unspecific, such as abdominal pain, malaise, mild fever, or weight loss. In the case of bile duct obstruction, jaundice may be the presenting sign. The differences in the clinical behavior of bile duct cancers are due to variation in the location and size of the tumor at the time of diagnosis. A tumor of the papilla of Vater or the distal common bile duct may cause jaundice at an early stage, while ICC—or gallbladder carcinomas—is often advanced before causing symptoms of obstruction. Gallbladder carcinoma is often found incidentally in a resected cholecystectomy specimen. Gallstones are present in most of the affected patients [1–3].

Imaging modalities, image-guided fine-needle aspiration (FNA), and endoscopic brush samples play a crucial role in the diagnostic work-up, although laboratory findings or tumor markers may also be suggestive of a tumor. However, there is no single modality capable of reliably detecting and accurately staging biliary cancers; hence, complementary modalities are usually needed.

This chapter will concentrate on the potential of different imaging modalities to respond to the challenge of how to diagnose and stage biliary cancers. The current state-of-the-art strategies are also discussed. Similar imaging modalities and diagnostic strategies are mainly used for both carcinoma of the gallbladder and carcinoma of the bile ducts. Therefore, the possibilities of each imaging method in both cancer types are presented under the subheadings of the modalities. Although jaundice with bile duct obstruction is typical for cancer of the bile ducts, it is also common in advanced gallbladder cancer.

The accuracy for diagnosing a bile duct carcinoma has been up to 84 % for ultrasound (US), 94 % for computed tomography (CT), and 95 % for magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP) [4]. However, comparative studies of the accuracies of modern MRI with MRCP and multidetector computed tomography (MDCT) in biliary cancers are sparse. It is also challenging to compare existing studies due to the differences in study design, algorithms, or equipment and the differences in the origin of the tumors. There is also rapid emergence of novel technology. The classification and nomenclature of bile duct tumors and classification for operability are variable, as well. Nevertheless, the conclusions of the pertinent literature are highlighted and discussed.

2 Spread, Staging, and Treatment of Biliary Cancers

With the exception of ampullary carcinoma, the prognosis of biliary carcinomas has been poor. In biliary cancers, the histologic type, the staging, and, in the case of carcinoma of the bile ducts, the location of the tumors are the most important prognostic factors. Papillary-type carcinomas have the most favorable prognosis. In general, resection provides the only chance of cure, and since advanced surgical techniques are increasingly used, there is a need for accurate preoperative staging and determination of the best therapeutic option.

Gallbladder carcinoma spreads early in its course. It invades the wall of the gallbladder and into the liver and spreads into the lymph nodes. Common bile duct, hepatic artery, portal vein, stomach, duodenum, transverse colon, pancreas, and omentum are at risk of tumor extension. It usually metastasizes to the peritoneum and liver and, occasionally, to the lungs and pleura.

ICC may spread to other intrahepatic locations, vessels, common bile duct, regional and more distant lymph nodes, adjacent organs, peritoneum, abdominal wall, diaphragm, lungs, and pleura. Klatskin tumors have a tendency to spread to adjacent hepatic parenchyma, vessels, bile ducts, and regional lymph nodes, especially hilar and pericholedochal nodes. It is characterized by intrahepatic ductal extension and spread along perineural and periductal lymphatic channels. Liver metastases are common and klatskin tumors may also metastasize to the peritoneal cavity, lungs, brains, and bones.

Distal bile duct cancer can spread to the vessels, lymph nodes, pancreas, duodenum, stomach, colon, or omentum. Distant metastases may occur in the liver, peritoneum, and lungs. Ampullary carcinoma may spread to the regional lymph nodes and adjacent structures, such as duodenum, the head of the pancreas, and extrahepatic bile ducts. Metastases may occur in the liver, peritoneum, lungs, and pleura.

In the case of a bile duct tumor, in addition to the spread, it is important to evaluate the location, length, and local invasion of the tumor. The TNM classifications of biliary tumors are used for staging. There are different staging systems. Separate staging schemes for gallbladder carcinoma, ICC, Klatskin tumors, distal tumors, and ampullary carcinoma may be used [1–3, 5].

Table 1 Primary Tumor (T) [3] (Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1	Tumor invades lamina propria or muscular layer
T1a	Tumor invades lamina propria
T1b	Tumor invades muscular layer
T2	Tumor invades perimuscular connective tissue; no extension beyond serosa or into liver
T3	Tumor perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure, such as the stomach, duodenum, colon, pancreas, omentum, or extrahepatic bile ducts
T4	Tumor invades main portal vein or hepatic artery or invades two or more extrahepatic organs or structures

The original source for this material is the AJCC Cancer Staging Handbook, Seventh Edition (2010) pulished by Springer Science and Business Media LLC, http://www.springerlink.com.)

Table 2 Bismuth classification of hilar cholangiocarcinoma [6]

Type I	Confluence of the right and left hepatic ducts not involved
Type II	Tumor involves the confluence of the hepatic ducts
Type III	Tumor involves the confluence of the hepatic ducts and extends into the right (IIIA) or left duct (IIIB)
Type IV	Tumor extends into both hepatic ducts and the confluence

Table 3 Criteria for unresectability in patients with hilar cholangiocarcinoma [8]

Medical comorbidities limiting the patient's ability to undergo major surgery
Significant underlying liver disease prohibiting liver resection necessary for curative surgery based on preoperative imaging
Bilateral tumor extension to secondary biliary radicals
Encasement or occlusion of the main portal vein
Lobar atrophy with contralateral portal vein involvement
Contralateral tumor extension to secondary biliary radicals
Evidence of metastases to N2 level lymph nodes[a]
Presence of distant metastases

[a] N2 lymph nodes, metastasis in the peripancreatic (head only), paraduodenal, periportal, celiac, superior mesenteric, and/or posterior pancreaticoduodenal lymph nodes.

There are various practices for the treatment of biliary cancers. In gallbladder carcinomas, surgery is the only curative therapy in properly selected patients. T1–2 tumors are potentially resectable, while T4 tumors are usually regarded as unresectable (Table 1). Patients with advanced cancer or significant comorbidities are candidates for biliary enteric bypass or biliary drainage, and adjuvant or palliative chemotherapy and radiotherapy are also possible [6, 7]. In the case of ICC, surgical exploration is carried out if imaging reveals that a complete resection is possible. A poor prognosis is associated with regional lymph node involvement and incomplete resection in patients treated with resection [3].

There is no universally accepted surgical approach for Klatskin tumors, and variable practices are employed. Bismuth staging is often used to describe the extent of tumor involvement within the ductal system (Table 2). Criteria for unresectability have also been published and are presented in Table 3. The operative goal is complete resection with negative histologic margins, which is the most important predictor of long-term survival. However, the proximity to the hepatic artery, portal vein, and hepatic parenchyma makes excision challenging. Partial hepatic resection or total hepatectomy with transplantation are also possible. Most patients have logoregional extension or distant metastasis that precludes resection. Factors impairing survival include vascular invasion, lobar atrophy, and lymph node metastasis [3, 6, 8]. The operative procedure for distal bile duct cancers consists of pancreaticoduodenectomy or local bile duct excision. Ampullary carcinoma is usually treated by pancreaticoduodenectomy. Endoscopic treatment or transduodenal excision may also be possible [6].

Patients with unresectable bile duct carcinoma may need palliative treatment for jaundice, which can be accomplished by biliary enteric bypass, percutaneous biliary drainage, or by inserting a plastic or metallic stent percutaneously or endoscopically. Catheters suffer from the risk of infection or dislodgement, and the major problems with plastic stents are displacement and occlusion with sludge. Self-expandable metallic stents inserted by radiologists have advantages over plastic stents, as they can be introduced on a small delivery catheter, have a large inner diameter, and remain in a fixed position after release. However, they may also cause infections or become occluded by tumor ingrowth or overgrowth. Radiotherapy and/or chemotherapy is used as adjuvant therapy or palliation, and photodynamic therapy and thermoablative procedures are also options [4, 9–11].

A few biostatistical terms will be defined here, as they are used widely in the literature and in subsequent chapters. Sensitivity is the proportion of true positives (TP) that are correctly identified by the test, and specificity is the proportion of true negatives (TN) that are correctly identified by the test. Positive predictive value is the proportion of patients with positive test results who are correctly diagnosed, and negative predictive value is the proportion of patients with negative test results who are correctly diagnosed. Accuracy is

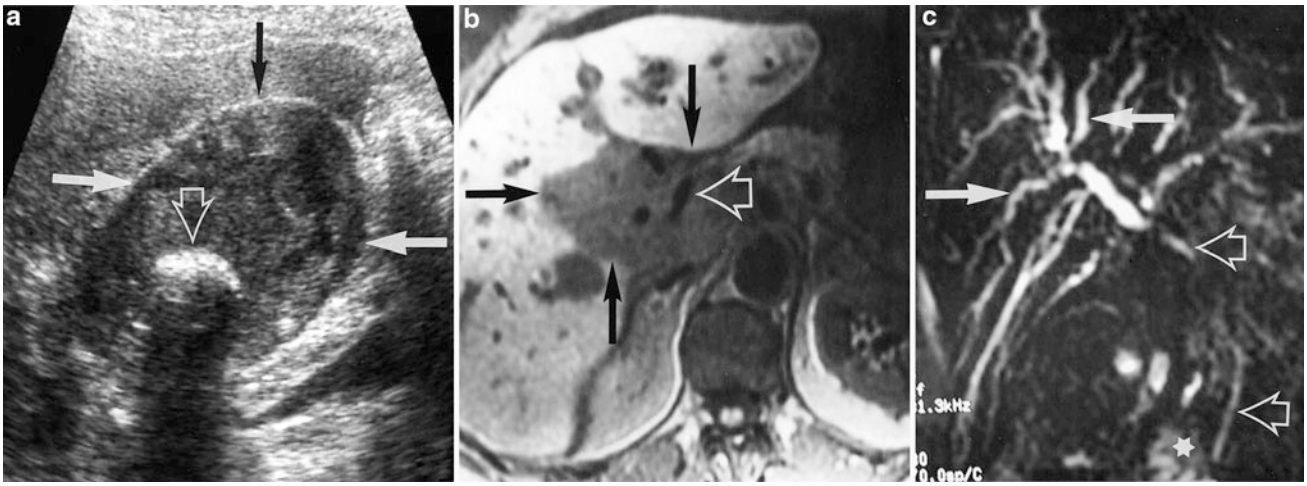

Fig. 1 Gallbladder carcinoma. **a** Sonography reveals tumorous tissue replacing the gallbladder (*arrows*). A gallstone is also seen (*open arrow*). **b** MRI (T1 fat-saturated gradient echo) shows tumorous tissue even in the hilar area (*arrows*). There are vessels inside the tumorous area (*open arrow*). **c** MRC reveals intrahepatic bile duct dilatation (*arrows*). Extrahepatic bile ducts are seen only partly (*open arrows*) because of the strictures caused by tumorous tissue. Duodenum (*) [2]

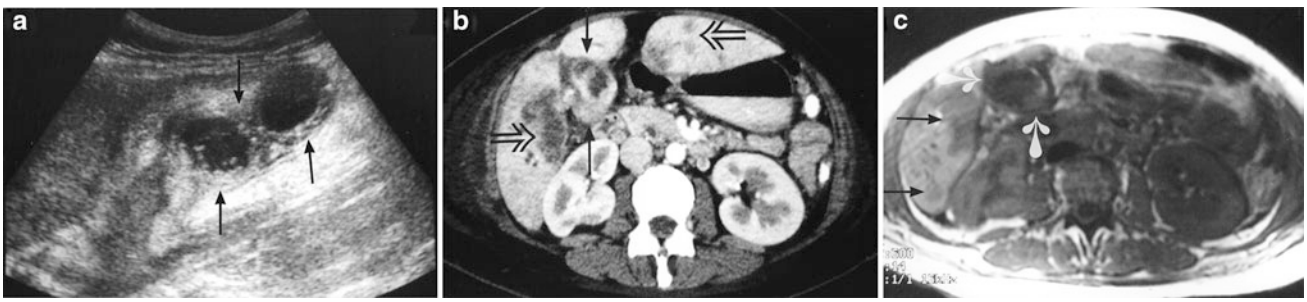

Fig. 2 Gallbladder carcinoma. **a** The gallbladder is thick-walled and deformed (*arrows*) due to carcinoma (sonography). **b** CT (arterial phase) also reveals a tumorous gallbladder (*arrows*) and metastases of the liver (*open arrows*). **c** The thickened gallbladder wall (*white arrows*) seen in MRI (T1 spin echo). Liver metastases are also visible (*black arrows*) [2]

the proportion of true results in the population. It is defined as a ratio of TP + TN and TP + FP + FN + TN (FP = false positive and FN = false negative).

3 Ultrasound

Transabdominal US is often the first imaging modality applied to patients with nonspecific gastrointestinal complaints or jaundice. It is a suitable method for even mild symptoms, and it is commonly available. US does not include any radiation, the examination can be performed at bedside, and it is relatively inexpensive. However, the value of US depends on the experience of the operator and the quality of the equipment. It may also be problematic in the case of obese patients and in the presence of bowel gas. The sensitivity of US to reveal a primary tumor of the gallbladder or the bile ducts has increased to over 90 % with technical development of the equipment, although problems do occur, especially with small bile duct tumors [12, 13].

3.1 Carcinoma of the Gallbladder

A tumor of the gallbladder may appear on US as a mass of variable echogenicity filling the entire lumen of the gallbladder (exophytic type) (Fig. 1). There may be tumor necrosis, and echogenic foci may be related to gallstones, porcelain gallbladder, air, or calcification of the tumor itself. Other manifestations are focal or diffuse thickening of the gallbladder wall, which can be hypo- or hyperechoic and often irregular (infiltrating type) (Fig. 2), or an intraluminal fungate mass with a nodular or smooth contour and variable

echogenicity (polypoid type). The mass type is the most common, and the infiltrating type has been the most difficult to detect by US. Gallstones may sometimes disturb the visualization of tumors [14–16].

US- or CT-guided FNA is necessary to reveal the malignant nature of the tumor. This technique has a diagnostic accuracy of 95 %. For differential diagnosis, tumorous sludge, other causes of wall thickening (e.g., cholecystitis), benign polyps, and other malignancies should be noticed.

Early-stage cancers have been difficult to detect sonographically. However, it has been reported that most early cancerous lesions appear polypoid at US, and high-resolution US can detect even small lesions. Single polyps, broad-based sessile polyps, or lesions larger than 1 cm are more likely to be malignant. There have been efforts to differentiate benign from malignant lesions with Doppler, and the results are suggestive at best [7, 17, 18].

For detailed analysis, endoscopic US (EUS) or intraductal US (IDUS) has also been promising. High-frequency EUS can provide high-resolution images, and it can reveal the layered structure of the gallbladder and gallbladder masses. It has been useful in differentiating polyps or wall thickening. In the presence of polyps, the internal echogenicity and contour of polypoid lesions are analyzed. EUS is also used to guide FNA procedures. However, EUS or IDUS are more invasive, less widely available, and more examiner-dependent. Contrast-enhanced US has also been a valuable adjunct for the differential diagnosis of polypoid lesions, and laparoscopic US may help to detect unsuspected cancer during laparoscopic cholecystectomy [19–22].

3.2 Carcinoma of the Bile Ducts

The most frequently seen abnormality due to carcinoma of the bile ducts at US is dilatation of the intrahepatic bile ducts, which may also accompany advanced gallbladder carcinoma (Fig. 3). In fact, such dilatation can be an indirect sign of a biliary tumor. The accuracy of US to define the level and cause of obstruction with surgical obstructive jaundice has been 95 and 88 %, respectively. Malignancies are found especially in obstructions at the distal or hilar level. The zone of transition from a dilated to a nondilated or nonvisualized duct should be evaluated regardless of the imaging modality. Bile duct carcinoma can also be visible as a mass (exophytic, nodular), an infiltrating tumor (sclerosing, periductally infiltrating), or a polypoid growth (papillary, intraductal growth). The infiltrating type has been especially difficult to detect. The polypoid type is rare and of low-grade malignancy [23–26].

The mass-forming type of ICC, Klatskin tumor, or extrahepatic carcinoma may present as a tumor mass with

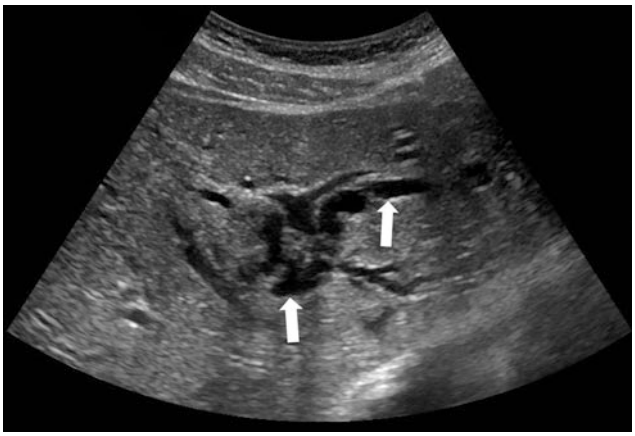

Fig. 3 Intrahepatic bile duct dilatation (*arrows*) seen at US

variable echogenicity (Figs. 4, 5). Carcinomas of the distal common bile duct are often small. The architecture is also dependent on the amount of fibrous tissue, mucin, calcification, and necrosis. An infiltrating tumor may show a diffusely abnormal liver echo pattern or focal irregularity of the ducts. However, in these two types, US may only reveal bile duct dilatation—a small mass or bile duct wall thickening may not be depicted. Intraductal carcinomas have a variety of imaging features. They may be single or multiple with variable echoes, and a mucin-secreting tumor (intraductal papillary mucinous tumor) may present as a cystic mass and sometimes severe bile duct dilatation. With bile duct cancers, peripheral bile duct dilatation, necrosis, satellite nodules, calcification, lobar atrophy, pressure effects, and, in the case of Klatskin tumors, segmental dilatation and nonunion of the right and left ducts may also be seen. Lobar atrophy may be caused by vascular or biliary obstruction [24, 27–29].

Contrast-enhanced US has been introduced to characterize focal liver lesions and has shown hyperperfusion in the arterial phase and punched-out defects in the late portal venous phase with ICC. It has also improved the detection and staging of malignant hilar obstruction (mostly caused by biliary malignancies) compared with unenhanced sonography [30, 31]. US- or CT-guided FNA may reveal the malignant nature of the tumor. However, FNA can be hazardous in the case of hilar tumors due to the adjacent big vessels. Differential diagnosis of bile duct cancer includes other malignant diseases (e.g., liver and lymph node metastases, hepatocellular carcinoma, pancreatic cancer, or gallbladder carcinoma), bile duct stones, and benign tumors or strictures (e.g., primary sclerosing cholangitis). Extrinsic tumors may displace, encircle, obstruct, or invade the bile ducts visualized by different modalities.

To get detailed information, laparoscopic US or EUS may show the presence and origin of a small hilar or common bile duct tumor. IDUS has also been valuable in

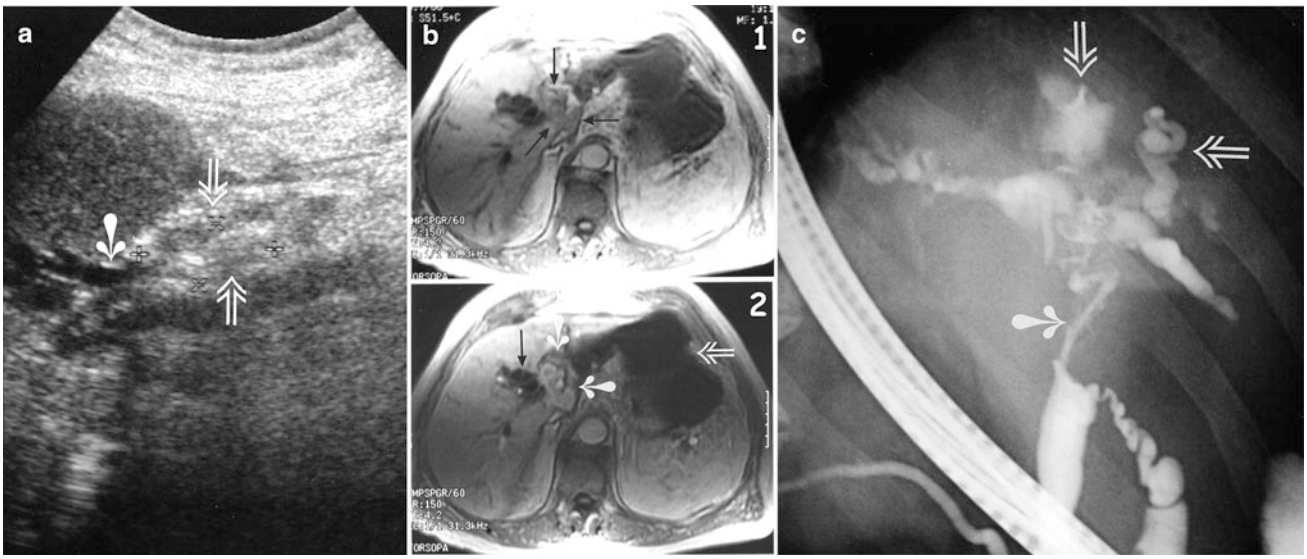

Fig. 4 Klatskin tumor. **a** Intrahepatic biliary dilatation (*white arrow*) ends in the hilar area, where sonography shows an unclear heterogeneous mass (*open arrows*). **b** MRI (T1 gradient echo) reveals slightly different tissue in the hilar area (*arrows*). *2* Gadolinium-enhanced MRI (T1 gradient echo) shows nonhomogeneously enhanced tissue in the hilar area (*white arrows*). Intrahepatic bile duct dilatation (*black arrow*) and a biloma (*open arrow*) are also shown. **c** ERC shows a long stricture of the common hepatic duct (*arrow*) and intrahepatic bile duct dilatation (*open arrows*) [2]

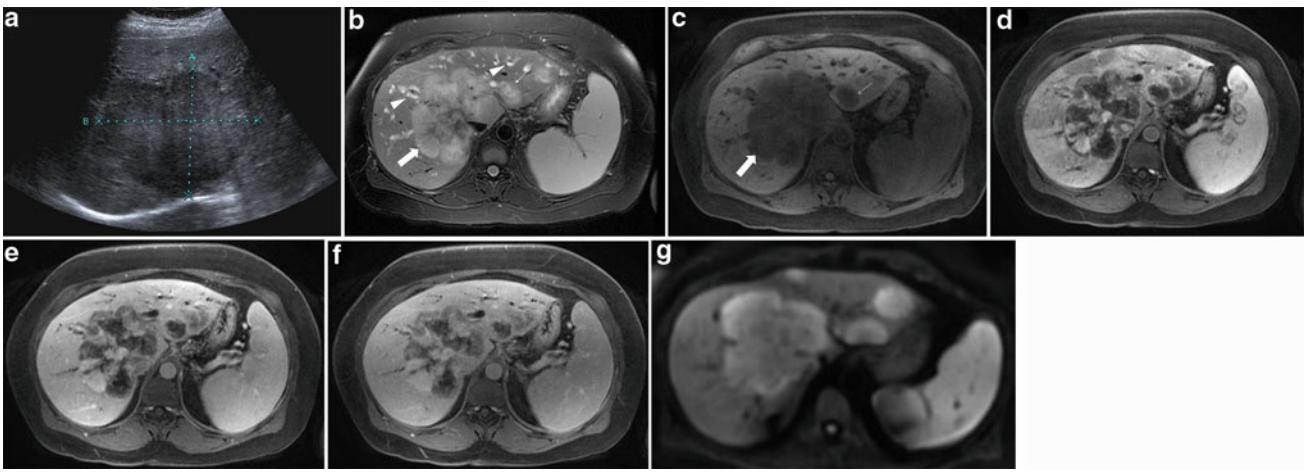

Fig. 5 Cholangiocarcinoma. **a** A large hypoechoic, heterogenic expansion is seen in the central area of the liver at US. **b** MRI (fat-saturated T2 axial FSE) reveals a large hyperintense, lobulated tumor (*thick arrow*) with intrahepatic metastases (*thin arrow*) and bile duct dilatation (*arrowheads*). **c–f** Gadolinium-enhanced MRI (T1 fat-saturated gradient echo) reveals heterogenic dynamic enhancement of the tumor (*thick arrow*) and the metastasis (*thin arrow*) (unenhanced, arterial, portovenous, and delayed phases). **g** Diffusion-weighted image shows the tumor and metastases

biliary strictures, and it can show tumor extension. EUS-guided FNA is useful in bile duct tumors, too. EUS with FNA has had a greater sensitivity for detecting malignant strictures than endoscopic retrograde cholangiopancreatography (ERCP) with brushings. However, it also has the potential for tumor seeding [9, 20, 22, 32–34].

In the case of an ampullary tumor, transabdominal US may only reveal the double-duct sign (dilatation of the bile duct and the pancreatic duct). Endoscopy with a biopsy, EUS, or IDUS may show the tumor itself, and EUS and IDUS are able to define the size, invasion, and extension of the tumor [34, 35].

3.3 Staging of Biliary Cancers by US

US may help to reveal the spread of a suspected malignancy. Doppler can be used to analyze hepatic vessels. In gallbladder carcinoma or Klatskin tumors, US with

Doppler can detect spread into the liver, the portal vein, and the bile ducts rather well, but it is not equally good in the detection of lymph node and especially peritoneal metastases. Advanced gallbladder carcinoma has been understaged by US. There are also controversial results about US in liver and lymph node invasion in gallbladder carcinoma. At any rate, other imaging modalities are also involved in the difficult analysis of pathologic, but normal-sized lymph nodes [12, 14, 27].

More invasive EUS, IDUS, or laparoscopic or intraoperative US has improved staging. EUS and IDUS are useful especially in evaluating the bile duct, the regional lymph nodes, or the vessels, but they are not suitable for the detection of distant metastases. EUS with FNA may be useful in lymphadenopathy. In addition, transabdominal or endoscopic US elastography might help to reveal malignancy of the tumors or the lymph nodes. Malignant expansions are stiffer than benign tissue [9, 13, 22, 33, 34].

4 Computed Tomography

Further investigations are usually desirable after US. Recent technological developments have led to improvements in CT and MRI. We lack large-scale comparative reports of MDCT and modern MRI with MRCP on the sensitivity and accuracy of finding and staging biliary cancers, which makes it difficult to rank these two methods. The choice of modality also depends on local expertise, capacity, and facilities. Sometimes both modalities are needed.

With MDCT, the liver can be imaged in a single breathhold, which eliminates artifacts from respiratory motion and slice misregistration. Thin, high-resolution images and high-quality multiplanar reformations of even curved structures are produced. The arterial and portovenous phases can be separated, and vascular structures can be displayed. CT angiography (CTA) with high-resolution three-dimensional (3D) angiograms, virtual CT cholangioscopy, or CT cholangiography with cholangiographic contrast medium are also possible. CT protocol should include CT acquisition (with intravenous contrast medium) with the early and late arterial phases and the portovenous phase. The early arterial phase is able to reveal the anatomy of the vessels. An additional delayed phase might reveal specific signs in the case of a bile duct tumor [36]. In spite of the marked improvement in image quality, modern MDCT has suffered from the high levels of radiation and possible allergy to the iodinated contrast medium.

4.1 Carcinoma of the Gallbladder

The sensitivity of CT in the detection of gallbladder carcinoma has been about 90 %. MDCT has been accurate in the diagnosis of the local extent of the cancer. The findings of gallbladder carcinoma may include a heterogenous mass replacing the gallbladder, wall thickening (Fig. 2), or a fungate (polypoid) tumor. The mass may have various retaining enhancement, an ill-defined contour, and low-attenuation areas of necrosis or calcification. Wall thickening may be irregular and enhance markedly. A polypoid tumor may also enhance, and the adjacent gallbladder wall may be thickened. There have been differences in the enhancement of the wall thickening between carcinoma and chronic cholecystitis. Protrusion of the quadrate lobe with lymphadenopathy has been reported to be unique to gallbladder carcinoma [16, 37–40].

4.2 Carcinoma of the Bile Ducts

Bile duct carcinoma often shows abrupt termination of bile duct dilatation at CT, which can be a finding in advanced gallbladder carcinoma as well. The accuracy of CT to determine the level and cause of obstruction has been 97 and 94 %, respectively. The sensitivity of CT to find bile duct carcinoma has been about 90 % [41]. However, CT may not readily detect a small mass or bile duct wall thickening.

A mass type tumor (Fig. 6) manifests as a low-attenuation mass, which may show peripheral enhancement during the arterial and portal venous phases. Delayed images with concentric retention of contrast are typical of highly fibrous content, and some tumors may only visualize on delayed images. This feature may help to differentiate them from hepatocellular carcinoma. Focal, eccentric wall thickening may have various enhancement patterns (Figs. 7, 8). A polypoid type tumor can be a single or multiple intraductal lesions with increased enhancement. In the case of excessive amounts of mucin, accumulated mucin can cause significant ductal dilatation, direct continuity of a cystic tumor to the ducts, and increased attenuation of the ducts caused by tumor casts or by diffuse spreading of the tumor. CT may have an important role in the diagnosis of papillary tumors [23, 24, 29, 42–46].

In the case of an ampullary tumor, CT may reveal both the double-duct sign and the tumor itself (Fig. 9) [35]. Bile duct carcinoma may also show calcification, biliary dilatation, nonunion of the right and left hepatic ducts, satellite

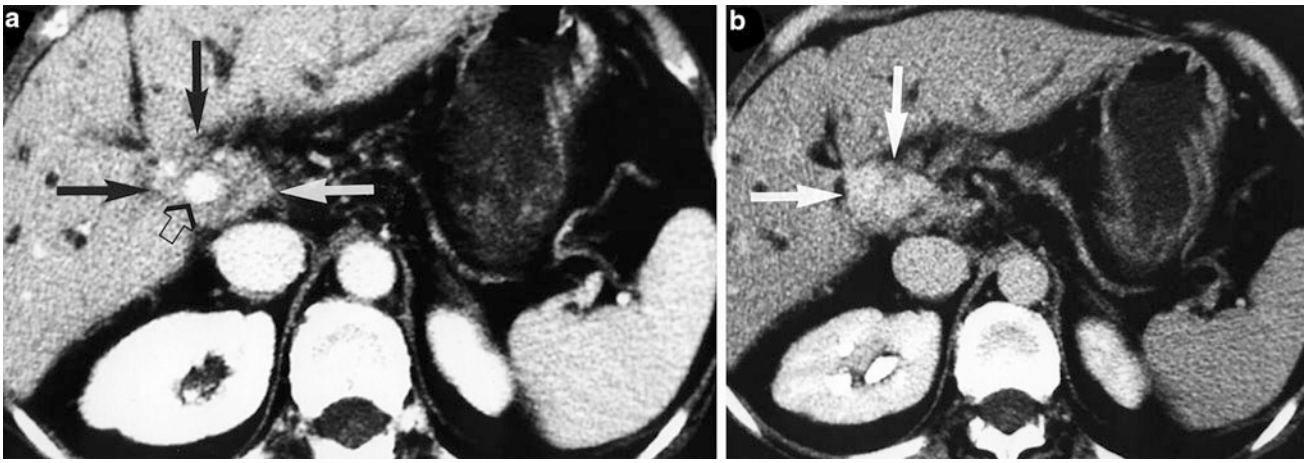

Fig. 6 Bile duct carcinoma. **a** CT in the venous phase shows a heterogeneous mass (*arrows*) in the hilar area around the portal vein (*open arrow*). The common bile duct is not seen because of obliteration caused by the tumor. **b** In the delayed phase, the mass shows enhancement (*arrows*) [2]

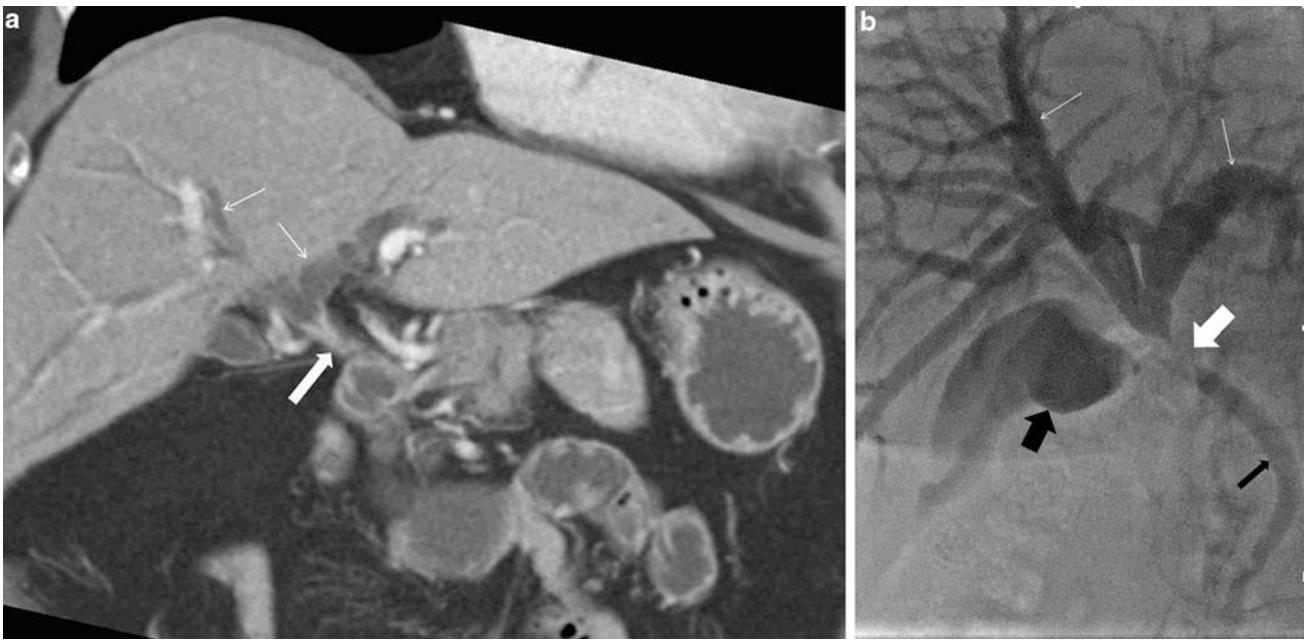

Fig. 7 Cholangiocarcinoma. **a** Coronal view reconstruction of contrast-enhanced CT shows a stricture with enhanced wall thickening of the common hepatic duct (*thick arrow*) and intrahepatic bile duct dilatation (*thin arrows*). **b** A stricture of the common hepatic duct (*white thick arrow*) and dilatation of the intrahepatic bile ducts (*white thin arrows*) are revealed by PTC. The gallbladder (*black thick arrow*) and normal-sized common bile duct (*black thin arrow*) are also seen

lesions, lobar atrophy, and capsular retraction. Stents inserted to relieve jaundice may limit the usefulness of CT in diagnosis and staging.

4.3 Staging of Biliary Cancers by CT

CT has been quite sensitive in assessing liver, vascular, and bile duct invasion of gallbladder carcinoma (Fig. 2) or bile duct tumor (Fig. 6), but not as good or variable in carcinomatous spread into lymph nodes, omentum, and peritoneum. In practice, however, CT seems to be the best modality for assessing peritoneal spread. As mentioned earlier, especially MDCT has provided good accuracy in the diagnosis of the local extent of carcinomas of the gallbladder (T staging). Invading gallbladder carcinoma may show irregular enhancement with regions of necrosis. The accuracy for local staging has been better for intraluminal mass types than for thickened wall-type tumors. Dual-phase helical CT has been reported to be a useful tool in assessing

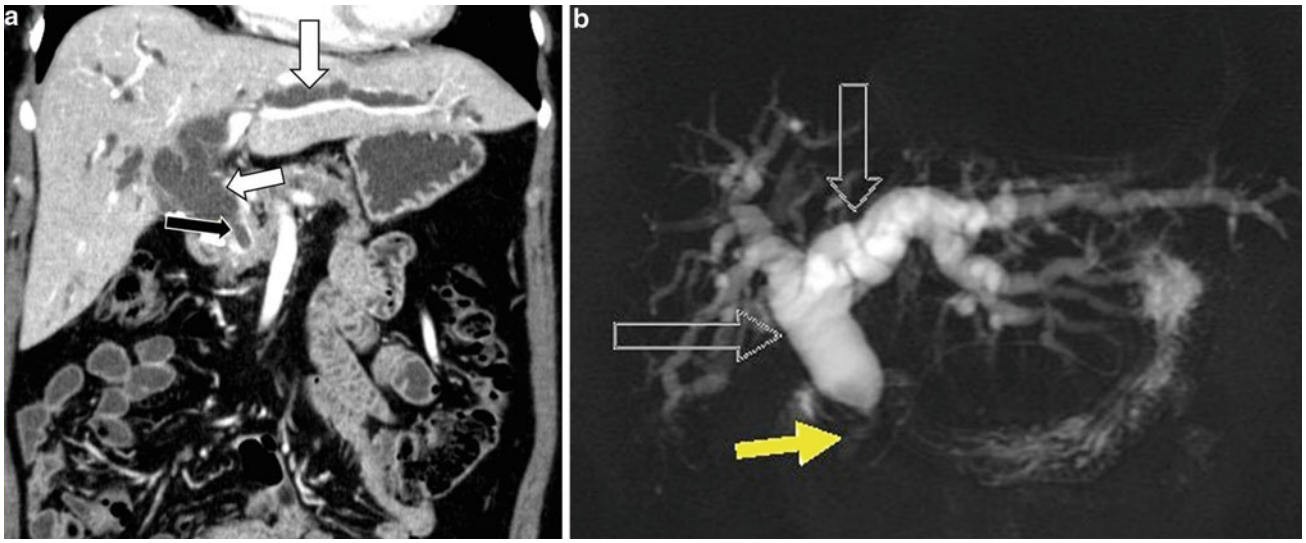

Fig. 8 Carcinoma of the common bile duct. **a** Coronal view reconstruction of contrast-enhanced CT reveals enhancement of the thickened wall of a 2-cm stricture in the distal common bile duct (*black arrow*) and marked intra- and extrahepatic bile duct dilatation (*white arrows*). **b** MRCP (4-cm-thick slab) visualizes a stricture in the distal common bile duct (*arrow*) and marked intra- and extrahepatic bile duct dilatation (*open arrows*)

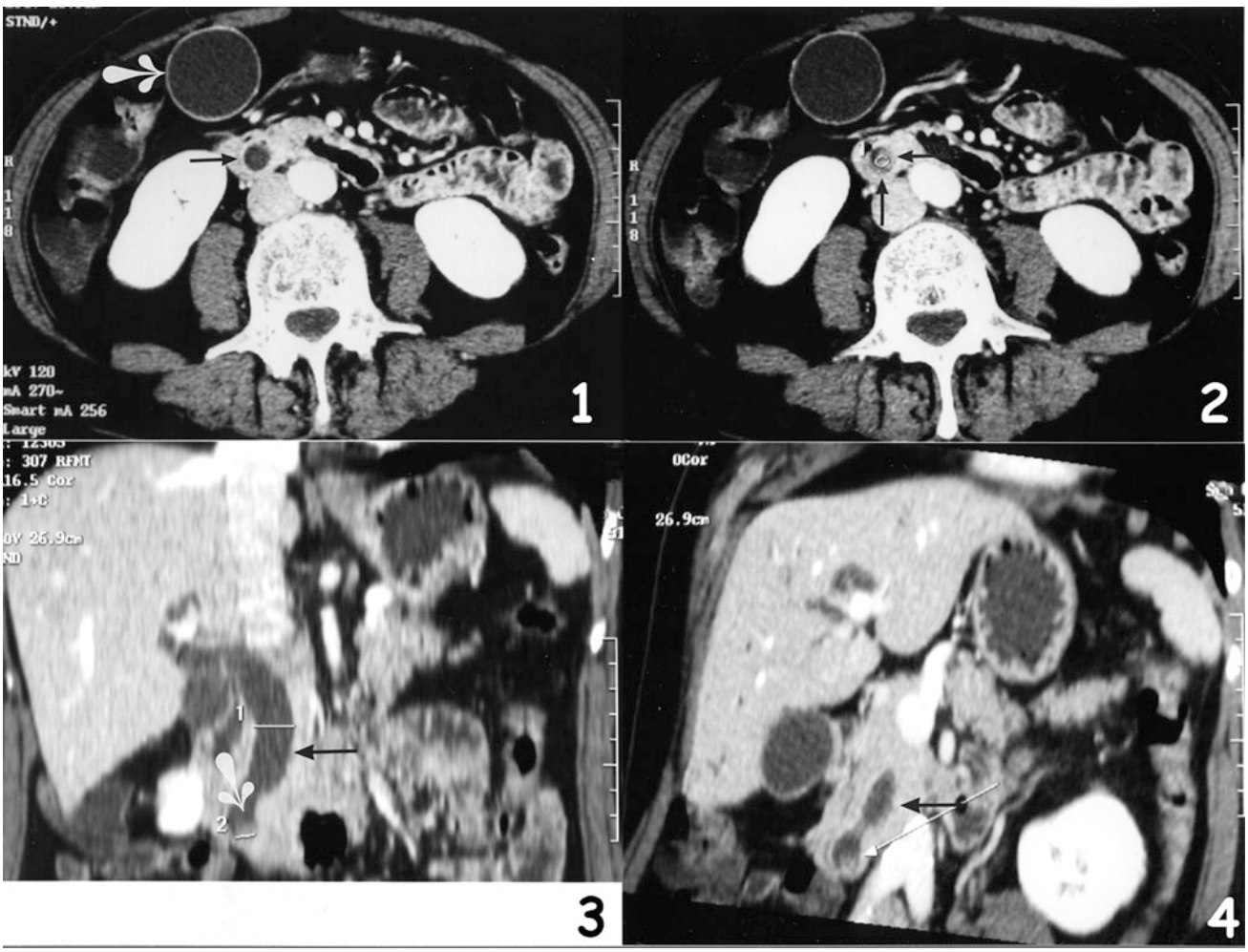

Fig. 9 Carcinoma of the papilla of Vater. Enhanced CT reveals a dilated gallbladder (*white arrow*) and a common bile duct (*black arrow*) (*1*) with an enhancing small mass in the ampullary area (*arrows*) (*2*). The coronary reconstructions show similar findings: the mass (*white arrow*) and the dilated common bile duct (*black arrow*) (*3*, *4*) [2]

the resectability of gallbladder cancers [28, 37, 38, 40, 41, 47–49].

The accuracy of MDCT has been 77 % in T staging of extrahepatic bile duct carcinoma, 63 % in N staging, and 97 % in M staging. In one report, 3D MDCT angiography and cholangiography with biliary contrast agent through a transhepatic drainage catheter showed the degree of vascular and biliary involvement of a Klatskin tumor. The diagnostic accuracy of portal vein and hepatic artery invasion was 94 and 89 %, respectively. Combined CT with direct cholangiography in Klatskin tumors has revealed 75 % accuracy for prediction of resectability. The accuracy for portal vein, arterial, and lymph node invasion was 86, 93, and 84 %, respectively. In general, metastatic lymph nodes are suspected if the short-axis diameter of a lymph node is longer than 10 mm, if central necrosis is present, or if attenuation is greater than for the hepatic parenchyma in the portal venous phase [49–52].

5 Magnetic Resonance Imaging and Magnetic Resonance Cholangiography

Fast-imaging techniques have made MRI more useful in biliary imaging. T1- and T2-weighted images of the liver can be obtained within a single breathhold. Using gadolinium chelate, it is possible to obtain images in the arterial, portal venous, and delayed phases.

Magnetic resonance cholangiography (MRC) is the least invasive mode of cholangiography, and it can show a detailed map of the biliary tree. Many studies consider MRC to be equally diagnostic as direct cholangiography in biliary diseases [53]. It is often a noninvasive alternative to ERCP or percutaneous transhepatic cholangiography (PTC), or when direct cholangiography fails. MR imaging also has high soft-tissue contrast and multiplanar capability, and it does not cause any ionizing radiation. However, there are certain contraindications to MRI as well, and interventions are usually not available.

Intrahepatic segmentary ducts are visible up to the first-order branches at MRC, and more peripheral ducts are seen in the case of dilatation. The accuracy of MRC to diagnose the presence and level of obstruction approaches 100 %, and it can show the bile ducts both above and below the obstruction as well as the severity of dilatation (Figs. 1, 8). Information on adjacent organs or extrinsic masses is also provided by MRC. However, the evaluation of obstruction in the case of bile duct carcinoma or advanced gallbladder carcinoma requires not only MRC, but also T1 and T2 images with gadolinium. Combined MRI/MRC has been superior to MRC or endoscopic retrograde cholangiography (ERC) alone in identifying malignant strictures in Klatskin tumors. Magnetic angiography (MRA) is able to provide images that resemble standard angiography [28, 36, 54, 55].

5.1 Carcinoma of the Gallbladder

There are only a few reports of MRI in the diagnosis of gallbladder carcinoma, but it has been considered a promising method. The tumor has been hypointense on T1 images (Fig. 2) and hyperintense or heterogenous on T2 images compared with the liver. With gadolinium, there may be early irregular enhancement, which persists throughout the dynamic study. Irregular wall thickening may also enhance markedly. Dynamic MRI has been used to differentiate different malignant gallbladder lesions from benign changes based on the enhancement pattern. The method has been promising [39, 56–58].

5.2 Carcinoma of the Bile Ducts

At MRC, bile duct carcinoma may typically show an irregular, asymmetric biliary stricture or obstruction with a dilatation above it (Figs. 8, 10). The morphology and length of the stricture can be evaluated by MRC. The accuracy of MRCP to differentiate extrahepatic bile duct cancer from benign stricture has been comparable with that of ERCP. However, differential diagnosis of a stricture may be difficult with MRC alone, and the discovery of a tumor at MRI may help to suspect a malignancy. MRC/MRI may show a mass type tumor, a polyp-type tumor, or a wall thickening. In view of recent technical improvements, a combination of single-shot thick-slab MRCP and thin-slice MRCP with MIP is the best choice for MRCP today. Biliary drainage can make bile duct assessment difficult, and MRC should hence be performed before biliary drainage [44, 59–62].

ICC and hilar tumors have been hypo- or isointense on T1 images (Figs. 4, 5), while the former have been hyperintense and the latter variable on T2 images. ICC may also have a hypointense central scar. There may be peripheral enhancement by gadolinium and concentric enhancement in the delayed phase. A high mucin content can cause high signal intensity on T2 images. Periductal infiltrating cancer with a thickened wall may show persistent enhancement (Fig. 10), and a papillary tumor may also enhance. Dilated ducts (Fig. 4), capsular retraction, satellite lesions, and lobar atrophy may also be seen, and segmental cholestasis may cause segmental hyperintensity on T1 images [29, 42, 43, 63].

An extrahepatic mass is often hypointense in both T1 and T2 images, and the malignancy may show strong enhancement in the delayed phase. A papillary tumor or wall thickening may also enhance. MRCP and 3D fat-saturated

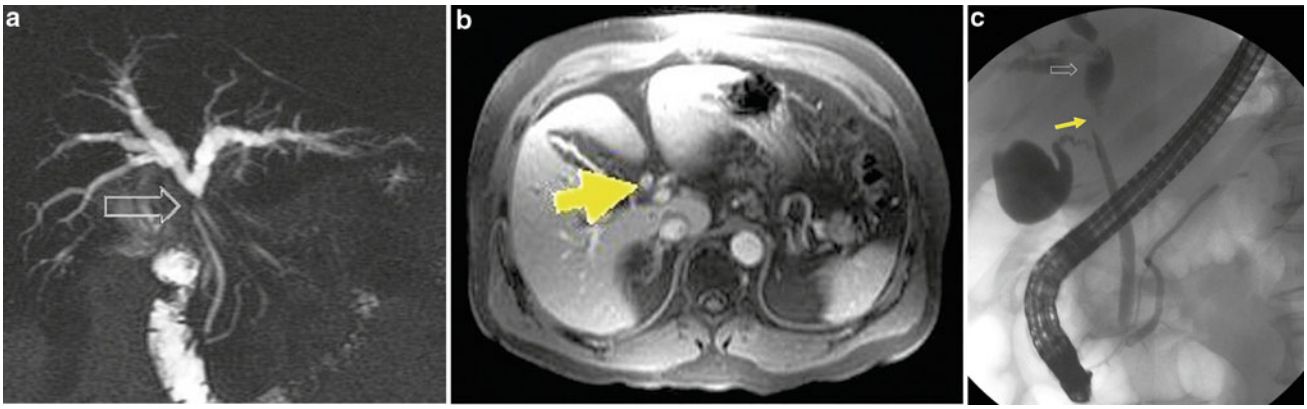

Fig. 10 Klatskin tumor. **a** MRCP (2-cm-thick slab) shows intrahepatic bile duct dilatation and a short, tight stricture in the common hepatic duct next to the bifurcation (*arrow*). **b** Gadolinium-enhanced MRI (T1 fat-saturated gradient echo) reveals enhancement of the wall thickening of the stricture (*arrow*). **c** ERC shows a short stricture in the common hepatic duct (*arrow*) and dilated intrahepatic bile ducts (*open arrow*)

thin-slice T1-weighted imaging with intravenous contrast at 3T MRI with enhanced spatial and temporal resolution has been superior in defining tumor margins and involvement of vascular and adjacent structures. Ampullary carcinomas have had low signal intensity on T1 and T2 images and have enhanced less than the pancreas. MRCP may reveal the double-duct sign. MRI with MRC is also useful in the differential diagnosis of periampullary carcinomas [44, 61, 63, 64].

5.3 Staging of Biliary Cancers by MRI

There is only scant information about the accuracy of MRI/MRC in the staging of biliary cancers. MRI with MRC and MRA has revealed liver invasion and spread into the bile ducts, vessels, lymph nodes, peritoneum, or pancreas and liver metastases in bile duct cancers. In gallbladder carcinoma, it has been sensitive in at least the first three groups of spread (Figs. 1, 2), but its status in for instance lymph node spread is still unclear. Dynamic MRI has been used to assess the depth of carcinoma invasion in gallbladder carcinoma. The signal intensity of the tumor in the liver is similar to that of the primary tumor. The T1 signal intensity contrast between the tumor and the surrounding tissues also facilitates the detection of tumor extension into surrounding structures.

The diagnostic accuracy of MRI with MRCP has been similar to that of MDCT with direct cholangiography for biliary and vascular involvement, lymph node metastases, and resectability in bile duct carcinomas. Both MRI and MDCT have had limitations in the assessment of lymph node and peritoneal metastases. When MRA and digital subtraction angiography have been compared for their ability to reveal arterial and venous invasion in bile duct carcinoma, similar diagnostic accuracies have been obtained [59, 61, 65–69].

6 Cholangiography

Traditionally, tumors causing biliary obstruction have been evaluated with direct cholangiography, i. e. ERC (Figs. 4, 10) or PTC (Fig. 7). This technique provides a detailed view of the anatomy of the biliary tree and detects the level of obstruction in 100 % of cases. It may provide the most accurate anatomic information because of its better spatial resolution compared to MRC. Brushings, biopsies, or bile cytology may also be simultaneously obtained, or more advanced cytologic techniques may be used to facilitate the final diagnosis. Cholangiography is performed for therapeutic purposes as well: A plastic or metallic stent may be inserted either endoscopically or percutaneously, or percutaneous biliary drainage can be accomplished. Direct cholangiography is still one of the main examinations, especially in the case of bile duct obstruction [9, 70].

At cholangiography, bile duct carcinoma may appear as an irregular stricture of variable length, a diffuse sclerosing change, or polypoid filling defects, or it may obstruct the duct (Figs. 4, 7). Luminal narrowing is usually abrupt, irregular, or uneven. Cholangiography can be essential to evaluate the disease extent. Advanced gallbladder malignancy may show bile duct changes or cause external bile duct compression. In ampullary carcinoma, PTC may show stenosis, obstruction, or an irregular polypoid filling defect, and ERCP may reveal the double-duct sign and the tumor itself. In a very small ampullary tumor, ERCP with its dynamic capability may be more diagnostic than MRCP [35, 70, 71].

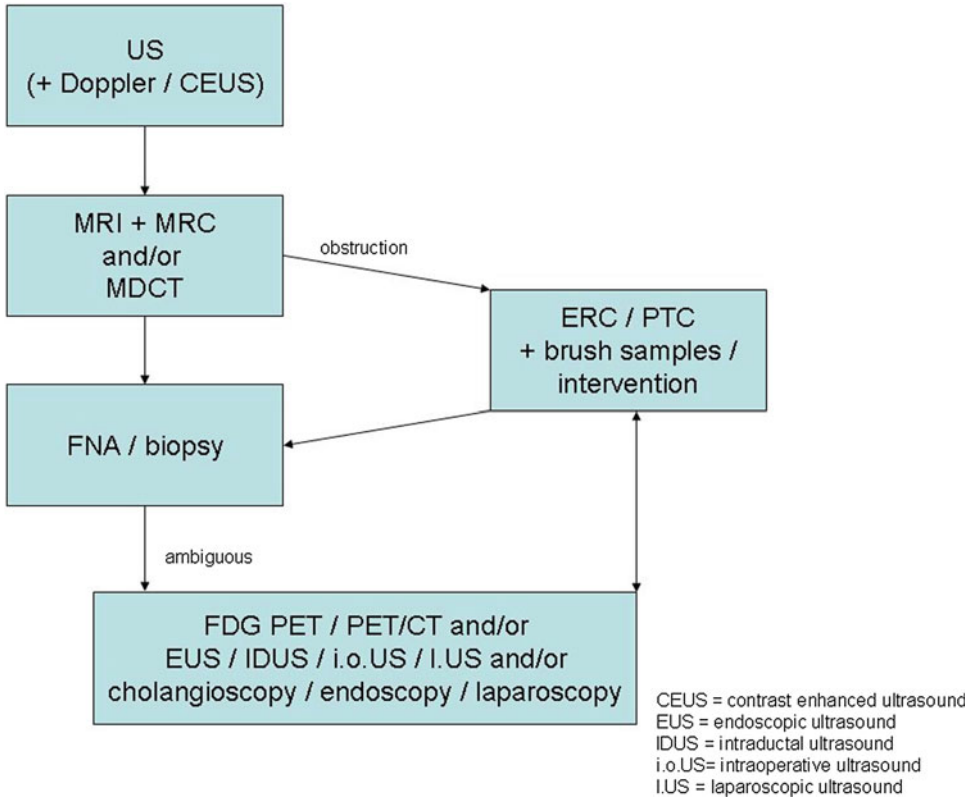

Fig. 11 Imaging strategies utilized in a typical case of a suspected biliary malignancy

However, direct cholangiography has its drawbacks. In cases of total obstruction, ERC does not show the cranial extent of the stricture, and PTC does not show the caudal extent. They are invasive procedures, not always possible, and carry the risk of complications. ERCP is associated with significant morbidity—pancreatitis, cholangitis, hemorrhage, perforation, and sepsis—and a mortality of 0.2–1 %. Cholangiography requires contrast medium and ionizing radiation, the technique is operator dependent, and it only provides information on the bile ducts.

7 Other Modalities

Angiography has had a major role in revealing encasement of the portal vein and hepatic artery by the malignancy. The recently improved versions of helical CT and MRI are increasingly replacing traditional angiography, unless there is a lack of capacity and facilities.

The 2-fluoro-2-deoxy-D-glucose-positron emission tomography (FDG PET) technique is based on the uptake of a radioactive-labeled glucose analog by rapidly metabolizing tumors. PET/CT combines functional and structural imaging. The sensitivity of FDG PET or PET/CT in revealing gallbladder or bile duct carcinoma has been quite high. FDG PET has also been helpful in assessing wall thickening of the gallbladder. However, its sensitivity in bile duct carcinoma has been dependent on the tumor subtype, being higher for the mass type than the infiltrating type and for the peripheral tumors than the hilar or distal tumors. FDG PET and PET/CT have improved diagnostics of regional lymph node metastases and distant metastases when compared with CT in biliary cancers. They may reveal occult metastases that have not been found by standard imaging. PET/CT has also had a slightly better accuracy than MDCT in assessing resectability in incidental gallbladder cancer with no distant metastases. Unfortunately, FDG PET has only limited spatial resolution and is not widely available [36, 66, 72–76].

Cholangioscopy with biopsies may reveal a small tumor or the longitudinal extent of a bile duct tumor. In the case of an ampullary tumor, endoscopy and biopsy may significantly contribute to the diagnosis. Sometimes, even laparoscopy and biopsies are necessary to reveal the extent of the biliary malignancy, e.g., to detect occult lymph node and peritoneal metastases.

8 Strategies of Imaging

A flow diagram of imaging strategies in a typical case of a suspected biliary malignancy is shown in Fig. 11. The prognosis of biliary cancers has been mainly dismal. However, recent advances in surgical techniques have led to

a need for improved detection and staging of these cancers. There has also been rapid development of radiological techniques, which has improved the diagnostic possibilities. Early diagnosis would be important in improving the prognosis, and careful staging would help in choosing the best possible treatment. All of this still remains a challenge. There is no single modality capable of reliably detecting and especially staging biliary cancers. In spite of these major advances, each modality seems to have its restrictions, and there are variable capacities and practices. Detailed recommendations cannot be given, and continuing advances will still modify the practice.

Transabdominal US is often the first imaging modality applied to patients with jaundice or nonspecific gastrointestinal complaints. It is noninvasive, nonradiative, and commonly available, and it is a suitable method for assessing even mild symptoms. US visualizes bile duct obstruction accurately, and it is able to reveal a gallbladder or bile duct tumor in about 90 % of cases, but less well able to reveal, especially small bile duct lesions. If a biliary malignancy is suspected, US-guided FNA is often able to confirm the final diagnosis. US is helpful, but of limited value, in staging.

Further investigations are usually performed after US. Technological developments have led to improvements, especially in MRI and CT. Both methods may yield additional information of the tumor and/or its extent. Fast-imaging techniques have made MRI potentially more valuable, and MRC is the least invasive mode of cholangiography, which is useful with MRI in the case of biliary obstruction. It is practical especially in patients who are unlikely to require any therapeutic intervention. The technique should include T1 and T2 sequences and gadolinium, often with MRC. There is ongoing discussion about the ranking of MRI and modern CT. The advantage of MRI is the absence of ionizing radiation.

Modern MDCT can produce multiplanar reconstructions of good quality, but the relatively high dose of radiation has made it problematic. The protocol should include triphasic CT acquisition when vascular structures can also be displayed. Simultaneously, CT of the thorax may reveal metastases of the lungs. Since comparative reports of the accuracies of modern MRI with MRCP and MDCT in biliary cancers are sparse, it is difficult to rank these methods. The choice also depends on the contraindications, local expertise, facilities, relative cost, and capacity. In ambiguous cases, both methods may be needed.

Direct cholangiography (PTC or ERCP) is still often necessary and may provide the most accurate anatomic information of the bile ducts. It is also needed for therapeutic purposes in the case of bile duct obstruction. Brushings, biopsies, or bile cytology may be obtained simultaneously, unless imaging-guided FNA is available. However, cholangiography is invasive, includes ionizing radiation, and carries the risk of complications.

Further, EUS and IDUS might help in the diagnosis and staging of the tumor as well, but they are invasive and not widely available and do not reveal distant metastases. PET and PET/CT have been promising ways to reveal the tumor and regional lymph node and distant metastases, and cholangioscopy may determine the longitudinal extent of a bile duct change. Sometimes, even laparoscopy with biopsies or laparoscopic or intraoperative US, when available, may be needed.

Detection of preneoplastic lesions of the gallbladder and microscopic tumor extension is a big challenge for the future. Again, large-scale comparison studies of the accuracies of MRI/MRC and MDCT in biliary cancers and their staging would be helpful. And the development of even better spatial resolution of MRC, tumor-targeted molecular imaging, and intervention-compatible MRI scanners and instruments would also be welcome.

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