



UPDATE IN RADIOLOGY

Bile duct tumors[☆]



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Abstract Bile duct tumors are benign or malignant lesions which may be associated to risk factors or potentially malignant lesions. They constitute a heterogeneous entities group with a different biological behavior and prognosis according to location and growth pattern. We revise the role of the radiologist in order to detect, characterize and stage these tumors, specially the importance of their classification when deciding an appropriate management and treatment.
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Tumores de la vía biliar

Resumen Los tumores de la vía biliar son lesiones benignas o malignas que pueden asociarse a factores de riesgo o a lesiones con potencial de malignización. Constituyen un grupo heterogéneo de entidades con diferente comportamiento biológico y pronóstico dependiendo de su localización y del tipo de crecimiento. En este artículo revisamos el papel del radiólogo para detectar, caracterizar y estadificar estos tumores y, sobre todo, la importancia de clasificarlos para planificar el manejo y el tratamiento.

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Introduction

Bile duct tumors originate in the epithelium of any bile duct segments, running from the small intrahepatic ducts to the choledochus,¹ and they are classified into different anatomical-pathological types: benign, premalignant and malignant, or cholangiocarcinoma (CC), of intra- and extrahepatic localization.² The anatomical location and morphological growth type (Fig. 1) allow us to categorize them into several groups with different prognoses requiring

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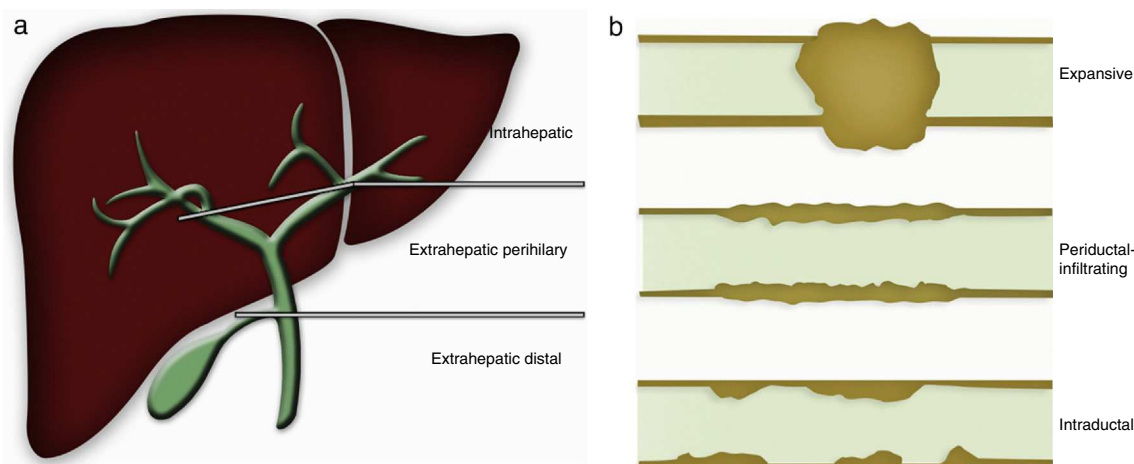


Figure 1 Graph illustrating the classification of bile duct tumors according to anatomical location (a): intrahepatic, perihilar and distal; and according to growth type (b): expansive, periductal-infiltrating and intraductal.

specific therapeutic strategies. The confluence of the secondary bile ducts sets the limit between intrahepatic and extrahepatic tumors, and the cystic duct junction to the common hepatic duct divides extrahepatic tumors into perihilar and distal tumors.²⁻⁴

Based on morphological growth four groups can be categorized: expansive, periductal-infiltrating and intraductal, or mixed if two of them coexist.⁵⁻⁷ Clinical presentation is variable, unspecific and generally late, and biliary obstruction signs are predominant in extrahepatic tumors, pain or weight loss in intrahepatic ones, or they appear as incidental findings in the image modalities.^{5,8} There are no specific tumor markers. CA 19-9 can be high (with a sensitivity of 40–70% and a specificity of 50–80%) as well as CA-125 in malignant tumors, in other tumors or in inflammatory cholangiopathies; so they are useful when assessed along other diagnostic modalities.^{5,9} This is why imaging techniques are essential to detect, characterize and classify these tumors. There is not such a thing as an ideal modality that allows us to make overall assessments so usually several additional image modalities are required.⁵

The radiologist's role in the finding, characterizing and staging of these tumors and above all the importance of categorization for therapy planning and managing is the aim of this article.

Diagnostic modalities

Abdominal ultrasound is the initial test in patients with suspicion of biliary obstruction due to its wide availability. It is very accurate to detect the obstruction and its level of obstruction but limited to detect and characterize the tumor and determine its extension and resectability.^{10,11} There is no evidence of the role that ultrasound contrast plays to detect extrahepatic tumors, although it may be relevant to distinguish them from biliary sludge¹² or for the guided biopsy of hard-to-see lesions. Multi-phase multidetector computer tomography (MDCT) has a great spatial resolution and wide coverage, which makes

it an excellent method to detect and stage bile tumors, both in vascular invasion and distant dissemination.^{10,13} When hepatectomy is considered the hepatic volume can be estimated more easily and accurately than with magnetic resonance (MR).¹⁰ MR is considered the best imaging modality to study bile ducts due to its higher contrast resolution. It allows us to obtain biliary anatomical information, the level of obstruction, the type of growth, the dimensions of tumor, the extension and vascular and nodal damage through conventional diffusion-weighted cholangiographic sequences and hepato-biliary contrasts.^{3,9,10,13,14} However, it is inferior to MDCT to detect distant metastasis.⁵ The contribution of positron emission tomography combined with CT (PET-CT) to detect CC is not too significant and even though it may be useful for the detection of metastases^{15,16} its use for staging purposes has not been validated.⁵

The endoscopic retrograde cholangiopancreatography (ERCP) has lost ground to MR to distinguish benign from malignant stenoses^{3,5} but it retains its role in obtaining anatomic-pathological samples and the implantation of palliative biliary prostheses.¹⁷ The percutaneous transhepatic cholangiography (PTHC or PTC) is useful when the endoscopic pathway is not accessible.¹⁰ Endoscopic ultrasound with fine-needle puncture is recommended when other techniques are not conclusive showing a 53% sensibility and a 89% specificity for the diagnosis of extrahepatic CC.¹⁷ It is much more accurate to assess ganglia than MDCT or PET is.¹⁸ Other modalities, such as intraductal ultrasound or transpapillary cholangioscopy, may provide relevant information, the former to detect and stage perihilar CC, and the latter to characterize stenosis, detect villous processes, ulcerated stenoses, intraductal nodules or to take biopsy samples, with a 90% sensibility and specificity for the diagnosis of CC.¹⁷

On occasion, intraoperative laparoscopy or ultrasound may be necessary to determine whether the lesion is irresectable.⁴ The anatomic-pathological sample is essential for diagnosis when resection is not indicated and hence puncture guided by imaging modalities

or invasive techniques can play an important role here.^{5,10}

Risk factors

Most CC appear sporadically and they are rare in patients younger than 40 years old.¹⁹ Only 30% are associated with risk factors, which have chronic inflammation of the bile duct as a common factor.^{5,13} Among the established risk factors, primary sclerosing cholangitis (PSC) is the most frequent in Western countries with a 5–15% prevalence.⁹ The duration of the disease is not a determining factor, and the mean interval between diagnosis and the appearance of CC is 2.5 years.^{5,20} Although there are no recommendations for screening the existence of CC should be investigated in the presence of clinical or analytical worsening.^{20,21} Other recognized factors are choledochal cysts, with a 6–30% incidence,²² intrahepatic lithiasis²¹ or infestation due to hepatobiliary parasites (*Opisthorchis viverrini* and *Clonorchis sinensis*) that are more common in Asia.¹⁹ There are other possible risk factors as well such as cholangitis and extrahepatic choledocholithiasis¹⁹ or cirrhosis and chronic viral hepatitis (more C than B) in intrahepatic CC.²³

Premalignant diseases

Three premalignant bile lesions are known: biliary intraepithelial neoplasia, bile duct papillary intraductal neoplasia and cystic mucinous neoplasia or cystadenoma.^{5,24} The former progresses into a tubular adenocarcinoma and is microscopic so it is not diagnosed through images. Bile duct papillary intraductal neoplasia includes borderline adenomas and tumors and it progresses to early CC (tubular or mucinous adenocarcinoma) and has a better prognosis than advanced carcinomas.^{1,14} They grow macroscopically within the lumen without invading the wall and spread superficially; this is why they can be detected and characterized through images. In most cases they produce great amounts of mucins that diffusely dilate bile ducts. Four growth patterns have been described here (Fig. 2): polypoid, mold-shaped, superficial and cystic. No study has shown any correlations among these types of growth, their location, anatomical–pathological characteristics or transformation into invasive carcinoma.^{24,25} There are several radiological signs that suggest intraductal growth (Fig. 3), such as nodules or intraluminal masses which are often more enhanced than the liver parenchyma, the absence of segmental atrophy and multiplicity of lesions.^{1,26} Biliary dilation without complete obstruction is considered an important finding for the diagnosis of these tumors.²⁷ MR with cholangiography has advantages as compared to CT and endoscopic cholangiography.²⁷ Diffusion-weighted MRIs provide relevant information both to distinguish bile papillary lesions and determine tumor invasion.²⁷ To be able to determine the tumor spread level with superficial mass and without growth the cholangioscopy can be useful.¹⁷ It is important to determine surgical treatment depending on the type of radiological growth. With complete resection, prognosis is more favorable than that of CC.¹ For the sake of differential diagnosis lithiasis need to be included since they can simulate an intraductal lesion. In the ultrasound, lithiasis

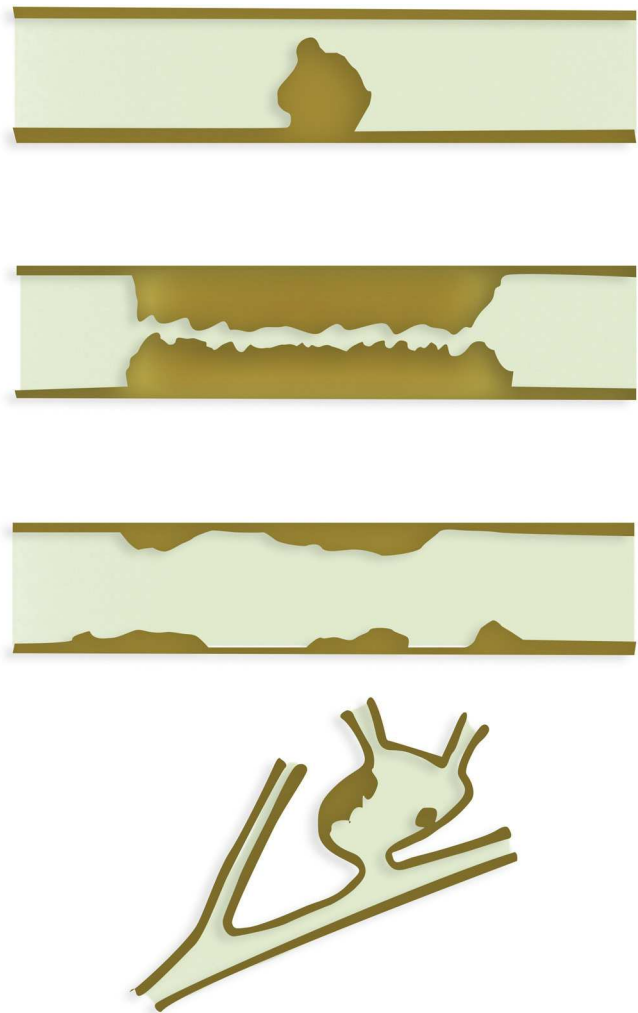


Figure 2 Graphs showing papillary intraductal tumor growth patterns, from the top down: polypoid growth, which is defined as a polypoid pedunculated or sessile mass whose length is less than 2 times the diameter of the bile duct where it stays; mold growth, when the mass fills all the dilated duct lumen, with a length twice as big as the diameter of the duct; superficial growth, when the tumor looks like a fine pitted jagged contour on the surface of the duct, the duct wall is >1 mm or there is diffuse segmental or lobar dilatation and the tumor cannot be seen; and cystic growth, with aneurismal dilatation of the affected duct with or without excrescences or mural nodes.

cast shadows in 80% of the cases.²⁸ In the CT the study without contrast is useful to determine the presence of calcium or enhancement, since both entities can show variable attenuation. Irregular edges, ductal stenosis or asymmetrical thickening of the wall suggest papillary tumor, while fine, angular edges are characteristic of lithiasis,²⁸ that also show a low signal in T1 and T2 (Fig. 4) unlike tumors whose signal in T2 is higher.²⁷

Differential diagnosis of these neoplasias with intraductal biliary metastasis should also be considered in patients with another extrabiliary malignant neoplasia. The tumors that metastasize in the bile duct are lung, breast, gallbladder, colon, testicle, prostate and pancreas tumors as well as melanomas and lymphoma.²⁹ Images can provide differential

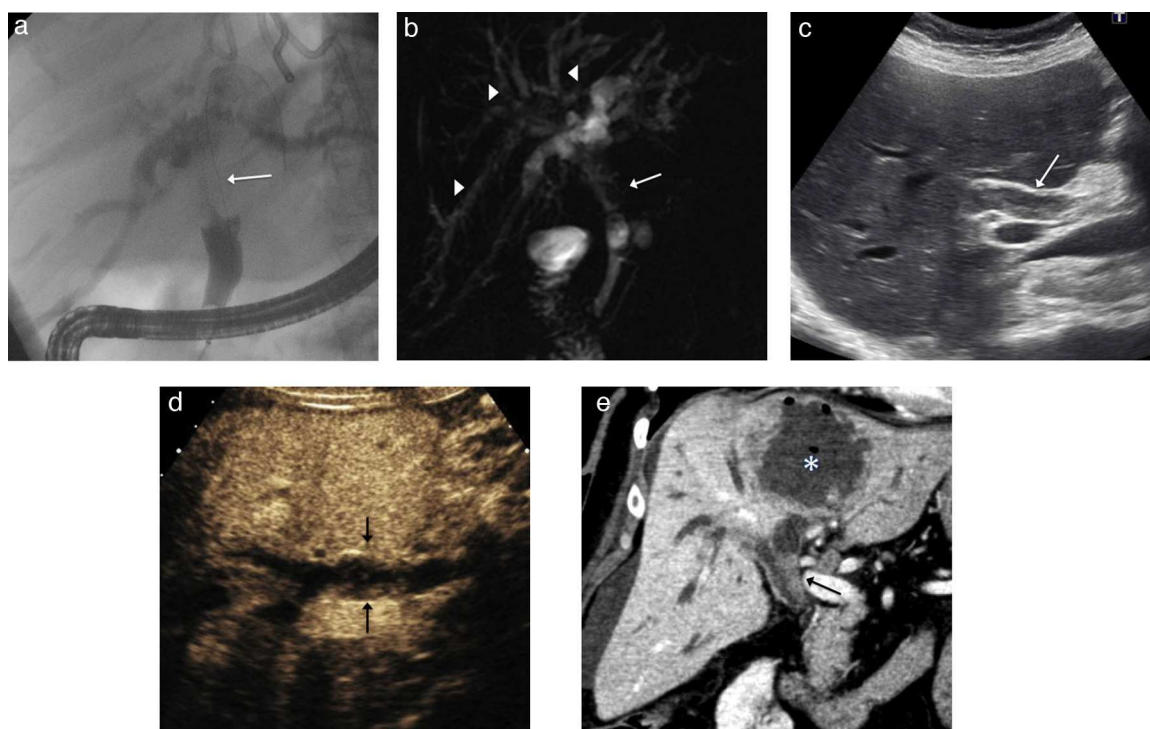


Figure 3 Multifocal intraductal papillary neoplasia with polypoid, mold-shaped growth. (a) Image of endoscopic retrograde cholangiopancreatography showing a mass of intraductal growth in the common hepatic duct (arrow) with marked stenosis that does not allow us to do a proper assessment of the proximal bile duct. (b) 2D coronal image of cholangio-MR of the mass (arrow) allowing us to see the proximal bile duct with multiple intraductal polypoid nodes (arrow heads). (c) Transverse oblique plane ultrasound of the hepatic hilum where the mold-shaped lesion is observed (arrow). (d) After the injection of contrast it is not as enhanced as the liver parenchyma (arrows) and it rules out biliary sludge. (e) CT coronal reconstruction showing intraductal lesion (arrow) not as enhanced as the parenchyma. It is possible to see an intrahepatic abscess due to cholangitis (asterisk).

signs: while the primary tumor is intraductal and polypoid, metastasis usually affects the parenchyma with expansive aspect.²⁹

The third type of premalignant lesion is mucinous cystic neoplasia or cystadenoma, which must be differentiated from the mucinous variant of biliary intraductal papillary neoplasia with cystic growth.³⁰ The latter communicates with the bile duct (Fig. 5) and can spread intraductally

(leading to intermittent obstructive symptoms) while the former is confined to a cyst usually closed to the duct. To diagnose it an ovarian stroma¹⁴ needs to be confirmed anatomopathologically.¹⁴

Mucin-producing biliary intraductal papillary neoplasia can be the biliary entity analogous to pancreatic mucinous intraductal papillary neoplasia, since they both show papillary epithelial proliferation with fibrovascular nucleus, have

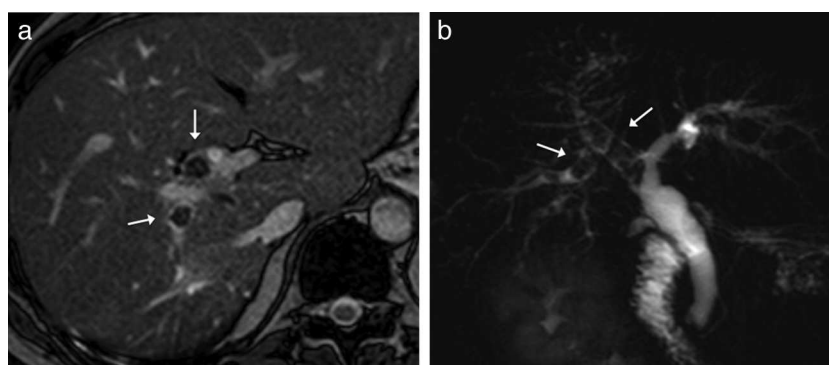


Figure 4 Intrahepatic lithiasis. T2-weighted transverse gradient echo MRI of the liver (a) and 2D coronal image of cholangio-MR (b) showing hypointense intraductal lesions (arrows) with smooth and angular edges in the right hepatic duct and secondary ducts associated with lithiasis.



Figure 5 Papillary intraductal neoplasia with cystic growth. (a) 2D coronal image of cholangio-MR showing a cystic, encapsulated lesion (arrow), without nodes and without a clear communication with the bile duct. (b and c) T1-weighted transverse images of hepatic gradient echo MR with fat suppression, with and without contrast (gadobenate dimeglumine) in hepatobiliary stage showing contrast passage to the lesion (arrow) due to the communication with bile duct.

no ovarian stroma on the wall, their histological phenotypes are similar, they produce mucin and tend to progress into carcinoma.³⁰

Malignant tumors

CC accounts for approximately 10% of hepatobiliary primary cancers and 2% of all cancers,³¹ though it has a wide geographic variability. The incidence of intrahepatic CC has grown during the last decades, with a concomitant decrease in extrahepatic CC;^{5,9} yet this is misleading information since perihilar CC has been considered as intrahepatic in several studies, and it is difficult to determine its origin in advanced perihilar CC stages.

Advanced CC has bad prognosis, with a mean life lower than 24 months.⁹ The only curative treatment is surgical resection, with survival rates at 5 years of 22–44%, 11–41% and 27–37% among intrahepatic, perihilar and distal CC, respectively.⁵ The second prognostic factor is nodal damage, with a 45% prevalence, more frequently in distal CC.⁴ Metastases are present in 30% of the cases at the moment of diagnosis.⁴ CC is a heterogeneous group of lesions with expansive macroscopic periductal-infiltrating or intraductal growth forms, of intrahepatic, perihilar or distal localization showing different biological behaviors and forms of dissemination. It has been proved that there is a significant correlation between type of growth and infiltration pattern and the survival rate. The intraductal subtype is characterized by a superficial and multiple mucous growth damaging

Table 1 Criteria for cholangiocarcinoma irresectability.

Intrahepatic cholangiocarcinoma (CC)	- Invasion of visceral peritoneum - Local invasion of extrahepatic structures - Periductal invasion: it includes the mixed pattern of growth (periductal and expansive) - Infiltration of regional nodes
Perihilar CC	- Distant metastasis (including celiac, periaortic and pericaval ganglia) - Vascular assessment criteria: deformity of the contour of vessel, stenosis or occlusion or vessel-tumor contact $\geq 180^\circ$ (93 and 85% accuracy for arteries and veins, respectively). The HCC portal invasion is triggered by the invasion of lumen - Bilateral affection of secondary ducts - Affection of the main portal vein or bifurcation - Invasion of portal branch or artery with contralateral lobar atrophy - Biliary invasion of secondary ducts with contralateral lobar atrophy - Invasion of one-sided secondary ducts with portal vascular invasion or contralateral artery
Distal CC	- Distant metastasis - Invasion of gallbladder, pancreas, duodenum or other adjacent organs with no affection of the celiac trunk or superior mesenteric artery - Invasion of celiac trunk or superior mesenteric artery - Infiltration of regional ganglia - Distant metastasis

Table 2 TNM-staging system of intrahepatic biliary tumors.

<i>Primary tumor</i>	
TX	The primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	In situ carcinoma (intraductal tumor)
T1	Only tumor with no vascular invasion
T2a	Solitary tumor with vascular invasion
T2b	Multiple tumors with or without vascular invasion
T3	Tumor perforating the visceral peritoneum or directly invading extrahepatic structures
T4	Tumor with periductal invasion
<i>Regional lymphatic ganglia</i>	
NX	The regional lymphatic ganglia cannot be assessed
N0	There is no metastasis in the regional lymphatic ganglia
N1	Metastasis in the regional lymphatic ganglia
<i>Distant metastasis</i>	
M0	There is no distant metastasis
M1	Distant metastasis

in a late onset the wall of ducts; hence prognosis is better than that of the periductal-infiltrating or expansive subtype that shows submucosal radial growth and perineural spread and invades the wall early.^{24,32,33} The former is characterized by showing less enhancement than the liver, while the others usually show early or progressive enhancement.³² Resectability is determined by the spread of the tumor toward the biliary tree, damage to liver parenchyma, vascular invasion, lobar atrophy and the presence of metastasis (Table 1).⁴

Intrahepatic cholangiocarcinoma (peripheral)

Approximately 20% of CC are intrahepatic.^{5,8} The expansive growth type is the most frequent, which disseminates through venous and lymphatic vessels. It is usually a large tumor, with irregular or lobulated outlines. Viable tumoral cells are generally located in the tumor's periphery being the center made up of variable amounts of fibrosis, coagulative necrosis or mucin.³⁴ The factors with the worst prognosis are multiple lesions (satellite lesions, hepatic metastasis or multiple tumors indifferently), vascular invasion and nodal metastases.^{35,36} Both MDCT and MR allow us to characterize and staged them correctly through the TNM staging system (Table 2).³⁷

In the ultrasound they are masses with variable echogenicity without a hypoechoic halo, unlike hepatocarcinoma (HCC), and in 31% of the cases with biliary dilation in the periphery of the tumor.³⁸ MDCT and MR are the most appropriate modality to assess tumor size, multifocality and vascular damage. MDCT is the best modality to determine resectability having an accuracy beyond 85%.^{36,39} In MDCT it is usually hypodense, and in MR its appearance is variable. It

Table 3 TNM-staging system of distal biliary tumors.

<i>Primary tumor</i>	
TX	The primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis	In situ carcinoma
T1	Tumor histologically confined to the biliary duct
T2	Tumor beyond the biliary duct
T3	Tumor invading gallbladder, pancreas, duodenum or other adjacent organs without invasion of the celiac trunk or the superior mesenteric artery
T4	Tumor celiac trunk or the superior mesenteric artery
<i>Regional lymphatic ganglia</i>	
NX	The regional lymphatic ganglia cannot be assessed
N0	There is no metastasis in regional lymphatic ganglia
N1	Metastasis in regional lymphatic ganglia
<i>Distant metastasis</i>	
M0	There is no distant metastasis
M1	Distant metastasis

usually shows hyperintense periphery in T2 and hypointense in T1 representative of cellular predominance. The center is characteristically hypointense in T2 due to fibrosis or coagulative necrosis, which are differentiated due to the presence or absence of enhancement,^{3,34} or it is hyperintense in the presence of mucin.³⁴ In both techniques it is common to have a minimal irregular and incomplete peripheral enhancement with centripetal progression in late stages^{13,40} (Fig. 6). It can be associated with differential findings such as capsular retraction, dilation and thickening of peripheral bile ducts or infiltration of vessels without visible thrombi (Fig. 6) (Table 3).

The use of hepatobiliary contrasts (gadoxetate disodium or gadobenate dimeglumine) can be useful since contrast allows us to better see the tumor and its edges and find multiple lesions and important information for surgical planning and prognosis (Fig. 6).^{41,42} With regard to the assessment of metastatic nodes the overall precision of the techniques is close to 77%.³⁶

The differential diagnosis of CC with expansive growth includes several entities. CC < 3 cm can have an atypical behavior in the cirrhotic liver, with enhancement in the arterial stage with or without washing in the portal stage,^{40,43,44} so differential diagnosis should be considered with HCC due to its different therapeutic management and prognosis. Washing in MDCT and MR confirms the diagnosis of HCC; however the pure intravascular distribution of contrast in the ultrasound does not allow us to distinguish between one and the other since both show washing. Target appearance in the diffusion-weighted MRI with high *b* values—translating central fibrosis, has proved to be a significant predictive, independent factor to distinguish CC from small HCC, with more sensitivity than T2-weighted images or

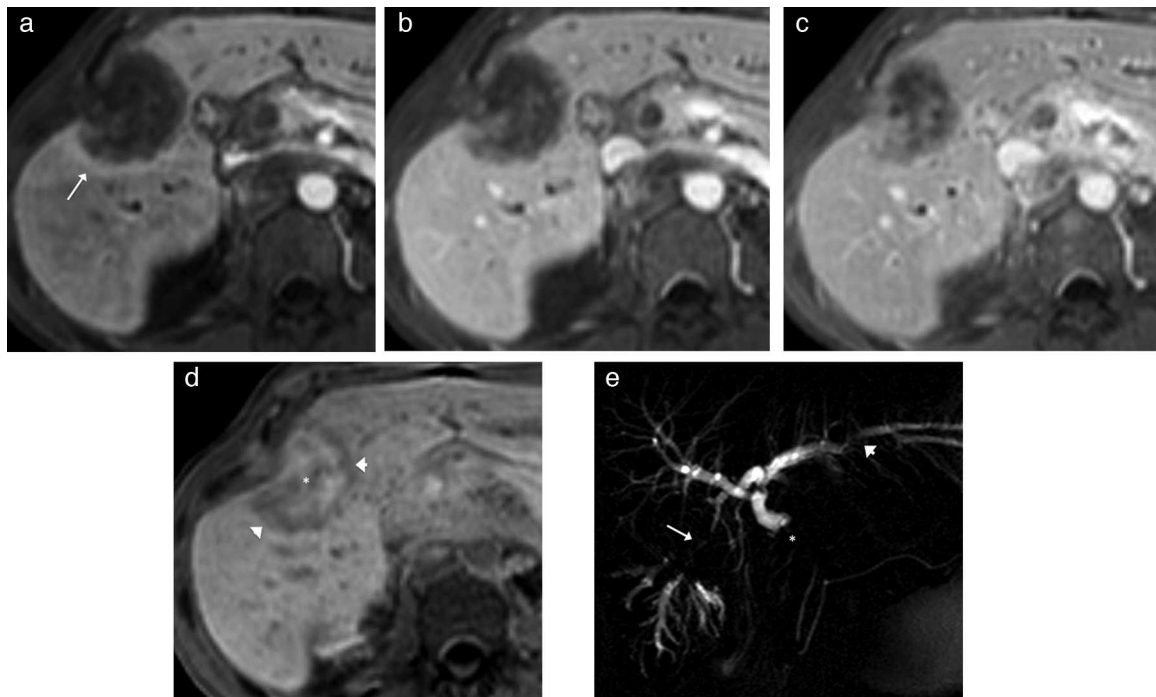


Figure 6 Intrahepatic cholangiocarcinoma with invasive growth. T1-weighted transverse liver MRI, fat suppression and hepatobiliary contrast (gadobenate dimeglumine) in late arterial (a), portal (b), balance (c) and hepatobiliary stages (d) showing a slight peripheral arterial enhancement (arrow in a) with centripetal and heterogeneous progression in late stages. In the hepatocyte stage, hepatic enhancement is observed better outlining the edges of the lesion (arrow heads in d) also showing a hyperintense center due to the persistence of contrast in the interstice through its fibrous component (asterisk in d). (e) 2D coronal cholangio-MRI where the mass-shaped defect is located in the right hepatic lobe (arrow) with dilatation of ducts proximal to the tumor and intraductal lesions in the left branches of the intrahepatic bile duct (arrow head), as well as extrinsic stenosis of extrahepatic bile duct due to adenopathies in the hilum (asterisk).

with hepatospecific contrast,⁴⁵ yet biopsy is still necessary.³⁵ Distinguishing it from colon carcinoma metastases can be very difficult since they can be hypointense in T2. Typical enhancement, findings associated such as dilation of the intrahepatic pathway and, above all, the presence of a primary tumor are key to be able to distinguish between the two.³⁴

Surgery achieves healing in less than 30% of the cases due to the positive surgical margins and nodal metastases, positive in 29% of patients after surgical procedure.^{8,39} There is no consensus as to whether lymphadenectomy is recommended during tumor resection.⁴⁶

Perihilar cholangiocarcinoma (hilar or Klatskin)

It accounts for 50–60% of CC.^{5,8} The most common type of growth is the mixed one, periductal-infiltrating with associated expansive mass,³⁵ and it disseminates predominantly through the perineural and nodal vias.¹ It grows across a dilated or stenotic bile duct while thickening the wall and then invading the liver parenchyma in 80%.⁴ Infiltrated lymphatic ganglia, tumoral differentiation and complete resection have been recognized as independent prognostic factors.³⁵ MR, MDCT, ERCP and, occasionally, endoscopic ultrasound are the most common used techniques for staging purposes.³⁹ There are different staging systems, but

none is used with a broad consensus. The most widely used is the Bismuth–Corlette modified system, based on the tumor's longitudinal spread along the biliary tree,⁴⁷ including 4 types (Fig. 7). This classification does not take into account vascular invasion, the presence of metastasis or the anatomical variants of the biliary tree. The TNM³⁷ system adds signs of radial growth (peribiliary tissues or vascular invasion) and distant nodal damage. Nevertheless it does not assess properly the tumor location in the biliary tree, which is important information to determine the possibility of local resection.³¹ Ipsilateral hepatic atrophy, vessel occlusion, stenosis or contour deformity or a tumor-vessel contact $\geq 180^\circ$ are regarded as vascular invasion.⁴⁸ A new classification has been introduced that takes into consideration both the tumor's longitudinal growth along the biliary tree and its radial growth while assessing arterial vascular or portal invasion.³¹ It classifies biliary and vascular damage in a very similar way to the modified Bismuth–Corlette system and it also considers other parameters relevant to resection, such as the size of the tumor, the type of growth, the potential volume of the remaining liver, nodal and distant damage, and the underlying liver disease. This system has shortcomings such as size or lobar atrophy that have no prognostic implications, or vascular invasion—valuable for resection purposes not for prognosis³⁵ (Fig. 8).

In the ultrasound, the most frequent finding is intrahepatic bile duct dilation; the hepatic duct juncture cannot

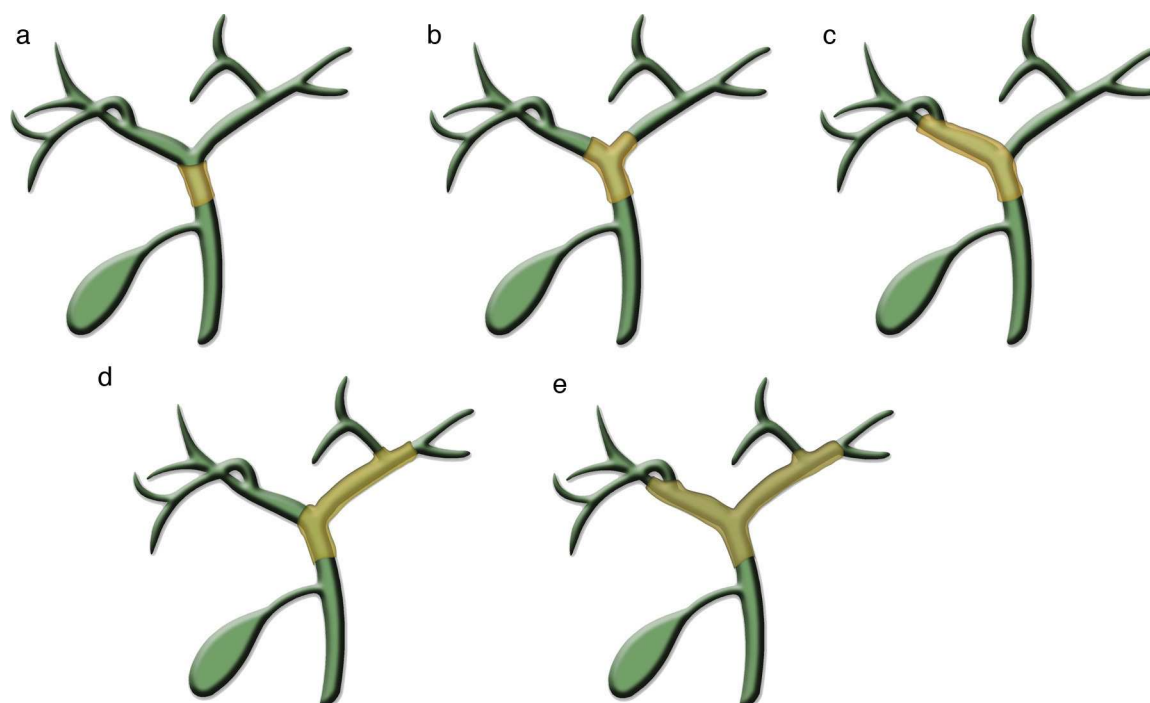


Figure 7 Illustrations representing the types of longitudinal growth of perihilar cholangiocarcinoma based on the modified Bismuth-Corlette system. (a) Type I—affectation on the common hepatic duct. (b) Type II—affectation on the hepatic duct confluence. (c and d) Type III—affectation on the secondary hepatic duct confluence of right (IIIa) or left (IIIb) hepatic duct. (e) Type IV—affectation of both hepatic ducts and the secondary confluence of both or at multiple and bilaterally discontinuous levels.

be seen and the distal bile duct has a normal caliber.³⁸ The lesion is usually as echogenic as the liver and it is hard to identify. The contrast of the ultrasound can enhance precision because the tumor is hypoechoic in late stages differing from the enhanced liver parenchyma.⁴⁹ Diagnosis is supported by the large number of dilated ducts and lobar atrophy. It is less frequent to observe mural and periductal thickening of the juncture or intraluminal mass.⁵⁰ The ultrasound, however, is not the proper modality to study dissemination and determine resectability.^{36,38} In the MDCT it looks like a focal thickening of the duct wall with

lumen stenosis and proximal dilation. We can have a mass with greater enhancement than the liver parenchyma in all stages (Figs. 9 and 10). It has a trend to underestimate the longitudinal spread, both in the periductal-infiltrating and intraductal forms.⁵¹ It assesses vascular and biliary infiltration and predicts resection accurately, for which reformatting techniques are useful.^{35,36,49,52} It underestimates nodal and peritoneal spread.^{52,53} The precision of MTCT to determine resection is 60–87.5%.^{4,36} The MRI is excellent to establish longitudinal spread in the biliary tree identifying alterations in the ductal shape and caliber or

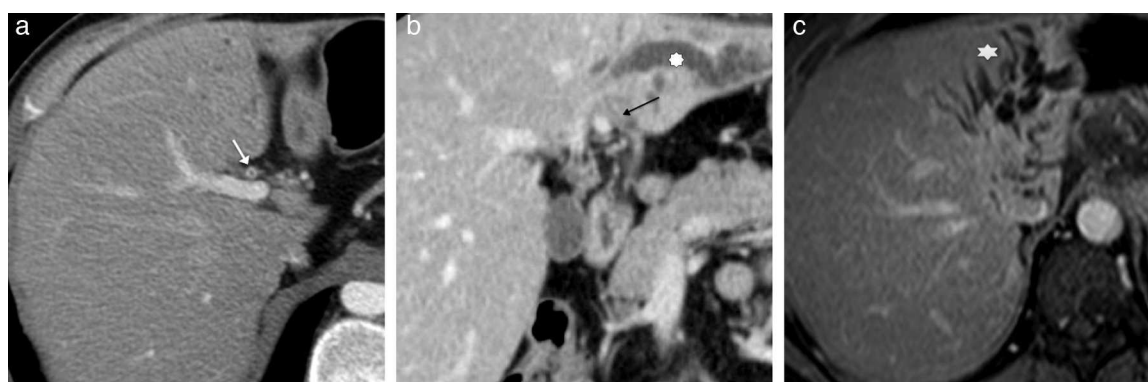


Figure 8 Forty year old-man with Type IIIb perihilar cholangiocarcinoma with periductal-infiltrating growth. (a) Transverse image of hepatic CT with contrast showing thickening and stenosis of left hepatic duct (arrow). (b) CT coronal plane with thickening of left hepatic duct and circumferential contact with one portal branch due to invasion (arrow) and dilation of the intrahepatic biliary duct (asterisk). (c) T1-weighted gradient echo MRI with contrast showing dilation of biliary duct and lobar atrophy due to vascular invasion (asterisk).

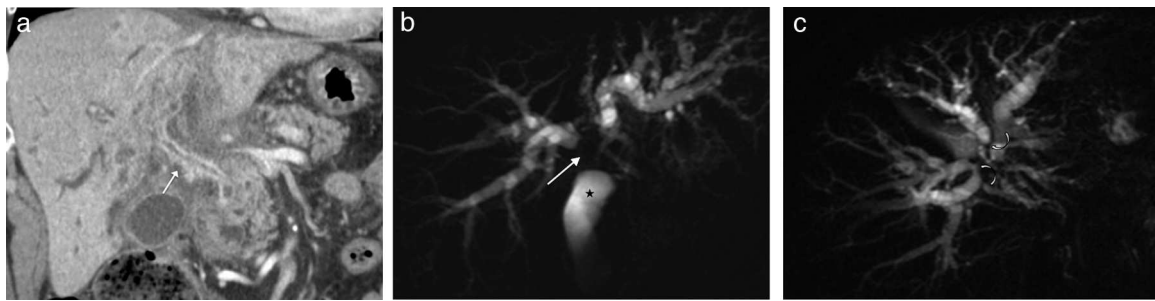


Figure 9 Seventy eight year-old man with Type IV perihilar cholangiocarcinoma. (a) CT coronal image with contrast in portal stage where thickening of extrahepatic bile duct wall and mass (arrow) can be observed invading the periductal structures due to mixed, periductal-infiltrating and invasive growth. (b) 2D coronal plane cholangio-MR showing lumen occlusion (arrow) of the bile duct; vesicle (star). (c) 2D transverse plane cholangio-MR showing longitudinal invasion toward the secondary ducts (curved arrows).

intraluminal polypoid lesions^{49,53,54} (Figs. 8 and 9). Late enhancement of the bile duct walls is a sign that improves the diagnostic accuracy of the MRI⁵³ since it is not an indirect sign like stenosis in cholangiographic modalities. The cholangioscopy might be necessary for intraductal extension since it shows multifocal superficial dissemination,^{48,54} and is also very accurate for liver infiltration and radial spread. Its main limitation is its lower spatial resolution, and the fact that it also underestimates nodal and peritoneal spread. Its precision for intervention is 72–83%.³⁶ The differential diagnosis is determined with entities that can be radiologically indistinguishable, such as benign iatrogenic stenosis, inflammatory or infectious diseases, IgG4-related disease, eosinophilic cholangitis, bile inflammatory pseudotumor or tumor lesions, such as metastasis or lymphoma.⁵⁵ Less than half of the patients are candidates to a curative surgical procedure through bilateral or contralateral vascular invasion and through secondary bile duct bilateral invasion.⁴⁹ Curative treatment requires resecting the extrahepatic bile duct, regional lymphadenectomy, cholecystectomy and in most cases a partial hepatectomy, including the caudate lobe.⁴ There is controversy on the need for preoperative bile drain that could improve the metabolic and regenerative requirements of the remnant hepatic function.³⁹

Distal cholangiocarcinoma

It amounts to nearly 20% of all CC.^{5,8} The periductal-infiltrating growth is the most frequent type,⁵⁶ there is

a trend to grow in depth (neural, vascular or pancreatic invasion) and toward nodal damage,³⁵—two factors driving prognosis.

The typical signs are a node or mass with late enhancement in the location of the stenosis or the concentric or asymmetric thickening of the duct wall. The ultrasound is the index diagnostic procedure^{38,57} capable of identifying proximal dilation. In rare occasions it is accompanied by an associated mass.³⁹

They are staged through the TNM system,³⁷ for which the MRI and MDCT are essential since they help outline the size of the tumor and the invasion of adjacent structures (Fig. 10).³⁶ The diffusion-weighted MRI with a *b* value of 800 is sensitive to find extrahepatic CC.⁵⁸

ERCP, percutaneous cholangiography and endoscopic ultrasound (EUS) with FNAP are useful diagnostic tools yet direct cholangiography is not very effective to see the tumor's longitudinal spread, since the growth can be either submucosal or extramural. The EUS allows us to assess more accurately node and vascular invasion.³⁹

Usually when no mass or lithiasis can be seen, a long, irregular, asymmetric stenosis suggests malignancy, unlike short, regular, symmetric stenosis that are usually benign.⁵⁶ Differential diagnosis includes benign stenosis, such as PSC, AIDS-related cholangiopathy, autoimmune pancreatitis, acute or chronic pancreatitis and malignant stenosis due to pancreatic or periampullary tumors³ (Fig. 10). Autoimmune pancreatitis affects the intrapancreatic choledochus in 67–96% of the cases narrowing it through wall thickening

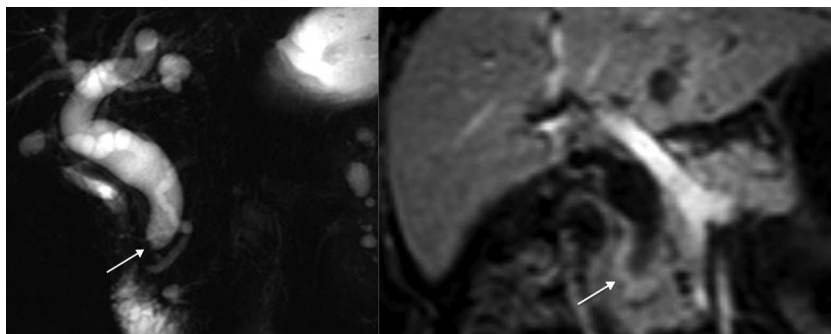


Figure 10 Distal cholangiocarcinoma. 2D coronal images of cholangio-MR and gradient echo MR with fat suppression and contrast showing irregular and asymmetric stenosis (arrows) due to distal cholangiocarcinoma of the periductal-infiltrating type.

which simulates a distal CC.⁵⁹ A concentric thickening of the duct wall, with a smooth outer edge, little enhancement and hourglass-like stenosis, limited to the intrapancreatic segment and multiple damage, are findings characteristics of cholangitis associated with autoimmune pancreatitis.⁵⁹ The extrahepatic unifocal bile duct damage is rare in PSCs.^{21,55} If there is a dominating stenosis (defined as a 1.5 mm stenosis in the choledochus or a 1 mm stenosis in the hepatic duct), a cytological study or biopsy is recommended to rule out underlying neoplasia.²⁰ Pancreatic carcinoma is hard to distinguish from a distal CC. The absence of invasion of main and accessory pancreatic ducts is suggestive of biliary origin.³ Lastly, periampullary tumors are classified separately in the TNM system³⁷ and they originate in the periampullary region, defined as the area that stretches radially for 2 cm from the major papilla. In an ampullary obstruction, the signs that define a periampullary neoplasia are a mass, papillary protrusion and irregular and asymmetric ductal stenosis, with dilatation of pancreatic duct.⁶⁰ The curative treatment of distal CC is surgical through Whipple procedure. Survival rate at 5 years is 27–50% when resection is complete, which is the most important predictive factor of all^{4,39} followed by nodal damage.⁸

Conclusion

Bile duct tumors are very variable due to their location and growth. Imaging techniques are essential to detect them and characterize them, and above all, to classify them into groups that make treatment planning and prognosis easier. In general, it is necessary to combine several image modalities and invasive techniques while surgical examination might be necessary too. These tumors need to be handled through multidisciplinary approach and this is why it is important for the radiologist to know both the radiological signs and roles of the different diagnostic modalities.

Ethical responsibilities

Protection of people and animals. Authors confirm that no experiments have been performed on human beings or animals.

Data confidentiality. Authors confirm that the protocols of their institution have been followed on the publication of data from patients.

Right to privacy and informed consent. Authors confirm that in this report there are no personal data from patients.

Author contributions

Manager of the integrity of the study; Study Design; Data Analysis and Interpretation: FD, JV, GM. Original Idea of the Study: JV, GM. Data Mining: FD, JV, GM, MJM. Statistical Analysis: Not applicable. Reference Search and Writing: FD, JV, GM, TR. Manuscript critical review with intellectually relevant contributions: TR, MJM. Final Version Approval: FD, JV, GM, TR, MJM.

Conflict of interests

Authors reported no conflicts of interests.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.rxeng.2014.10.001>.

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