Radiological findings of biliary obstructive causes

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Received: 28 October 2024, **Accepted:** 17 November 2024, **Published:** 20 November 2024

Abstract

Background: Radiological imaging plays a crucial role in diagnosing biliary obstruction, providing detailed visualization of the biliary tree and adjacent structures. This abstract reviews the characteristic radiological findings across various imaging modalities used to identify the cause and location of biliary obstruction.

Ultrasonography (US) is often the initial imaging modality, offering a non-invasive assessment of biliary dilation and identification of gallstones as a common cause. While US has limitations in visualizing the distal common bile duct, its ability to detect intrahepatic duct dilatation, gallbladder wall thickening, and pericholecystic fluid collection provides valuable diagnostic clues. Furthermore, US can readily demonstrate masses impacting the biliary tree, including pancreatic cancers, cholangiocarcinomas, and lymph node enlargement. Computed tomography (CT) offers superior anatomical detail compared to US, enabling precise localization of the obstruction and better characterization of the causative lesion. CT cholangiography (CTC) or magnetic resonance cholangiopancreatography (MRCP) provides direct visualization of the biliary ducts, offering detailed assessment of ductal dilation, strictures, and stones. CT excels in identifying extrahepatic causes of obstruction, such as pancreatic masses, lymph node involvement, and vascular compression. MRCP, on the other hand, avoids the use of ionizing radiation and offers excellent visualization of the biliary tree without the need for contrast administration, making it a valuable alternative, especially in patients with compromised renal function. Diffusion-weighted imaging (DWI) offers valuable supplementary information to magnetic resonance cholangiopancreatography (MRCP) in differentiating the causes of obstructive biliary disorders. While MRCP excels at visualizing biliary anatomy and identifying strictures or stones, it provides limited tissue characterization. DWI, sensitive to microscopic tissue motion, enhances the ability to differentiate benign from malignant biliary strictures and assess the characteristics of peribiliary masses. The addition of DWI allows for improved characterization of the lesion's cellularity and vascularity, providing crucial information regarding tumor grade, aggressiveness, and potential for invasion. In malignant biliary obstruction, DWI typically reveals restricted diffusion reflecting cellular density and impaired water mobility within the tumor tissue, manifested as low apparent diffusion coefficient (ADC) values. Conversely, benign strictures, such as those caused by inflammation or scarring, usually exhibit higher ADC values reflecting less cellular density. This improved tissue characterization afforded by DWI helps refine diagnostic accuracy, improves pre-operative planning for surgical resection or minimally invasive interventions, and aids in the stratification of patients for appropriate therapeutic management. The combined use of MRCP and DWI therefore reduces diagnostic uncertainty and potentially improves patient outcomes by facilitating more accurate and timely intervention. Further research is needed to fully elucidate the role of DWI in optimizing the management of various biliary obstructive pathologies and defining optimal ADC thresholds for differentiating benign and malignant processes..

Keywords: *Radiological findings, biliary obstructive causes*

Introduction

In Western countries, iatrogenic injury (cholecystectomy, LT) is the most common cause of benign biliary stricture [1]; other causes include PSC, IgG4-SC, CP, Mirizzi syndrome, recurrent pyogenic cholangitis, acquired immune deficiency syndrome (AIDS)-associated cholangiopathy, and chemotherapy-induced sclerosing cholangitis [1].

I. Primary sclerosing cholangitis

PSC is a chronic liver disease of unknown aetiology, characterized by inflammation and concentric periductal fibrosis that may involve the intra- and extra-hepatic bile ducts, leading to multifocal biliary strictures. Its incidence ranges from 0.5 to 1.3 per 100,000 person-years, with a prevalence of 1–16 per 100,000 persons. It is predominantly seen in men (male/female ratio: 2/1) with a peak of incidence in the third and fourth decades.

Secondary sclerosing cholangitis is characterized by a similar multifocal biliary stricturing process due to identifiable causes such as long-term biliary obstruction by choledocholithiasis [2].

Clinical features

Approximately half of patients are asymptomatic at the time of diagnosis. Non-specific symptoms such as fatigue and pruritus are common at presentation. Fever, jaundice, and right upper quadrant pain may also be present due to transient bacterial cholangitis. Continued destruction of bile ducts may lead to end-stage liver disease and portal hypertension [3].

Strictures may be present in both the intra- and extra-hepatic bile ducts (70%), or the intra-hepatic (25%) or extra-hepatic (<5%) bile ducts alone. The gallbladder and cystic duct may also be involved. A dominant stricture develops during follow up in 36–50% of patients; this is defined at ERCP as a stricture with a diameter of $\leqslant$1.5 mm in the common bile duct (CBD) and/or $\leqslant$1.0 mm in an hepatic duct within 2 cm of the main hepatic confluence [4].

Cholangiography is normal in <5% of patients who have “small-duct PSC” but 20% of them will develop large-duct PSC over a 7- to 10-year period. Small-duct PSC is associated with a lower risk of LT and death without LT than large-duct PSC. Inflammatory bowel disease (IBD) is associated with 60–90% of PSC in European and North American populations, with ulcerative colitis (UC) five times more frequent than Crohn’s disease. PSC patients with UC present a higher risk of LT or death without LT compared with patients with Crohn’s disease (hazard ratio (HR), 1.56; $p < 0.001$) or without IBD (HR, 1.15, $p = 0.002$) [5].

PSC-related complications include CCA, gallbladder stones (25% of patients) and carcinoma, colon carcinoma as well as cholestasis-associated problems. The annual incidence of CCA is 0.5–2% in PSC, with a lifetime risk of 10–20%. The diagnosis of CCA is difficult, particularly in the presence of a dominant biliary stricture. These should be carefully evaluated, particularly if they are discovered soon after the diagnosis of PSC (approximately half of CCAs are diagnosed within the first year after PSC diagnosis) [6].

Risk factors for CCA include older age at the time of PSC diagnosis (HR, 1.02 per 1-year increase in age), smoking, alcohol consumption, a long history of IBD, and coexisting UC with colorectal neoplasia. No screening strategy is recommended but a sensible attitude is, if the patient opts for surveillance after information about risks, to propose annual screening using magnetic resonance imaging (MRI) and CA19-9; if a dominant biliary stricture and/or rise in CA19-9 is observed, biliary brushings for conventional and fluorescence in situ hybridization (FISH) cytological examination should be obtained, or cholangioscopy performed [7].

Rapid clinical deterioration associated with a progressive biliary dilatation in the setting of a dominant biliary stricture should raise a strong suspicion of CCA. PSC increases the risk of colorectal cancer and dysplasia with an odds ratio (OR) of 3.2 when compared with patients with IBD without PSC.

Gallbladder mass lesions develop in 3–14% of patients [1].
Due to the high risk of malignancy associated with gallbladder polyps in PSC and the potential for increased cholecystectomy-related morbidity in these patients, guidelines recommend cholecystectomy either for gallbladder polyps of any size, or with a lower size threshold than in non-PSC patients. Cholestasis-related complications include metabolic bone disease, fat-soluble vitamin deficiencies, and choledocholithiasis [8].
The estimated median survival until LT or PSC-related death is 20.6 years with the main causes of mortality being CCA (32%) followed by liver failure (18%), LT complications (9%), and colorectal carcinoma (8%). The Amsterdam cholangiographic classification of PSC correlates with patient prognosis [9].
Diagnostic work up
At diagnosis, serum aminotransferases are typically <300 IU/L and serum bilirubin is within normal values. Increased serum IgG4 values have been reported in about 10% of patients; IgG4-SC should be differentiated from PSC [10].
The major diagnostic criteria for PSC are multifocal, short, annular strictures of the intrahepatic and/or extrahepatic bile ducts, alternating with areas of normal or slightly dilated segments, giving a “beaded” appearance; secondary sclerosing cholangitis should be excluded (Figure 33).

With the progression of fibrosis, the peripheral ducts become poorly visible, giving a “pruned tree” appearance. MRCP has gained priority over ERCP for diagnosing PSC due to its non-invasive character; the overall diagnostic accuracy of MRCP is 90% (97% for ERCP) [11].
Liver biopsy is not required to diagnose large-duct PSC; it is required only to diagnose small-duct PSC or a coexisting disease such as overlapping autoimmune hepatitis. The most typical, but infrequent, histopathological finding is fibrous obliteration of small bile ducts with periductal concentric replacement by connective tissue in an “onion skin” pattern [2].

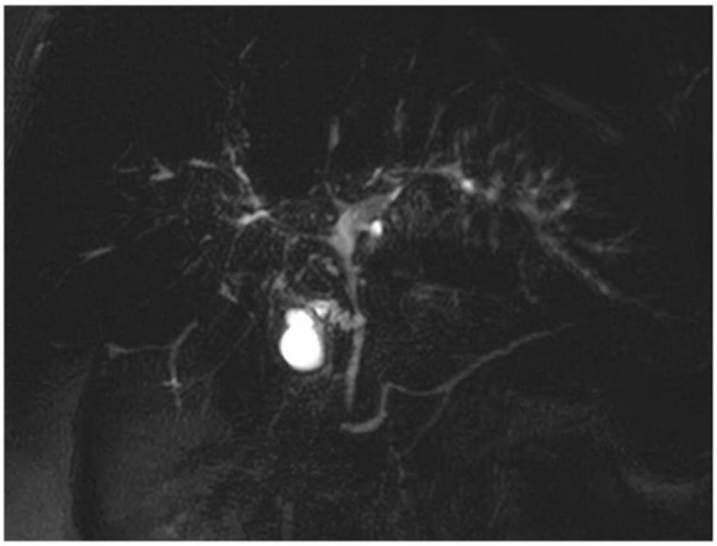

Figure 1: A 31-year-old man with severe ulcerative pancolitis and primary sclerosing cholangitis. MRCP demonstrates diffuse irregularities of the common bile duct and intrahepatic bile ducts with multifocal strictures and mild upstream dilatation [1].

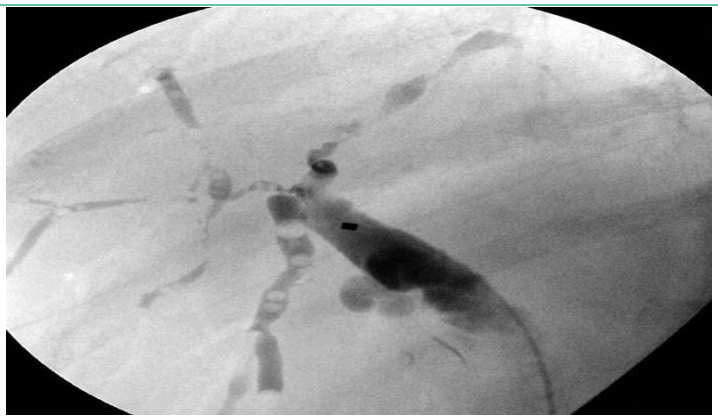

Figure 2: Multiple intrahepatic biliary strictures with intervening dilatation. Features of primary sclerosing cholangitis [12].

Differential diagnosis

Secondary sclerosing cholangitis may be caused by many diseases, including malignancy, and some of these are detailed below [1].

Recurrent pyogenic cholangitis is predominantly seen in Southeast Asia, where malnutrition and biliary parasites are endemic. Approximately 5% of patients develop CCA. Repeated attacks of cholangitis result in scarring, intrahepatic and extrahepatic biliary strictures, intraductal pigment stones, dilatation of the central hepatic bile ducts with minimally dilated peripheral bile ducts, lobar atrophy, and abscesses (Figure 34). Multifocal strictures favor a diagnosis of PSC, whereas multiple ductal stones favor a diagnosis of recurrent pyogenic cholangitis [14].

IgG4-related sclerosing cholangitis refers to the manifestation of IgG4-related systemic disease in the biliary tree; it may be isolated or, more frequently, associated with AIP. Affected organs are infiltrated by IgG4-positive plasma cells and present obliterative phlebitis and storiform fibrosis. Compared with PSC, IgG4-SC presents more frequently as painless obstructive jaundice (75% versus 5–30% of cases) and at an older age (62 versus 40 years), but both are more common in men. Cholestasis and increased serum IgG4 levels are the hallmarks of the biochemical changes in IgG4-SC. CA19-9 may be increased. Four different patterns of biliary strictures are described in IgG4-SC (Figure 35). The finding of >10 IgG4-positive cells per high power field in ampullary or biliary biopsy samples may help to differentiate IgG4-SC from PSC. Several diagnostic criteria have been proposed; the most widely used is the HISORt (Histology, Imaging, Serology, other Organ involvement and Response to therapy) adapted from AIP diagnostic criteria. Some features that are helpful for differentiating IgG4-SC from PSC include the fact that, unlike PSC, IgG4-SC responds to steroid therapy within 2 months, is not associated with IBD, and does not transform into CCA. At MRI/MRCP, accurate predictors of IgG4-SC rather than PSC include continuous, as opposed to skipped, bile duct strictures, gallbladder wall thickening, CBD wall thickness >2.5 mm, absence of liver parenchymal abnormalities, and presence of associated pancreatic or renal involvement [10].

Ischaemic cholangiopathy is due to impaired blood supply from the peribiliary vascular plexus, coming from hepatic arteries, to the bile ducts. This may result from vascular injury during biliary surgery, in particular LT, mechanical obstruction by multiple venous collaterals (portal cavernoma), intra-arterial chemotherapy, and drug-induced intravascular thrombosis. Clinical manifestations suggest biliary obstruction and liver chemistries reveal a cholestatic pattern. Occasionally, patients develop ascending cholangitis and liver abscesses. Cholangiographic findings consist of multiple intra- and extra-hepatic smooth strictures with diffuse irregularity (Figure 36) or ductal disruption with extravasation of bile. Liver biopsy is rarely useful as histopathology reveals only evidence of biliary obstruction, and, in some

cases, features of ischaemic cholangiopathy [1].

AIDS-associated cholangiopathy is an uncommon form of sclerosing cholangitis that typically occurs in patients with advanced AIDS and a CD4 count <100/mm3. Opportunistic infections (cryptosporidium, microsporidium, cytomegalovirus) are the most common causes. Large intrahepatic bile ducts are predominantly affected. Four cholangiographic patterns have been reported. A papillary stenosis, present in approximately 70% of patients, is highly suggestive of this diagnosis (Figure 37) [15].

Secondary sclerosing cholangitis in critically ill patients. This disease develops in patients with no prior history of liver disease and no known pathologic process or injury responsible for bile duct obstruction prior to intensive care treatment. It is thought to develop due to ischaemic injury of intrahepatic bile ducts and biliary casts are present in most patients at early stages of the disease. It is associated with rapid progression to liver cirrhosis and poor survival with limited treatment options other than LT [1].

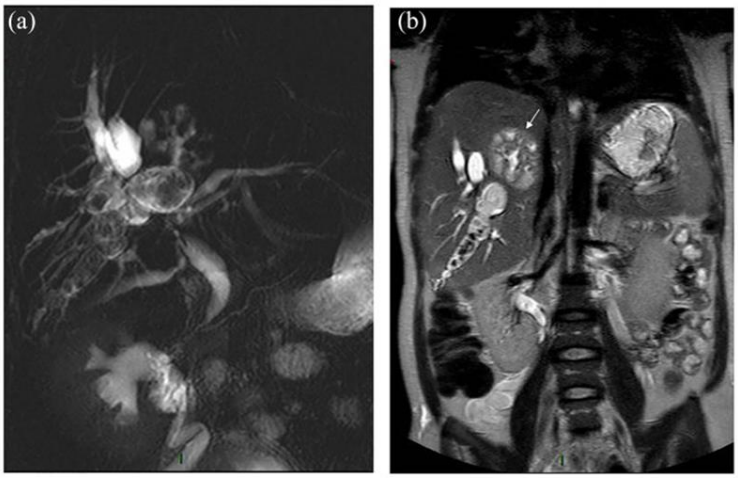

Figure 3: A 30-year-old Vietnamese woman with acute cholangitis, septicaemia, and shock. MRCP (A) shows a major dilatation of the right posterior intrahepatic bile duct filled with large stones and lithogenic material. Coronal MR T2-weighted image (B) shows a multilocular abscess of segment VII of the liver (arrow). Diagnosis was recurrent pyogenic cholangitis (oriental cholangitis) [1].

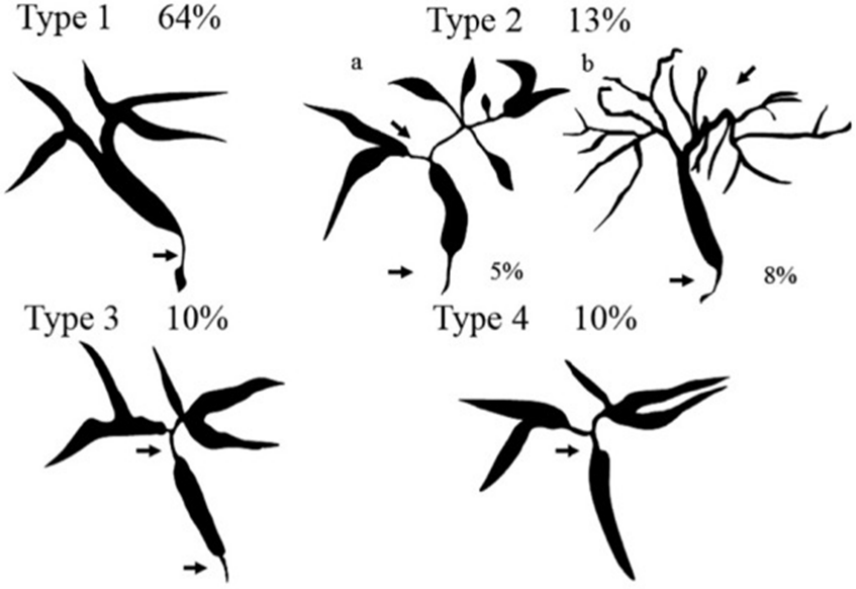

Figure 4: Types of biliary strictures in IgG4-SC. Type 1: isolated stricture of the distal common bile duct. Type 2: diffuse strictures of the intra- and extra-hepatic bile ducts with (Type 2a) or without (Type

2b) prestenotic dilatation. Type 3: hilar stricture and distal common bile duct stricture. Type 4: isolated hilar stricture. IgG4-SC, IgG4-related sclerosing cholangitis [1].

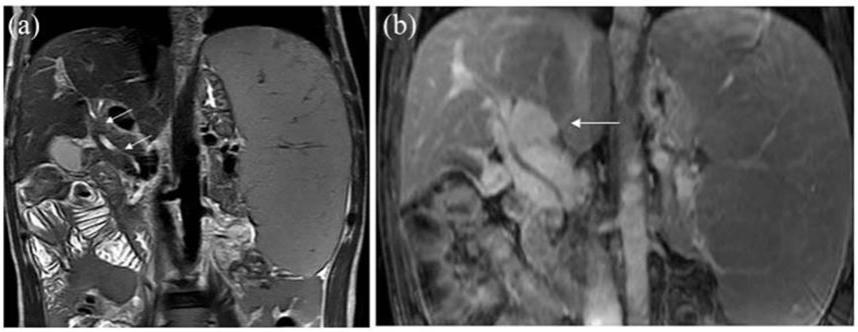

Figure 5: A 36-year-old man with asthenia, abdominal pain, and pruritus. Coronal MR T2-weighted image (A) and contrast-enhanced MR T1-weighted image (B) show multifocal smooth strictures of the common bile duct (arrows) because of extrinsic compression by a portal cavernoma (B, arrow) developed secondary to an extrahepatic portal stenosis. Diagnosis was primary myelofibrosis associated with portal hypertensive cholangiopathy [1].

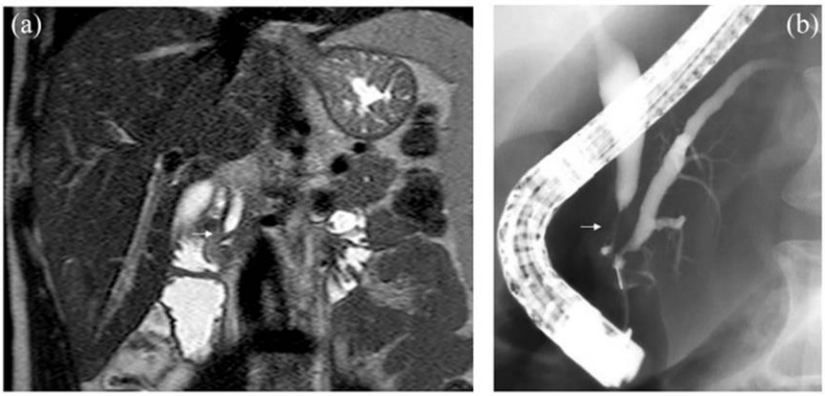

Figure 6: A 36-year-old man with recurrent abdominal pain and fever. AIDS had been diagnosed 12 years previously and treated episodically with antiretroviral drugs. Coronal MR T2-weighted image (A) and endoscopic cholangiogram (B) show focal distal common bile duct stricture (arrow) with mild upstream dilatation. Diagnosis was AIDS-associated cholangiopathy [1].

II. Bile Stone

When obstruction by a gallstone is suspected and the calculus cannot be found, continue to search. When faced with a clinical and laboratory picture suggesting obstruction by a calculus (migration, cholangitis, pancreatitis), the potential severity of the complications means that in all cases the explorations must be continued until a formal conclusion can be drawn as to whether there is a calculus in the CBD, or not [16].

A CT scan, when performed, is only of use if it shows the presence of calculi, but if it does not show any, they still cannot be excluded: even though the detection of calculi by CT can be optimised by non-injected slices being analysed by carefully adjusting windowing for optimal contrast, 20% of calculi are missed (too close in density to the bile and too small). A CT scan is therefore less effective than ultrasound for detecting vesicular calculi and less effective than MRCP for those in the common bile duct (CBD) [17].

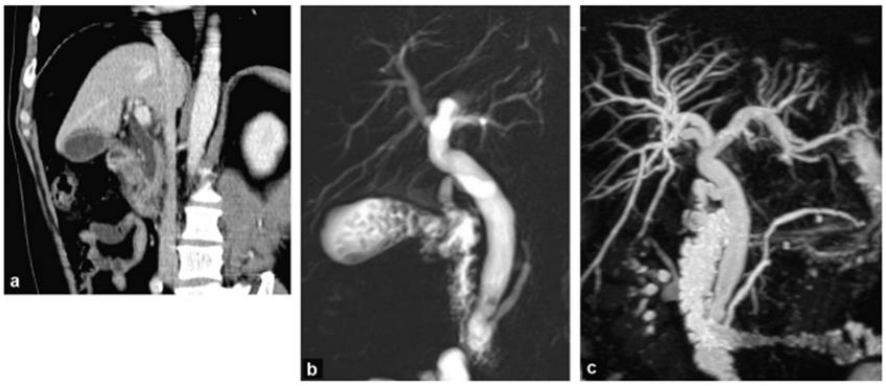

Figure 7: Male patient with acute pancreatitis: a: CT (coronal oblique reconstruction) before and after injection shows dilatation of the common bile duct (CBD) but with no aetiological pointer; b: MRCP (2D coronal oblique acquisition) shows several vesicular calculi and lower bile duct lithiasis, invisible in CT; c: this calculus is too small inside the dilated CBD to be visible on the MIP from a thin slice 3D acquisition: analysis of native MRI slices is therefore essential [17].

Clinicians are not always aware of the poor negative predictive value of CT for biliary calculi. It may therefore be useful to make this explicitly clear in the radiological report by noting: ‘‘absence of calculi that are sufficiently dense to be visible on the CT scan’’. However, gallstone aetiology can sometimes be asserted without any visible calculus: thus, according to work by Delabrousse et al., visualisation in a CT scan of a choledochal ring sign (difference of enhancement of the wall of the common bile duct greater than 15 HU relative to the pancreas) confirms the biliary origin of acute pancreatitis with a positive predictive value of 100% [18].

After the 1st line ultrasonography, the strategy recommended for exploring a patient with suspected obstruction by a calculus is set out in Figure 39. In theory, this strategy avoids having to perform MRCP when intraoperative cholangiography or endoscopic ultrasonography is in any case indicated. In practice however, MRCP is tending to become more and more systematic. Indeed, surgeons often prefer diagnosis of CBD lithiasis and a biliary map to be made preoperatively by MRCP rather than during intraoperative cholangiography. Similarly, gastroenterologists expect MRCP to confirm for them at the outset that endoscopic ultrasonography will be followed by therapeutic measures during ERCP [17].

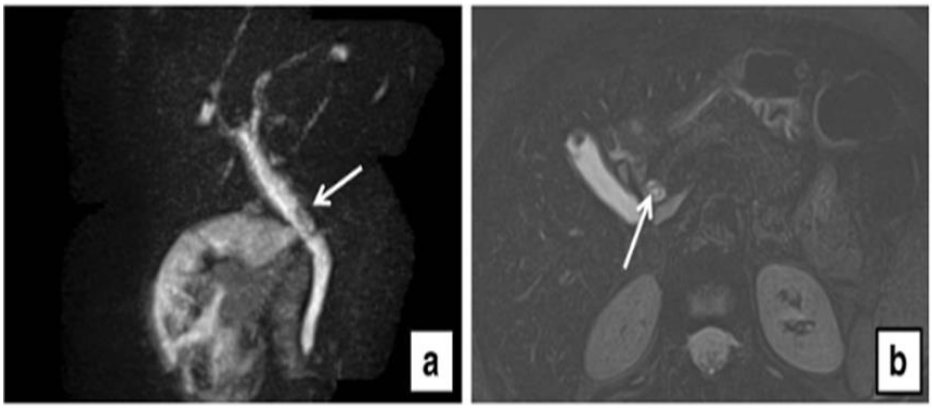

Figure 8: (a) Sagittal thick-slab magnetic resonance cholangio pancreatography (MRCP) shows a filling defect in a dilated common bile duct (CBD) (arrow). (b) Axial fat-saturated T2-weighted magnetic resonance imaging (MRI) of the same patient shows a dishomogeneous filling defect in a dilated CBD (arrow).

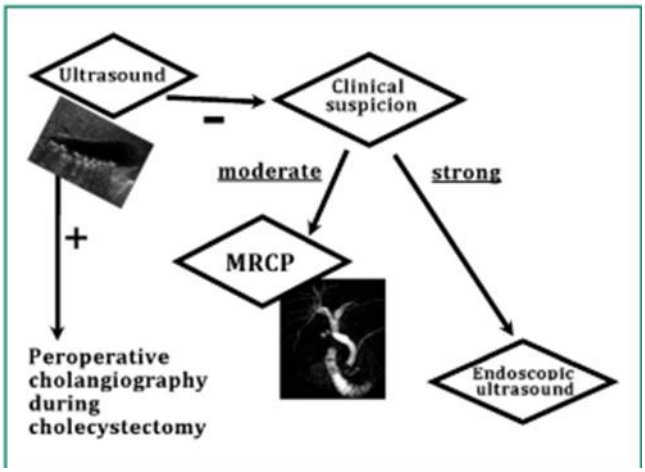

Figure 9: Theoretical strategy for exploring a symptomatic patient, suspected of having gallstone migration or obstruction. If ultrasound shows calculi in the gallbladder, cholecystectomy is indicated. In principle MRCP is not necessary, since the surgeon can check for the presence of stones in the common bile duct by cholangiography directly during his operation. In cases where there is moderate clinical suspicion of common bile duct calculi, we can stop exploration after a negative MRCP. In contrast, if the clinical suspicion is strong, a negative MRCP does not sufficiently exclude the possibility and endoscopic ultrasonography must be additionally performed. The latter can be proposed from the outset instead of MRCP; furthermore, it can be extended into a therapeutic procedure using endoscopic retrograde cholangiopancreatography (ERCP) during the same period of anaesthesia. In practice, however, the surgeon or endoscopist may request an MRCP before surgery, regardless of the situation, if it would be useful in helping him plan his treatment [17].

MRCP

It should be remembered that, given the risks of ERCP, current recommendations exclude its use for purely diagnostic purposes. Endoscopic ultrasonography is the reference examination, in principle, for the diagnosis of CBD lithiasis, with sensitivity and specificity of more than 95%. However, if the MRCP technique is optimal, it is also highly efficient for detecting CBD calculi, with sensitivity of 80–100% and specificity of 90 to 100% depending on the series. In addition, MRCP has the advantage of exploring both the CBD and the intrahepatic bile ducts and of being non-invasive [19].

One cause can hide another: so make sure you have found the right one. Once calculi have been found, it is easy to suggest that they explain a biliary obstruction. However, while calculi can be a cause, they can also be just the result of an obstruction. Where there is an obstruction by a gallstone, an underlying disease (malignant or benign stenosis) should therefore be sought, particularly in the following two cases [17]:

• when there are episodes of recurrent biliary obstruction
• when the site of the obstruction is not choledochal but concerns the intrahepatic bile ducts.

Generally speaking, where there is biliary obstruction, we must be sure that we have actually found the real causal pathology, so we must earnestly continue to search for the aetiology. Figures 40-42 illustrate situations where the initial diagnosis of the cause of the obstruction was confirmed or challenged [17].

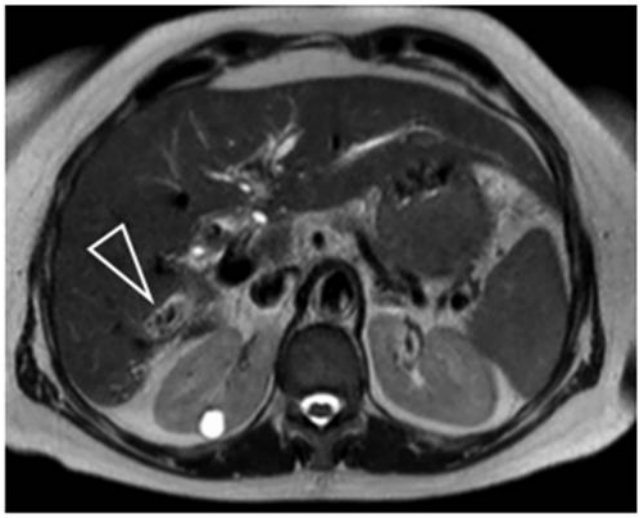

Figure 10: Dilatation of the intrahepatic bile ducts, associated with the presence of several calculi (arrowhead). Retrograde catheterisation was performed with cytological sampling by aspiration of bile and biliary brushing. Here the calculi were a consequence and not the cause of the obstruction: cytology showed the presence of an underlying cholangiocarcinoma [17].

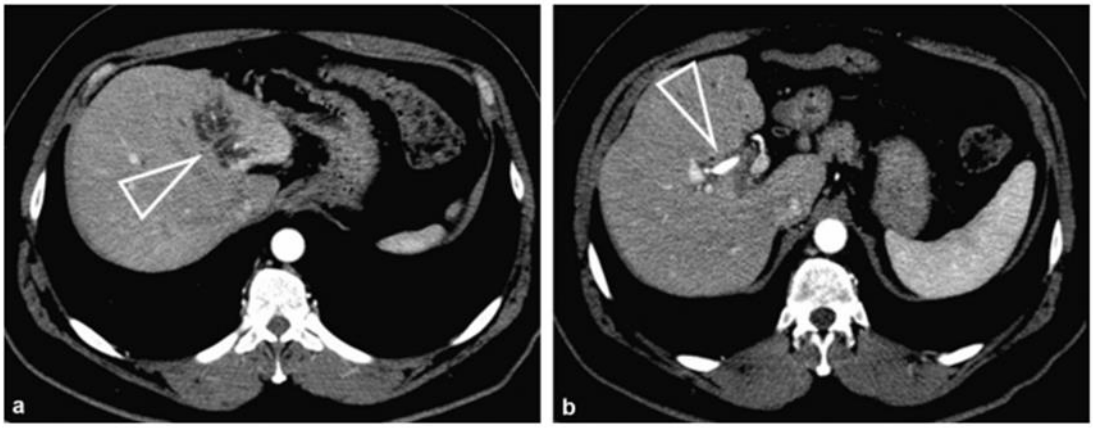

Figure 11: Obstruction of the superior biliary confluence responsible for dilatation of the left (a) and right intrahepatic bile ducts, drained by a plastic prosthesis (b). A cholangiocarcinoma (Klatskin tumour) was suspected. After left hepatectomy, histopathological examination found no carcinomatous cells: it was actually autoimmune cholangitis (IgG4-associated cholangitis). This disease, causing stenosis of the bile ducts, and characterised by infiltration of the bile ducts by IgG4 plasma cells, is frequently associated with autoimmune pancreatitis. It regresses in a spectacular way with simple corticosteroid treatment; measurement of serum IgG4 can provide the diagnosis [17].

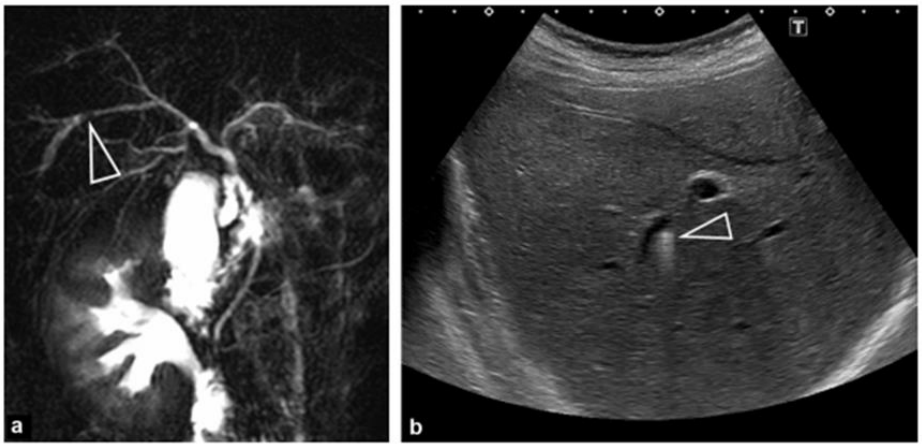

Figure 12: Two different female patients: a: intrahepatic calculi found by MRCP; b: cholesterol

deposited along the small intrahepatic bile ducts, visible with ultrasound in the form of a classic comet tail image, but which requires careful targeted exploration to be detected. These patients with a history of obstetric cholestasis, presenting biliary symptoms before 40 years of age, with recurrence after cholecystectomy, have, with the imaging, all the diagnostic criteria for low phospholipid-associated cholelithiasis (LPAC). This predisposition to biliary disease can be confirmed by genetic research and lead to medical treatment and family screening [17].

III. Acute/chronic pancreatitis

In the setting of pancreatitis, a CBD stricture may develop because of acute pancreatitis, compression by a pseudocyst, or, in the case of CP, periductal fibrosis. Biliary strictures complicate the course of CP in 3–23% of patients, usually in its advanced stages, and may be transient [15].

Clinical features

The clinical presentation of biliary stricture secondary to CP is variable. Some patients remain asymptomatic, whereas jaundice develops in 30–50% of patients. Secondary biliary cirrhosis occurs in 7% of patients [15].

Diagnostic work up

CT-scan or MRCP shows biliary obstruction and possibly compression by a pseudocyst. Other features of CP (e.g. parenchymal atrophy, calcifications, dilated main pancreatic duct) may be visible [20].

Differential diagnosis

Autoimmune pancreatitis (AIP) is a rare type of CP that may involve the distal CBD. AIP typically develops in old men and is associated with increased serum IgG4 levels, whereas idiopathic duct-centric pancreatitis, previously known as type 2 AIP, typically develops in younger patients with normal serum IgG4 levels and IBD. AIP belongs to the group of IgG4-related systemic diseases that may involve the pancreas, bile ducts, salivary glands, retroperitoneum, and kidneys. Unlike usual CP, AIP is relatively painless. The HISORt diagnostic criteria are commonly used. Typical imaging features at CT-scan or MRI include a diffusely enlarged pancreas with featureless borders (“sausage-shaped” appearance) and delayed enhancement with or without a capsule-like rim. MRCP may reveal a diffuse irregular narrowing or a focal stricture of the main pancreatic duct (Figure 43) [21].

Pancreatic cancer. Special attention should be paid to concurrent pancreatic cancer in patients >50 years, of female gender, of white race, presenting with jaundice, in the absence of calcifications, or in the presence of exocrine insufficiency. A malignant aetiology of the biliary stricture should always be thoroughly sought in these patients, particularly in the first years after diagnosis. In the particular context of CP, a meta-analysis has found a sensitivity/specificity of MRI with diffusion-weighted imaging of 86%/82% for the diagnosis of pancreatic malignancy [22].

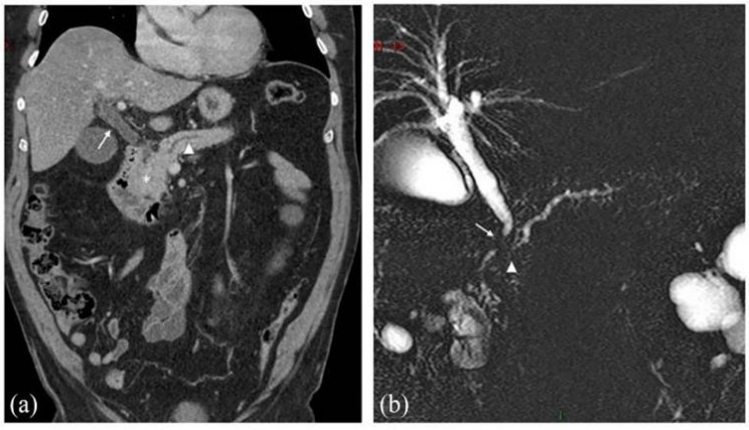

Figure 13: A 76-year-old man with painless obstructive jaundice, increased bilirubin (6 mg/dl, normal values <1.2 mg/dl) and IgG4 (4.96 g/l, normal values <1.26 g/l) in the serum. CT-scan in the portal venous phase (A, coronal plan) shows dilatation of the common bile duct (arrow) and main pancreatic

duct (arrowhead) upstream from a pancreatic head mass (star). At 2D-MRCP (B), a stricture of the distal common bile duct (arrow) and main pancreatic duct (arrowhead) associated with mild irregularities of the secondary pancreatic ducts are demonstrated. Diagnosis was autoimmune pancreatitis [1].

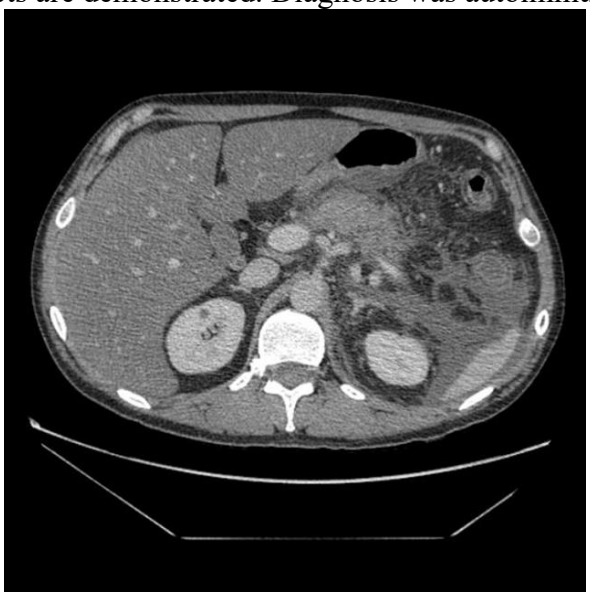

Figure 14: Diffuse pancreatic parenchymal enlargement predominantly affected the body and tail with decreased attenuation. Indistinct pancreatic margins with surrounding retroperitoneal fat stranding. Thickened edematous large bowel at the hepatic and splenic flexures. Multiple peripancreatic and periportal lymph nodes [23].

IV. Post-surgical biliary strictures

In Western countries, iatrogenic strictures account for up to 80% of all benign strictures [1].

Post-cholecystectomy. Although the incidence of biliary injuries at laparoscopy recently decreased to figures similar to those reported with open cholecystectomy (0.08–0.3%), cholecystectomy remains a frequent cause of biliary stricture. These most often involve the CBD, the hilum, or the right hepatic duct (Figure 46). Patients typically present with jaundice or pain, sometimes associated with cholangitis. Various classifications of post-surgical biliary strictures have been proposed. MRCP can be used to identify not only the level of the stricture but may also reveal a bile leak, an obstructed segment lacking continuity with the biliary tree, or a focal liver atrophy [24].

Post-liver transplantation. Biliary strictures may be anastomotic or non-anastomotic. Anastomotic strictures complicate approximately 6–12% and 34% of deceased and living donor LT procedures, respectively. Non-anastomotic strictures are located >5 mm proximal to the anastomosis and account for 10–25% of all strictures complicating LT; they may result from ischaemia (e.g. hepatic artery thrombosis or stenosis, prolonged cold or warm ischaemia) or from receiver disease (e.g. PSC). They are usually multiple and longer than anastomotic strictures (Figure 47), and may progress to the intrahepatic ducts. Endoscopy has become the first-line treatment; it is technically more difficult for non-anastomotic strictures than for anastomotic strictures, and, in the case of hepatic artery thrombosis, it is mostly ineffective if the arterial blood flow cannot be restored [25].

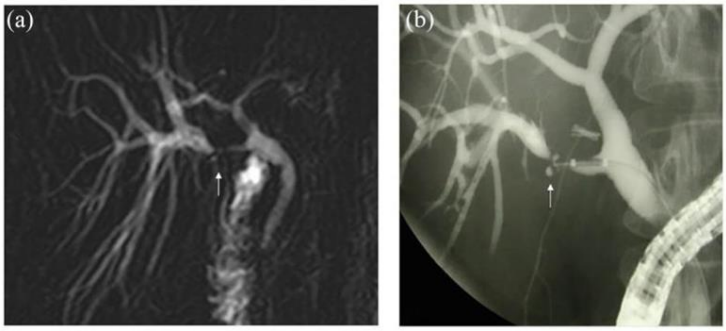

Figure 15: Post-cholecystectomy stricture of an aberrant right posterior biliary duct (low insertion on the common bile duct) shown on 2D-MRCP (A, arrow) and endoscopic cholangiogram (B, arrow) [1].

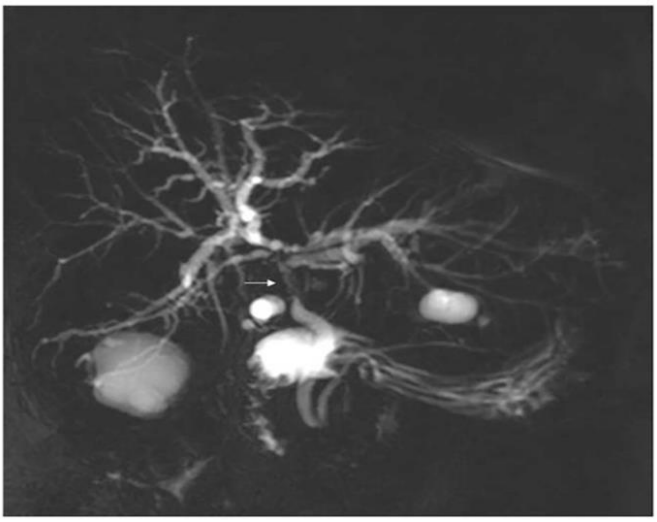

Figure 16: A 62-year-old woman with cholestasis 8 months after liver transplantation for hepatocellular carcinoma developed cirrhosis related to hepatitis C virus. 2D-MRCP discloses a long stricture extending from the anastomotic site to the hilar confluence (arrow) with upstream biliary dilatation. Diagnosis was ischaemic biliary stricture [1].

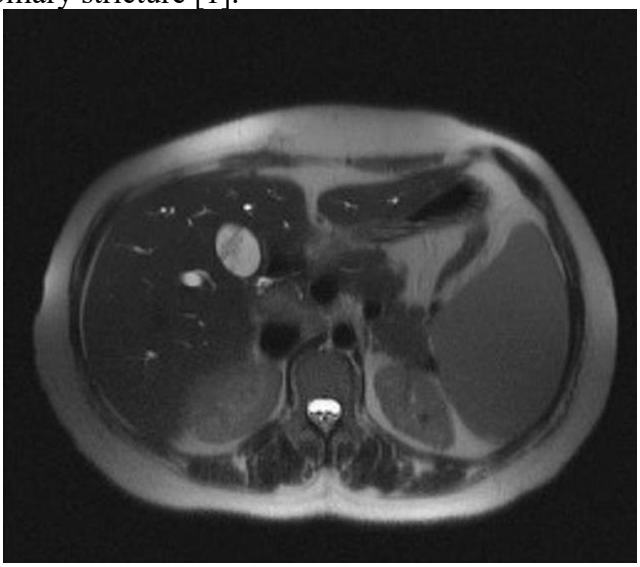

Figure 17: Abrupt smooth cut-off of common hepatic duct approximately 1 cm from the hilar confluence. There is proximal dilatation of intrahepatic biliary tree [4].

V. Mirizzi syndrome

Mirizzi syndrome, the obstruction of the common hepatic duct by a gallstone impacted at the gallbladder neck or cystic duct, occurs in 0.1% of gallstone disease. Common presenting symptoms include fever,

right upper quadrant pain, and obstructive jaundice [26].

MRCP or even ultrasonography may be diagnostic, showing stone(s) within the cystic duct or neck of the gallbladder as well as extrinsic narrowing of the common hepatic duct with upstream dilatation. It has been classified into four types, depending on the presence and importance of a defect in the common hepatic duct. Differential diagnosis with an underlying CCA or gallbladder carcinoma should be made [27].

VI. Others

Other extremely rare causes of benign biliary strictures include sarcoidosis, adenomyomatosis, inflammatory cholangiopathy related to mastocytosis, eosinophilic cholangitis, and follicular cholangitis. Some features of benign biliary strictures may suggest a diagnosis (Table 1) [1].

Table 1: Benign biliary strictures [1].

	Clinical features	Imaging features	Diagnosis	Other specific features
Large-duct PSC	Cholestatic clinical pattern*	Multifocal IH and/or EH BD strictures ("beaded" appearance)	MRI/MRCP	• Association with IBD (UC)
Small-duct PSC	Cholestatic clinical pattern*	Normal cholangiography	Liver biopsy	• May progress to large-duct PSC • Low-risk phenotype
IgG4-SC	More often painless obstructive jaundice	4 patterns of biliary strictures	↑ serum IgG4 IgG4-positive Immunostaining in ampullary/bile duct biopsy	• Association with AIP • Response to corticosteroids • Other organ involvement (pancreas, kidneys, etc.)
AIDS cholangiopathy	Cholestatic clinical pattern*	4 patterns of biliary strictures Papillary stenosis in 70% of cases	MRI/MRCP	• Advanced AIDS (CD4 count <100/mm^3) • Opportunistic infections
Secondary sclerosing cholangitis in critically ill patients	Prolonged stay in intensive care unit and need for mechanical ventilation	Biliary casts and irregular strictures/dilatations in the intrahepatic ducts with relative sparing of the common bile duct.	MRI/MRCP	Lack of prior history of liver disease and no known pathologic process or injury responsible for bile duct obstruction
RPC	Recurrent acute cholangitis	Multiple IHBD strictures (mainly affects the left lateral and right posterior intrahepatic ducts) Intrahepatic stones Biliary abscesses	MRI/MRCP	• Disease of Southeast Asia
Ischaemic cholangitis	Cholestatic clinical pattern*	Proximal IHBD strictures Bile duct necrosis Bilomas, abscesses, biliary casts	MRI/MRCP	• EH portal vein obstruction with portal cavernoma • After LT or intra-arterial drug infusion
Chronic/Acute pancreatitis	Recurrent/Acute pancreatic pain	Distal CBD stricture Pancreatic calcifications, pseudocyst and MPD abnormalities	MRI/MRCP CT-scan	• Exocrine/endocrine pancreatic insufficiencies

A. Malignant biliary strictures

CCA and pancreatic cancer are the two most common causes of malignant biliary strictures [28].

I. Pancreatic cancer

The incidence of pancreatic cancer varies between 7.7 (Europe and North America) and 2.2 (Africa) per 100,000 people, with little difference between genders and a peak incidence in the seventh and eighth decades. Due to its low survival rate (9% at 5 years), it is the seventh leading cause of cancer death in industrialized countries, and the third leading cause of cancer death in the United States (US). Risk factors include cigarette smoking, increased body mass index, heredity, CP, and diabetes [29].

Clinical features

Approximately 60–70% of tumors occur in the cephalic area and typically cause jaundice, weight loss, and steatorrhea, whereas tumors in the body and tail usually cause pain and weight loss. Pancreatic cancer should be considered in patients presenting with acute pancreatitis and no causative factor, a recent onset of diabetes, or unexplained thrombophlebitis. Physical findings may include a dilated gallbladder (Courvoisier's sign), and, rarely, an abdominal mass, ascites, and left supraclavicular adenopathy [30].

Diagnostic work up

A meta-analysis (52 studies, 5399 patients) found that CT-scan, MRI, transabdominal ultrasonography, and EUS present similarly high accuracies for the diagnosis of pancreatic cancer (90%). Guidelines recommend CT-scan for the detection, staging, and assessment of resectability of suspected pancreatic cancer [31].

A hypoattenuating pancreatic mass associated with secondary signs such as biliopancreatic ductal dilatation, parenchymal atrophy, or contour abnormalities is highly suggestive of pancreatic cancer (Figure 49). Fluorodeoxyglucose positron emission tomography (F-FDG PET)/CT may detect masses not seen at CT-scan and differentiate pancreatic malignancy from CP and AIP [32].

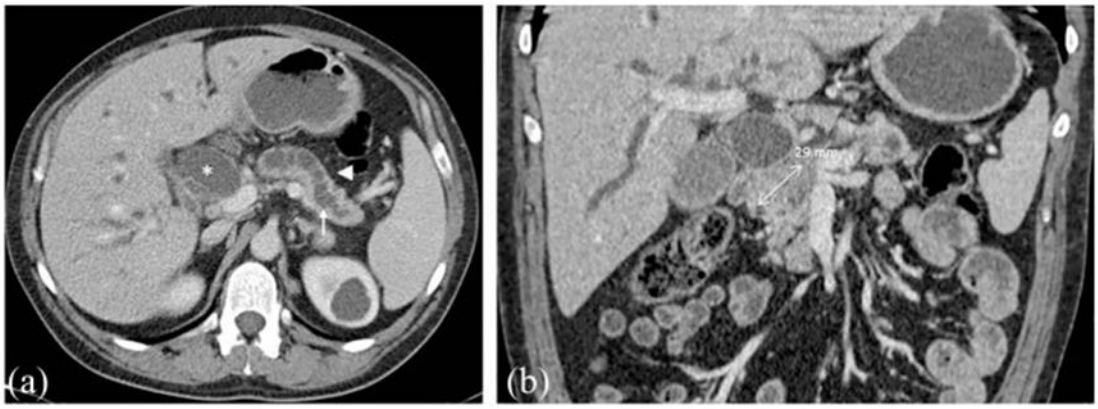

Figure 18: A 48-year-old man with painless obstructive jaundice, loss of weight, and increased CA19-9 serum level (14,000 U/l, normal values <37 U/l). CT-scan in the portal venous phase shows, in the axial plane (A), a double duct sign [dilatation of both the common bile duct (star) and the main pancreatic duct (arrow)] as well as pancreatic parenchymal atrophy (arrowhead) and, in the coronal plane (B), a low-density mass in the head of the pancreas measuring 29 mm in diameter. Diagnosis was pancreatic cancer [1].

Differential diagnosis

Focal CP and AIP are the two benign processes most commonly mistaken for pancreatic malignancy. A history of prolonged alcohol abuse and smoking, young age, and diffuse pancreatic ductal changes favor CP, whereas AIP is suspected in the presence of increased levels of serum IgG4. In a meta-analysis (11 studies, 1294 patients), the sensitivity/specificity of IgG4>130–140 mg/dl for distinguishing AIP from pancreatic cancer was 72%/93% [33].

Some authors have suggested increasing the IgG4 cut-off value to avoid missing a cancer (280 mg/dl: specificity of 99%). Other features that may help to diagnose AIP from pancreatic cancer include biopsy (infiltration by IgG4-positive plasma cells), other organ involvement, and a corticosteroid trial if

diagnostic criteria are not fulfilled. Differential diagnosis also includes pancreatic neuroendocrine tumors, lymphoma, and a variety of other rare conditions [1].

II. Cholangiocarcinoma

CCA is rare (incidence in the US, 1.3 per 100,000/year) but it is becoming more frequent worldwide. CCA occurs slightly more often in men, (male/female ratio, 1.3:1) during the sixth to eighth decade. CCAs are classified according to their location as intrahepatic, perihilar (also called Klatskin tumours, two-thirds of CCAs), and distal, or according to their macroscopic appearance as mass-forming, periductal-infiltrating, or intraductal growth [34].

Klatskin tumours are further classified according to the level of biliary obstruction from type I to IV using the Bismuth-Corlette classification. Risk factors include hepatitis C virus infection, chronic biliary inflammation (e.g. PSC, parasitic biliary infestation), and some types of choledochal cysts and anomalous pancreaticobiliary junctions [35].

Clinical features

Tumour location dictates the symptoms and signs of CCA. Intrahepatic CCAs may cause a dull constant pain in the right upper quadrant, whereas hilar and extrahepatic CCAs cause jaundice, pain, and weight loss. Cholangitis is rare at presentation. At clinical examination, hepatomegaly, tumor mass, or Courvoisier's sign may be detected [1].

Diagnostic work up

All guidelines recommend MRI or CT-scan for the diagnosis of CCA. At imaging, upstream biliary tract dilation is detected, except in the case of peripheral intrahepatic CCAs, but the tumour itself may not be detected. MRI/MRCP is highly accurate (98%) for identifying biliary obstruction (Figure 50), but is less able to differentiate benign from malignant causes. CT-scan and MRI protocols continuously improve, with the latest techniques currently involving T1- and T2-weighted sequences as well as diffusion-weighted imaging and late-phase sequences with hepatocyte-specific contrast agents [36].

This has allowed for marked improvements but some aspects still remain problematic with both MRI and CT-scans (e.g. evaluation of the longitudinal extent of the lesion). The performance characteristics of CT-scan and MRI for diagnosis and staging of CCA have recently been reviewed. Another technique, F-FDG PET/CT, has demonstrated sensitivity and specificity of 82% and 75% respectively, for diagnosing CCA, with better performance for intra- than extra-hepatic CCA [1].

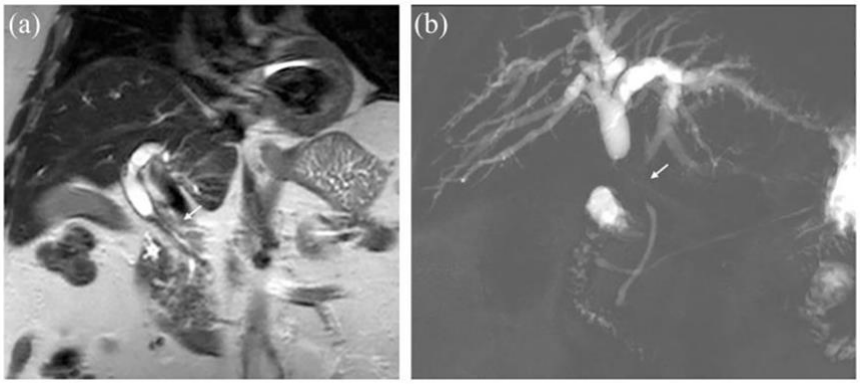

Figure 19: A 74-year-old man with cholestasis, loss of weight, and increased CA19-9 serum level (190 U/l, normal values <37 U/l). Coronal MR T2-weighted image (A) and 2D-MRCP (B) show a long common bile duct stricture with upstream dilatation and no mass. After a 2-week negative steroid trial, the patient underwent surgery and pathological analysis revealed a T2N0 cholangiocarcinoma [1].

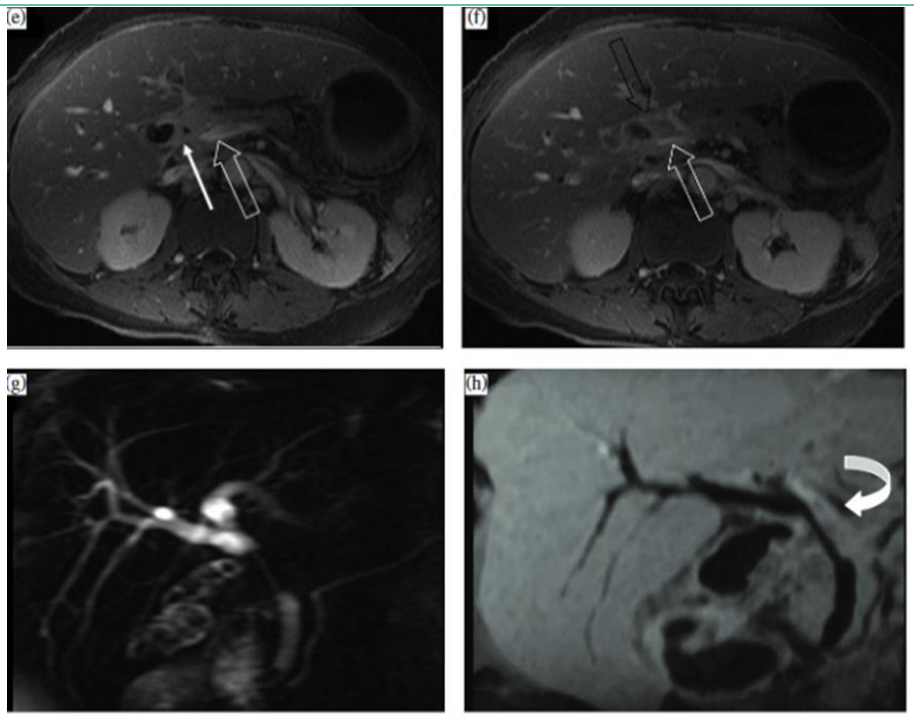

Figure 20: Inoperable perihilar cholangiocarcinoma in a 64-year-old female who presented with painless jaundice and had focal stenosis of the common bile duct on ERCP. There is a perihilar mass (arrow), which is hypointense to liver on (a) axial T1W in-phase SGRE, mildly hyperintense on (b) T2W FSE with fat saturation, has little to no arterial enhancement on (c) the arterial-dominant phase gadolinium-enhanced axial T1W 3D SGRE, mild enhancement on the (d) 2 min post-gadolinium image, and the tumor becomes mildly hyperintense to liver on the (e) 15 min post-gadolinium image. The tumor surrounds and narrows the main portal vein (white open arrow), and the right main hepatic artery (black open arrow) on a (f) higher slice. (g) Coronal thick slab T2W single shot fast spin-echo (SSFSE) MRCP image demonstrates long segment narrowing of the common hepatic and proximal common bile duct, with a stent traversing the stenotic segment as well as dilation of the intrahepatic bile ducts. (h) A corresponding minimum intensity projection (Min IPreformatted image demonstrates the mildly enhancing mass surrounding the narrowed segment of common hepatic duct (curved arrow).

III. Gallbladder carcinoma

The incidence of gallbladder carcinoma widely varies in the world, with the highest incidences in India and South America (it is the primary cause of cancer death among women in Chile). Gallbladder carcinoma affects two to six times more women than men, its incidence steadily increases with age with a peak in the sixth and seventh decades. Gallstones are present in 65–90% of patients with gallbladder carcinoma; other risk factors include porcelain gallbladder, gallbladder polyps, and anomalous pancreaticobiliary junction [37].

Clinical features

Early diagnosis is difficult because most patients present with non-specific findings of right upper quadrant pain, jaundice, and weight loss. Jaundice has been associated with unresectable disease. Patients with advanced disease may also present with a palpable gallbladder mass, hard nodular liver, and malignant ascites [1].

Diagnostic work up

Three major patterns of presentation have been described on ultrasonography, CT-scan, or MRI: a focal or diffuse mural thickening (20–30%), an intraluminal polypoid mass originating from the gallbladder wall (15–25%), and a subhepatic mass replacing or obscuring the gallbladder (45–60%) [38].

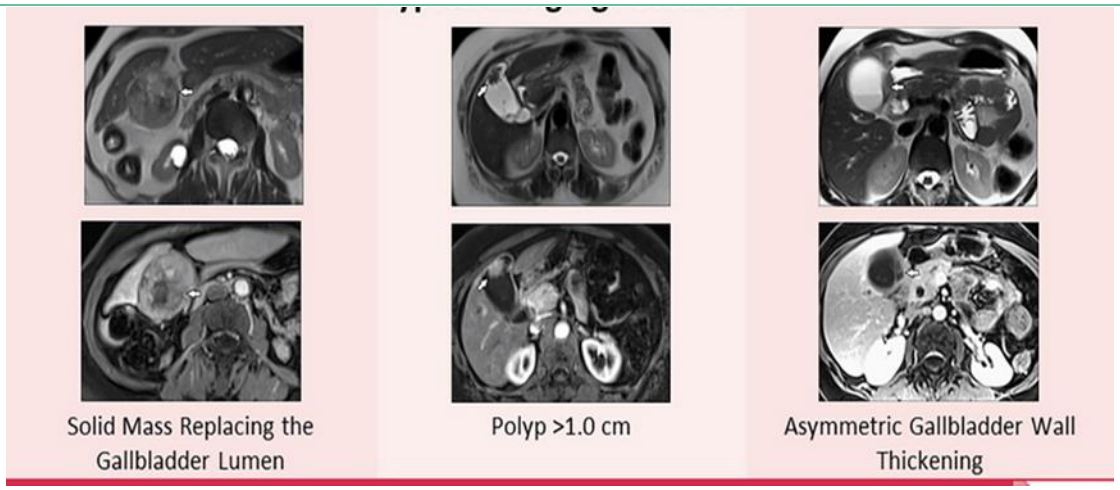

Figure 21: Gallbladder carcinoma and its differential diagnosis at MRI.

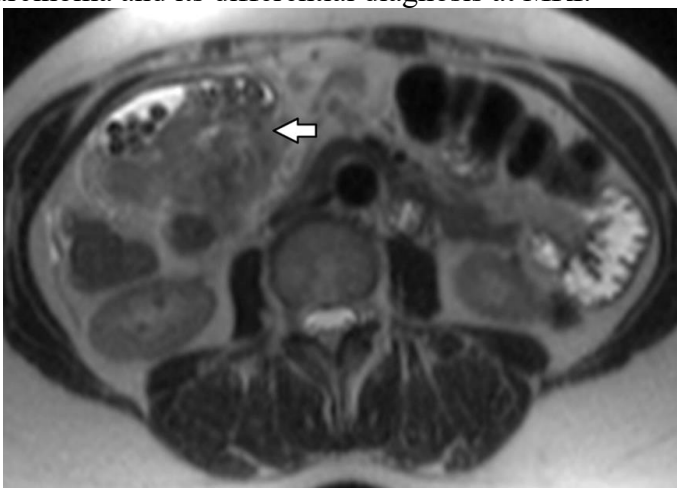

Figure 22: Gallbladder adenocarcinoma in a 54-year-old woman with weight loss and abdominal pain. (a) Axial T2-weighted MR image shows a heterogeneous gallbladder mass (arrow) with gallstones. (b) Axial T1-weighted image shows that the mass (arrow) is isointense to the liver parenchyma. (c) Axial contrast-enhanced T1-weighted image shows heterogeneous enhancement of the mass (arrow). The mass arising from the gallbladder and invading surrounding fat was pathologically confirmed to be gallbladder adenocarcinoma. The tumor was stage IV (T4) and unresectable, with peritoneal and colonic involvement.

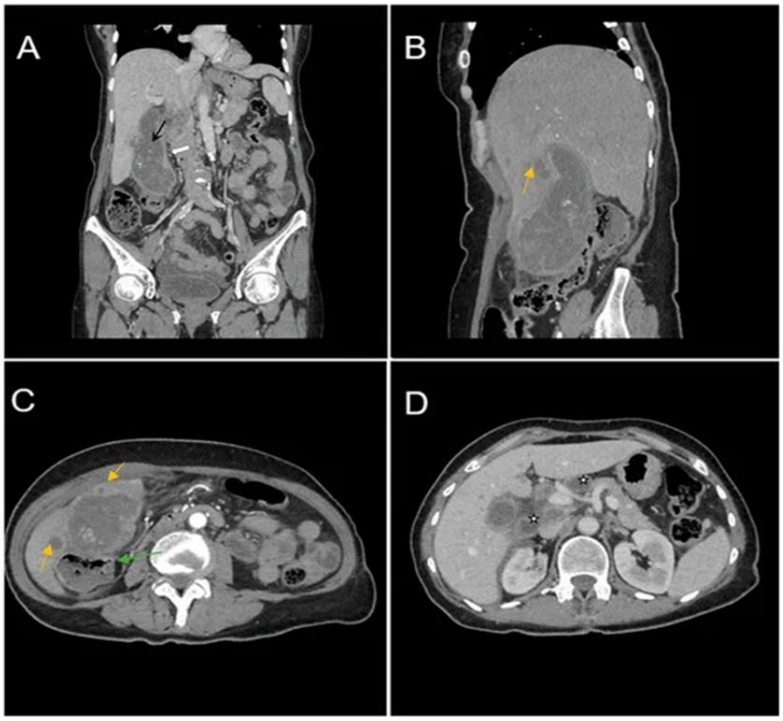

Figure 23: Multiplanar sections of contrast-enhanced CT acquisitions richly illustrating a low differentiated gallbladder adenocarcinoma. (A) Gallbladder hydrops (>40 mm transverse measurement, 142 mm longitudinal measurement) with asymmetric gallbladder mural thickening, 7 mm (white arrow), and multiple intraluminal mixed stones, 5–8 mm (black arrow). (B,C) Liver metastases—hypodense nodular hepatic lesions with rim contrast enhancement (yellow arrow). (C) Tumoral extension into IV, V segments of the right hepatic lobe and contact with the ascending colon (green arrow). (D) Lymphatic metastases (white stars).

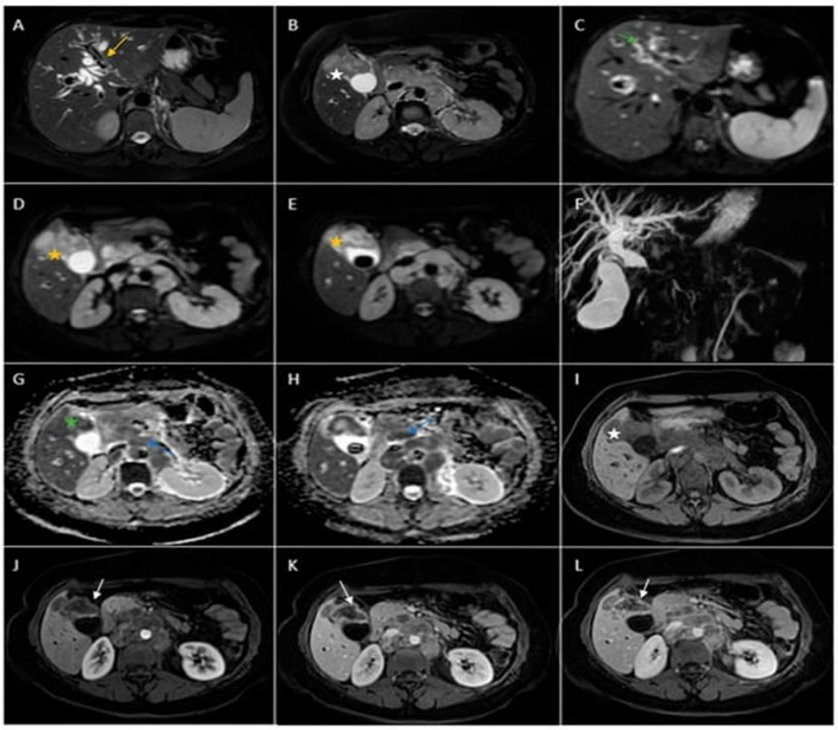

Figure 24: Abdominal MRI vividly illustrating synchronous gallbladder and biliary tract carcinoma with multiple large lymphadenopathies localized in the hepatic hilum, surrounding the cephalic region of the pancreas and in the celiac region. (A) Axial T2-weighted FS showed significant intrahepatic biliary

dilatation in both hepatic lobes (yellow arrow). (B) Axial T2-weighted FS showed hypointense intraluminal gallbladder mass (white star) and multiple large lymphadenopathies. (C) Axial diffusion-weighted imaging (DWI B800) showed irregular, asymmetrical thickening of the walls of the intrahepatic bile ducts with high signal intensity suggestive of cholangitis (green arrow). (D,E). DWI B800 highlighted the gallbladder mass; inhomogeneous areas of high signal (yellow stars). (F) Coronal 3D MRCP showed enlarged gallbladder with an intraluminal gallstone and dilated intrahepatic and extrahepatic biliary tree. (G,H). On apparent diffusion coefficient (ADC) map, the gallbladder mass is dark, illustrating markedly diffusion restriction (green star). Multiple large lymphadenopathies are also observed mainly in the lombo-aortic region, in the cephalic pancreatic region and in the hepatic hilum (blue arrow). (I) Axial T1-weighted image showing hypointense irregular tumoral gallbladder mass (white star). (J–L). Axial contrast-enhanced (arterial phase followed by venous phase) T1-weighted image showing rim-enhancing of the tumoral gallbladder mass (white arrow).

The clinical approach to biliary strictures

The diagnostic approach begins with a careful patient history and physical examination: a history of surgery (cholecystectomy or LT), autoimmune disease (IBD or AIP), pancreatitis, gallstones, HIV status, or chemotherapy is vital knowledge needed to narrow the differential diagnosis [1].

Figure 25 summarizes the initial work up proposed for patients with a cholestatic clinical pattern. Abdominal ultrasonography reveals the level of obstruction with an accuracy of >90%. It may also show the cause of obstruction but it is highly operator dependent. CT-scan or MRI is the next step to identify the cause of obstruction. Some authors suggest to prefer MRI and CT-scan for intrahepatic and distal bile duct strictures, respectively; however, the evidence supporting this diagnostic approach is limited [39].

Duct hyperenhancement and thickness ⩾3, 4, or 5 mm are independent predictors of malignancy, while other criteria may also be helpful (longer, irregular, and asymmetric biliary stricture, regional lymph node enlargement >1 cm, abrupt cut-off on cholangiography, or a mass lesion). In patients with CP, MRI with diffusion-weighted imaging may be particularly useful. At this stage, standard biochemical tests should be complemented with complete blood count, CA19-9, CEA, IgG, IgG4, and HIV serology [1].

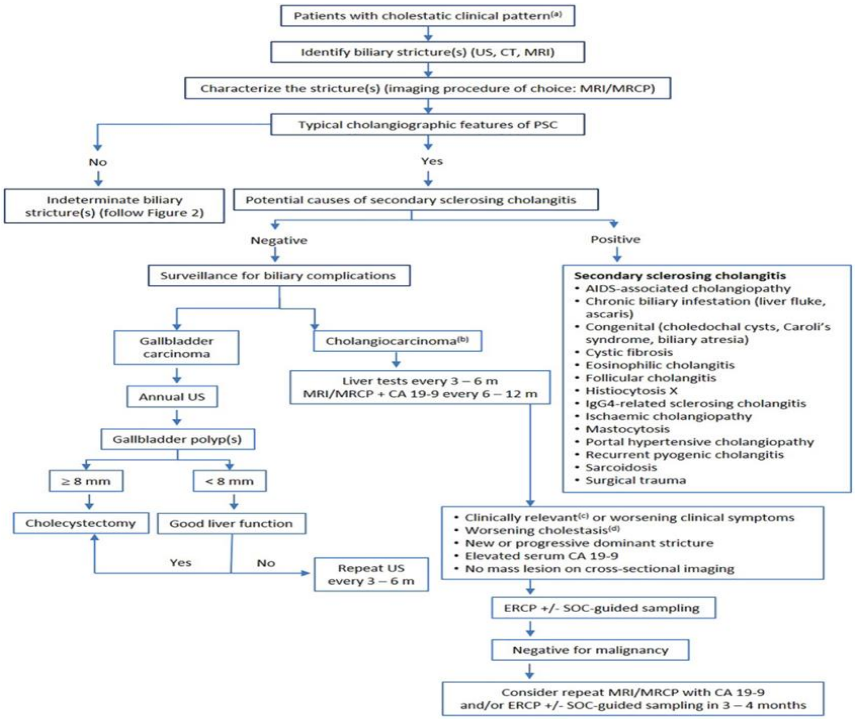

Figure 25: Algorithm for the evaluation of patients with a cholestatic clinical pattern caused by biliary stricture(s). The first step is to identify biliary stricture(s) by imaging procedures. The next step is to characterize the stricture(s). (a) Cholestatic clinical patterns include one or more of pruritus, dark urine,

light stool, jaundice, increased serum levels of alkaline phosphatase, γ glutamyl transferase, bilirubin. (b) Particularly for the high-risk phenotype of PSC, that is, patients with large-duct PSC and ulcerative colitis as well as older patients, but not for patients with small-duct PSC or patients <20 years old. (c) Pruritus, jaundice, bacterial cholangitis, weight loss. (d) ⩾20% increase in cholestatic liver enzymes (alkaline phosphatases, γ glutamyl transferase) [1].

Biliary strictures that remain indeterminate will likely require invasive procedures that allow sampling and, in the case of EUS, detection of masses missed by other techniques and locoregional tumor staging. After a complete work up, some patients still have no diagnosis and exploratory surgery may be indicated. This should be discussed in a multidisciplinary team and with the patient as about 15% of patients with suspected perihilar CCA are found to have a benign diagnosis after resection and post-operative mortality remains about 10% in many Western referral centers [40]..

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