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Ultrasound of the gallbladder and hepatobiliary system

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Introduction

Biliary system diseases are common pathology in medical practice. After obtaining the patient history and performing a physical examination, conventional B-mode and Colour Doppler imaging (CDI) are the first-line imaging methods of choice. In fact, ultrasound (US) is now a routine examination in daily clinical practice and in many clinical presentations. Additionally, it is used in asymptomatic patients as a screening tool [(1)]. It is an accurate imaging modality when performed by a qualified and experienced operator. Furthermore, it is safe, non-invasive, inexpensive, easily accessible and a repeatable imaging modality, which is highly sensitive and specific for the detection of many biliary diseases.

It is unusual for the biliary tree to be scanned in isolation due to the complexity of the pathophysiology of the hepatobiliary system. Rather, the biliary tree is scanned as part of an upper abdominal ultrasound examination. Therefore, ultrasound imaging can frequently demonstrate an alternate diagnosis as the cause of a patient's symptoms when the biliary system is normal [(2, 3)]. However, it is a highly operator dependent imaging modality and its diagnostic success is also influenced by variables such as non-fasting, obesity, presence of surgical dressings and a distended abdomen due to gastrointestinal (GI) gas. In the hands of an experienced practitioner, ultrasound has become a diagnostic tool equal in importance to endoscopy. However, the limitations of ultrasound must be appreciated by the operator, recognising that successful diagnostics of some hepatobiliary disease requires a multimodality approach [(4)].

Topography and gross anatomy

The gallbladder is a saccular shaped hollow sac that has a pear or teardrop shape in long-axis cross section. Its function is to store and concentrate bile, which is expelled into the duodenum after eating. Topographically, it is commonly located in the right hypochondrium in the mid-clavicular line, just below the right lower costal margin, beneath the anterior abdominal wall. Anatomically, it is situated on the inferior surface of the liver in the gallbladder fossa of the posterior right hepatic lobe, lateral to the second part of the duodenum and anterior to the right kidney and transverse colon.

The gallbladder comprises a fundus, body, infundibulum and neck. The fundus is the rounded, distal portion of the gallbladder that typically projects below the inferior surface of

the liver in the mid-clavicular line. The body is the largest portion that tapers to the infundibulum and neck. Sometimes, there is a saccular outpouching from the infundibulum/neck known as Hartmann's Pouch, which is a common location for gallstones to become lodged, causing cholestasis.

The cystic duct (CD) of the gallbladder arises from the superior aspect of the gallbladder neck and transmits bile from and to the main bile duct. The CD contains a spiral series of mucosal folds, referred to as the spiral valves of Heister that prevent collapse or over-distension of the gallbladder due to sudden position changes. The cystic artery, a branch of right hepatic artery, is the main arterial supply to the gallbladder.

Impact of body habitus on gallbladder position

The gallbladder typically lies obliquely within the abdomen. However, its position and orientation vary with differing body habitus. There are four typical body habitus types – hypersthenic, sthenic, hyposthenic and asthenic [Table 1]. It is important for the ultrasound practitioner to understand this variation in the position/orientation of the gallbladder position to correctly align the ultrasound transducer to optimally image the long and short axes of the gallbladder [Figure 1].

Table 1 Variable positions of the gallbladder dependent upon body habitus type.

Body habitus type	Typical gallbladder position and orientation
Hypersthenic 5% population (wide, deep, chest, Wide abdominal cavity)	The diaphragm, liver and gallbladder tend to lie high in the abdomen in the right upper quadrant, under the thoracic cage. Consequently, the liver and gallbladder are often difficult to access using ultrasound, requiring a flexible and adaptable scanning technique. Intercostal approach and decubitus/erect patient positions can facilitate imaging. The stomach is also high, and this can create problems with US imaging access to deeper structures due to overlying gas and food residue. The gallbladder is also often horizontally orientated rather than in its normal oblique orientation.
Sthenic (Average build)	The liver and gallbladder tend to lie as expected in the right upper quadrant with the gallbladder fundus projecting just below the lower costal margin in the mid-clavicular plane and with the gallbladder lying in its typically oblique orientation.

Hyposthenic (Tall, thin, narrow, chest not deep in AP diameter)	The liver and gallbladder tend to lie lower than in hypersthenic/sthenic types; often located in the right lumbar abdominal region and the gallbladder is frequently more vertically orientated.
Asthenic (Extreme variant of above)	The liver and gallbladder tend to lie low down in the abdomen, sometimes as low as the right iliac fossa. The gallbladder tends to lie in a more vertically orientated than above body habitus types.

Impact on Ultrasound Scanning technique

An understanding of these variable positions of structures is essential for successful ultrasound scanning technique. It is suggested that the practitioner looks at the patient as they enter the scan room and assigns them to a body habitus type. This will help the ultrasound practitioner to know where to find the gallbladder and other structures and how to align the ultrasound transducer to show the long and shorts axes of the gallbladder [Figure 1, Table 1].

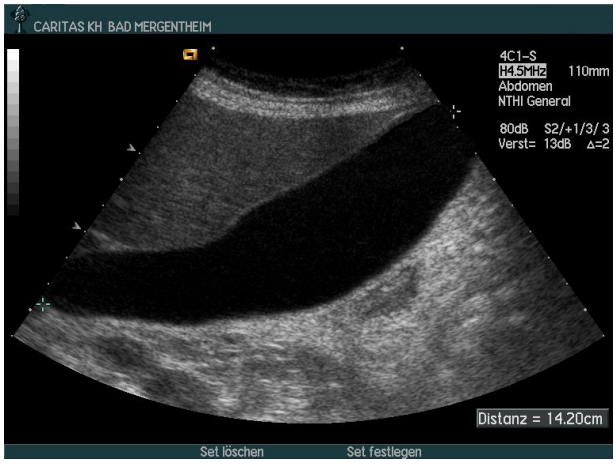
Gallbladder measurements

The normal gallbladder size is reported to be 7-10 (length) x 2-4 (AP diameter) x 2-4 (transverse diameter) cm, but it obviously depends on the volume of bile present [(5)]. Typical bile volume is normally 40 - 60 ml, measured by a rotating ellipsoid [(5)]. However, volume estimates using ultrasound are unreliable, showing a wide intra- and inter-operator variability [(5, 6)]. Cholecystomegaly in patients with diabetes mellitus or during long standing fasting periods may reveal gallbladder diameters up to 15 x 6 x 6 cm without clinical relevance [Figure 2], in contrast to clinically important hydrops associated with right upper quadrant pain and fever.

Gallbladder volume can be estimated before and after a test meal and this can be used to assess gallbladder function to a limited degree. Contraction of >60 % is regarded as normal. It is difficult to locate the gallbladder after a test meal as it is usually contracted. A useful tip

is to mark an X on the abdominal wall at the site of the gallbladder when it is distended to facilitate its location after the test meal. Normal contraction is a requirement before gall stone treatment with, for example, ursodeoxycholic acid. The normal gallbladder wall thickness is ≤ 3 mm on ultrasound.

Figure 1 **Long axis section of the gallbladder showing clinically insignificant large, thin walled gallbladder (+…..+). This is often seen in the elderly, known as a physiological atonic gallbladder. A large gallbladder (up to 15 cm in length) might be found in older people, diabetics and many other unspecific disorders [(6)].**



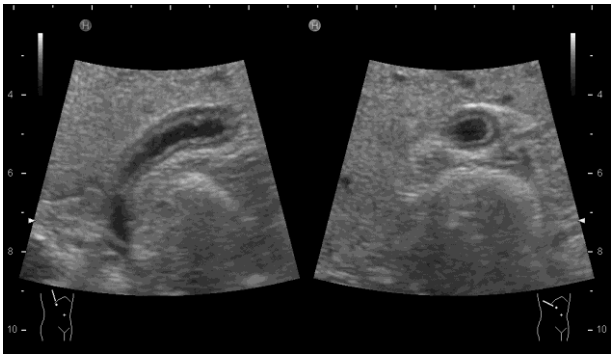
Ultrasound Examination technique

Patient Preparation

It is recommended that a patient undergoes a 6-8 hours period of fasting and non-smoking, prior to imaging of the gallbladder and biliary tree to maximise the distension of the gallbladder. However, a patient may take small amounts of still water by mouth prior to the scan, particularly for taking any medications. Additionally, fasting reduces food residue and gas in the upper gastrointestinal (GI) tract, which may reduce image quality or preclude

imaging of the gallbladder and biliary tree due to overlying GI contents. Inadequate fasting and smoking are likely to result in the gallbladder being partially or completely contracted; consequently, the walls will appear thicker than normal mimicking pathological gallbladder wall thickening – a misdiagnosis [Figure 2].

Figure 2 **Small contracted gallbladder (left: long axis section; right: short axis section section): gallbladder lumen is very narrow, the layers of the contracted and thickened wall are visible.**



In emergency situations, however, ultrasound can be performed without fasting. If a conclusive diagnosis is not reached, a repeat scan after fasting is recommended if the clinical status of the patient permits. Alternately, other imaging modalities such as MRI can be used.

Patient history and physical examination

It is recommended that a short history is taken and that the abdomen is examined/palpated before the ultrasound examination commences. This is to ensure that the ultrasound practitioner has the complete clinical picture and coupled with the ultrasound findings, can be integrated to ensure that the clinical question is addressed.

Ultrasound Examination of the gallbladder and biliary tree

The gallbladder and biliary tree are usually examined as part of a complete upper abdominal survey. However, targeted scanning of these structures is sometimes undertaken where there is a robust history/presentation, typical gallbladder/biliary tree pathology or in follow-up cases. The examination is not confined to the gallbladder. Rather, it must include the ducts of the intra- and extra hepatic biliary tree.

Ultrasound Equipment

Routinely, a convex, wide band, multi-frequency (e.g. 2-6 MHz) transducer is used for the evaluation of the gallbladder. However, lower frequencies may be used when an increased depth of penetration is required, for example in obese patients or when the gallbladder is deep (e.g. hypersthenic patients). In very slim patients (e.g. asthenic/hyposthenic types) [Table 1] where the gallbladder maybe very superficial, a wide band high frequency range convex or linear transducer (e.g. 4-12 MHz) should be used to optimise image quality.

Anatomical Landmarks

Topographically, the gallbladder is usually located in the midclavicular line at the level of the lower costal margin. Useful landmarks to identify the gallbladder on ultrasound are the inferior edge of the right lobe of liver and the liver hilum. In the right subcostal oblique section, the landmark structure to be used is the interlobar fissure and the gallbladder will be found by aligning the probe with the fissure. The gallbladder will be located inferiorly or laterally to the fissure (between liver segments IV and V).

Image acquisition

Conventional real-time ultrasound produces images of thin slices of the liver/biliary tree on the screen, and so it is essential that the operator scans the structures systematically, in at least two anatomical planes, to be entirely convinced that the entire volume of the liver and biliary tree and structures has been imaged. The operator must then synthesise this 2-dimensional information to develop a 3-dimensional map of the individual patient`s

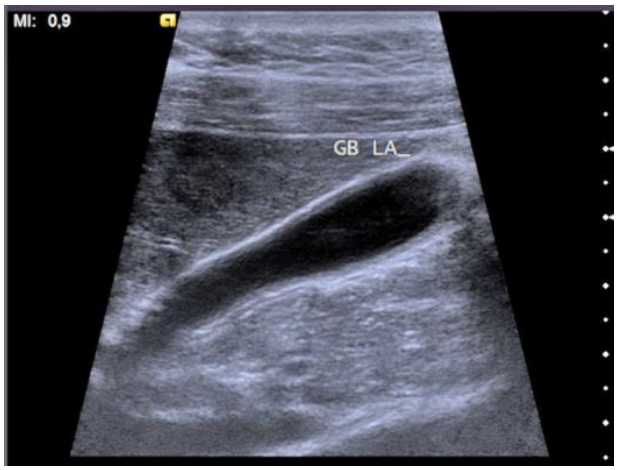
liver/biliary tree anatomy and pathology. This requires good hand-eye-brain coordination and spatial awareness.

Ultrasound scanning technique of the gallbladder and biliary tree

The gallbladder and biliary tree can be examined initially with the patient in a supine position. This is to be encouraged as a first-line approach to minimise the risks of operator repetitive strain injury to the operator due to overreaching. Successful examination of the gallbladder and biliary tree also often requires the patient to be examined in a left posterior-oblique or left lateral decubitus position. These latter positions cause the liver/gallbladder to rotate antero-medially under the influence of gravity and this may optimise the use of the liver as an acoustic window for imaging the gallbladder or make the gallbladder more readily accessible below the thoracic cage.

In an 'average'/sthenic patient, the transducer can be placed in the right mid-clavicular line on the anterior abdominal wall at the lower costal margin and its position is adjusted until the gallbladder is located, usually just visible beneath the liver. The operator should try to use the liver as an acoustic window and avoid scanning through bowel by angling cranially. The patient may be asked to take a suspended deep breath-in to cause the liver/gallbladder to descend below the lower costal margin. The transducer is then rotated over the gallbladder until the true long axis section of the gallbladder is achieved [Figure 3]. There is often a temptation for novice practitioners to freeze an image as in Figure 3. However, one must remember the gallbladder is a 3-D structure and so the transducer must be angled medially>laterally, to ensure that the ultrasound beam is swept through the gallbladder, ensuring that the whole gallbladder has been imaged in its entire long axis.

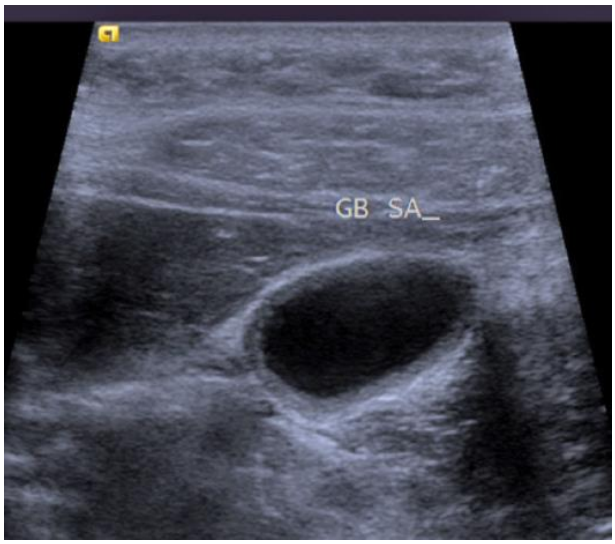
Figure 3 Long axis section of the gallbladder in a sthenic patient. Once this plane is achieved, the transducer must be angled to ensure all the gallbladder has been scanned thoroughly in this plane.



The normal gallbladder wall is thin and measures ≤3mm in the antero-posterior diameter. Many operators do not measure the normal wall thickness as is it difficult to measure such a small structure accurately. If a measurement is made, the gallbladder should be aligned so that the long axis lies horizontally on the screen, with the walls perpendicular to the ultrasound beam [Figure 3]. The anterior wall of the gallbladder should always be measured as it is closer to the transducer; it should be measured 'in line'/parallel with the ultrasound beam to optimise the axial resolution of the ultrasound beam.

In this plane, the fundus of the gallbladder is frequently not seen as it lies parallel to the ultrasound beam; an artefact. An inexperienced practitioner might recognise this apparent 'absence' of the wall as a perforation. This highlights the importance of understanding the physics of ultrasound artefacts and their impact on diagnosis. After scanning the gallbladder in long axis, the transducer should be rotated over the gallbladder, through 90 degrees towards the practitioner, to image the gallbladder in its true short axis section [Figures 3 and 4]. Again, the transducer should be angled (cranial-caudal) to ensure thorough imaging of the gallbladder in this plane from cystic duct to fundus.

Figure 4 Short axis section through the gallbladder. The transducer must be angled from cranially to caudally to ensure that the entire gallbladder has been imaged in this plane.



Movement of the patient is essential where there is sludge or stones present in the gallbladder to assess whether they move as the patient moves. Erect imaging is particularly useful to assess whether gallstones are mobile, as they will normally descend into the dependent part of the gallbladder (fundus) with the patient erect, with the assistance of gravity.

The demonstration of the cystic duct is easiest in deep inspiration with the patient in the supine or left lateral decubitus position. It is visualised by tracking the duct from the infundibulum of the gallbladder [Figure 5]. Sometimes the echogenic structures of the spiral valves of Heister may be depicted. This structure is important to recognise on ultrasound as it may be confused with real septae [Figures 6 and 18]. Moreover, it can cause acoustic shadowing, which may sometimes be mistaken for a calculus in the neck of the gallbladder. Scanning from multiple angles and different positions can aid diagnosis [Figure 16]. The distal segment of the cystic duct is best visualised with the patient supine, in the plane through the hepatic portal, anterior to the portal vein.

Figure 5 Cystic duct, originating at the gallbladder infundibulum (*). The course of cystic duct is marked by arrowheads.

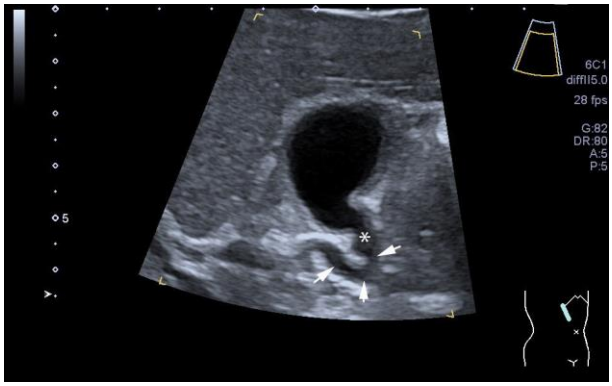
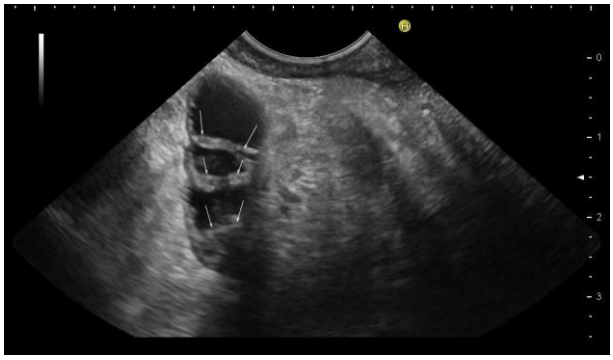


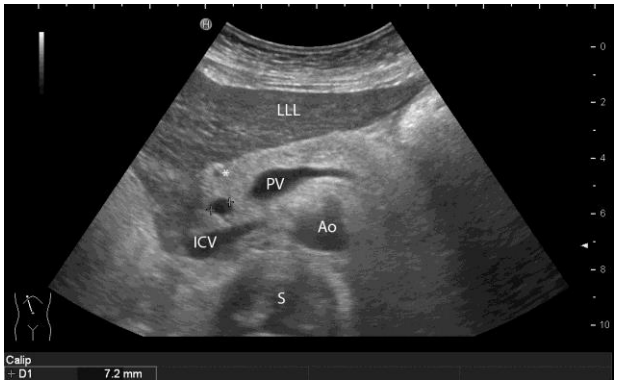
Figure 6 Spiral valve of Heister in the infundibulum of gallbladder and proximal cystic duct (arrows), visualized by longitudinal endoscopic ultrasound with the transducer positioned in the gastric antrum towards the liver hilum.



The main bile duct (MBD) with the common hepatic duct (CHD, region of the liver hilum) and the common bile duct (CBD, choledochal duct) in most patients can be easily displayed using transabdominal ultrasound. In supine position a cross section of the CBD may be found in the dorsal part of the pancreatic head [Figure 7].

Figure 7 Cross section of the CBD in the posterior part of the pancreatic head (between calipers: 7.2 mm diameter). The other cross section of a tubular structure (in

the ventral part of the pancreatic head) is the gastroduodenal artery (*; Ao: Aorta; ICV: inferior caval vein; LLL: left liver lobe; PV: portal vein; S: spine).



When found in cross section, the course of the MBD may be delineated by rotating the transducer in an oblique position. With the patient in a left posterior oblique or left lateral decubitus position the liver can be used as an acoustic window for imaging the hilar and extra hepatic biliary tree in a longitudinal section. The MBD often lies obliquely and is more lateral superiorly, hence it can usually be imaged by placing the transducer below the right costal margin in the region of the mid-clavicular line; an oblique position is required to align the transducer parallel to the long axis of the bile duct to image it along its length in a single plane (“shoulder – navel – section”). To follow the course of the extrahepatic bile duct requires slight rotation of the transducer in direction to a sagittal plane.

The MBD appears as a tubular structure usually typically situated anterior to the portal vein. Often, the bile duct is imaged with the transducer parallel to the midline. In this section, the hepatic artery will normally appear as a round structure between the MBD and the portal vein [Figures 8 - 10]. However, the practitioner must be mindful of the anatomical variants of the vessels/tubes in this region. Consequently, colour Doppler imaging is useful to ensure that the operator is in fact imaging and measuring the bile duct (no flow) and is not inadvertently mistakenly measuring another vessel, such as the hepatic artery/portal vein (7) [Figures 8 - 11].

Figure 8 **Anatomy of the hepatic hilum with the plethora of tubular structures which lie in the region of the porta hepatis (CBD: common bile duct; CHD: common hepatic duct; Duo: Duodenum; Gb: Gallbladder; MBD: Main bile duct).**

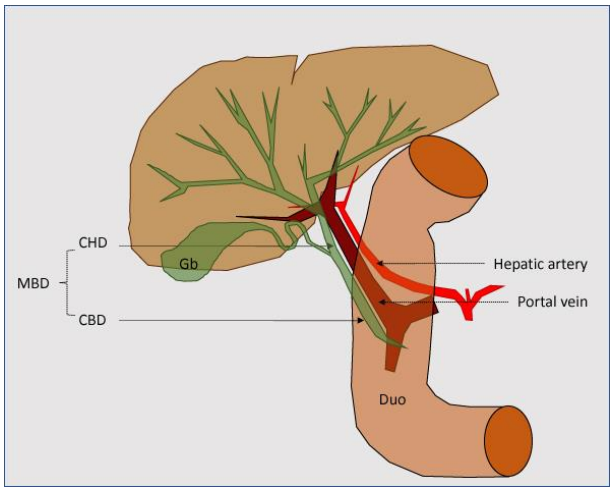


Figure 9 **Sono-anatomy of the hepaticum hilum: schematic drawing: hepatic artery in between the common hepatic duct (ventrally) and the portal vein (dorsally)**

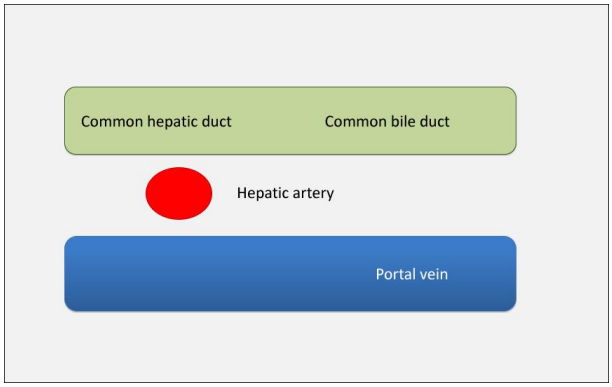


Figure 10 Oblique section (direction: right shoulder to navel) showing the length of the CHD anterior to the portal vein and passing into the region of the head of pancreas (between calipers: 6.2 mm; Ah: hepatic artery; Duo: Duodenum; portal vein).

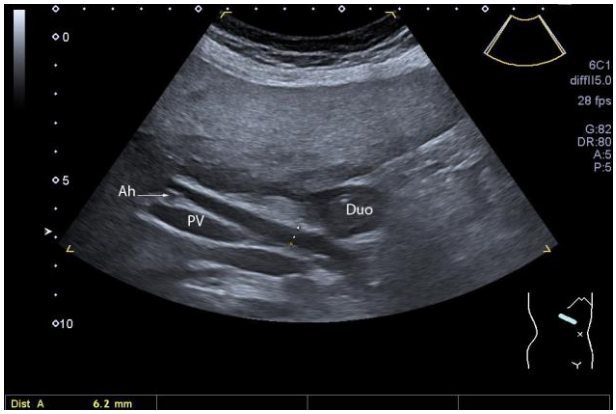
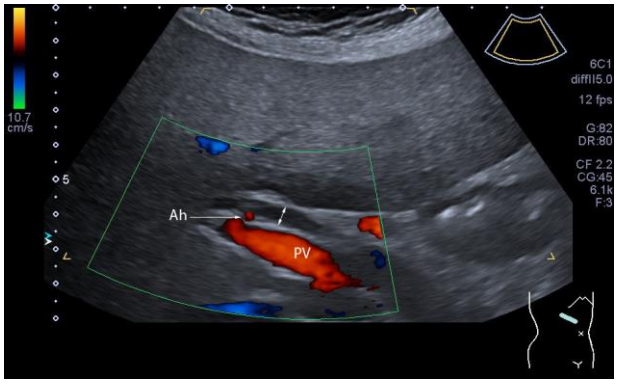


Figure 11 Colour Doppler image showing hepatopetal flow in the portal vein (PV: red); the CHD can be found anteriorly with no Doppler flow (marked with double-head arrows), which confirms that one is truly imaging and measuring the CHD (Ah: transverse section of the hepatic artery in between CHD and PV).



The CHD and the CBD should be followed from the hepatic hilum to the pancreatic head and the papilla [Figure 12]. In some patients, the hepatopancreatic ampulla or Papilla of Vater (at the end of the CBD) can be nicely displayed using transabdominal ultrasound [Figure 13]. Complete and high quality delineation of the bile duct from hepatic hilum may be impaired by obese patients and in case of gas artifacts (stomach, duodenum, transverse colon). In

case of clinical suspicion of bile duct disease, endoscopic ultrasound or magnetic resonance imaging (MRI) including MR cholangiography are necessary [Figure 14].

Figure 12 Delineation of the extrahepatic bile duct (arrows) from the hepatic hilum (common hepatic duct, CHD), continuing to the extrahepatic part (common bile duct, CBD) down to the papilla (arrowheads) with the patient in a left lateral decubitus position (Duo: descending duodenum; GB: Gallbladder; PV: Portal vein).

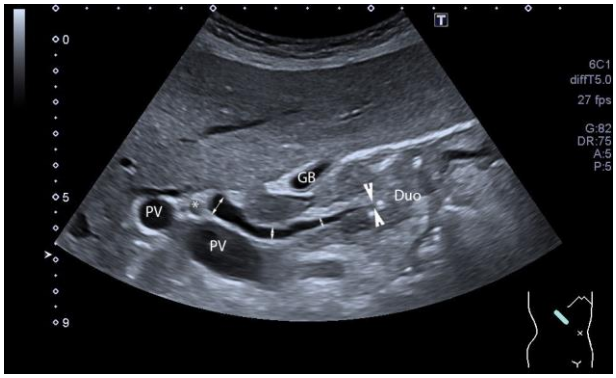


Figure 13 Visualisation of the common bile duct (CBD) and the main pancreatic duct (8) converging to the papilla (arrowhead; Duo: descending duodenum).

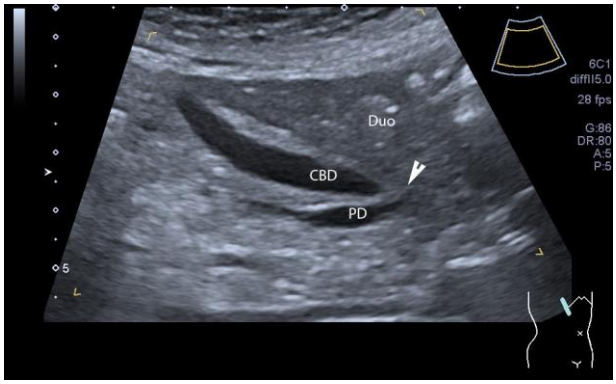
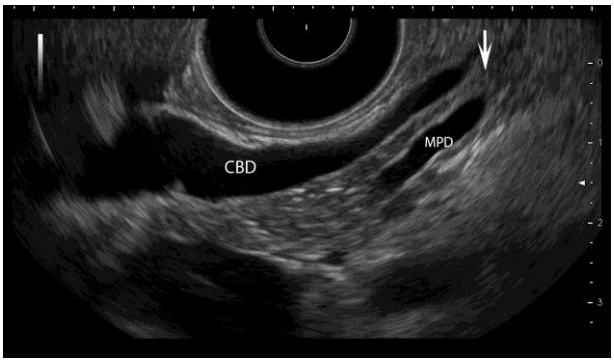


Figure 14 The reference standard for sonographic imaging of the extrahepatic bile duct is endoscopic ultrasound (CBD: common bile duct; MPD: main pancreatic duct; arrow: papilla)



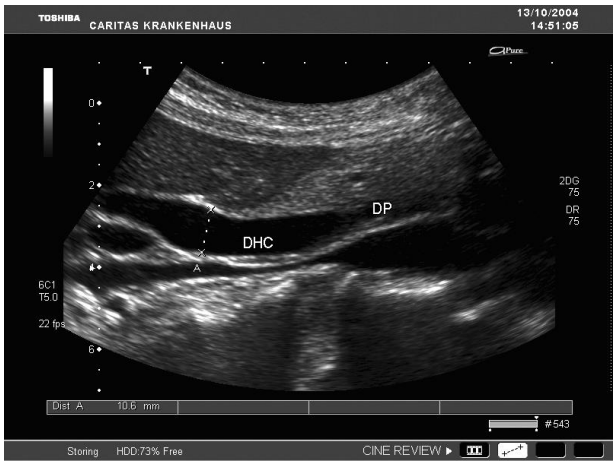
Frequently, the main bile duct is measured at the hepatic hilum, from inner wall to inner wall, in line with the axial resolution of the ultrasound beam to achieve greater accuracy. However, a single measurement of the bile duct at this level can be misleading, as the bile duct (common hepatic duct) may be normal at this point and be distended lower down (common ibile duct) in early obstructive jaundice; it is therefore recommended that the duct be imaged along the entire length and measured at several points, including near to the head of pancreas. The duct should be evaluated for size and any variants in its shape, wall thickness and any contents in the lumen. The normal bile duct dimensions are given in table 2 [(9, 10)].

Table 2 Normal variation of the diameter of the bile ducts.

Level	**Normal diameter**
Intrahepatic bile ducts	≤ 1 mm (lumen not visible)
Right and left hepatic duct	3 mm
Common hepatic duct anterior to hepatic artery	4 – 5 mm
Common bile duct (with gallbladder in situ)	6 - 7 mm
Common bile duct post cholecystectomy	≤ 8 – 10 mm, large variation of diameters, diameter increases with time after cholecystectomy

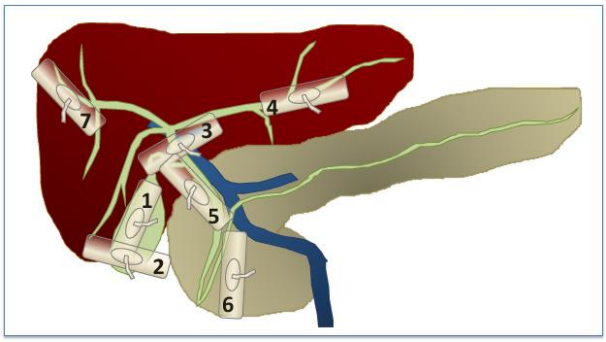
The diameter of the main bile duct typically becomes wider after eating, due to the expulsion of bile from the gallbladder, which transits to the duodenum. Slight dilatation of the MBD may be also observed in patients with a juxtapapillary duodenal diverticulum.
Additionally, the duct typically increases in size by 1 mm per decade over the age of 60 years and post-cholecystectomy [(11)]. Figure 15 shows a mildly distended main bile duct, and it is essential for the operator to assess the cause of the distension and to determine whether it is pathological or simply increased with age or post cholecystectomy. The left lateral decubitus position is helpful for adequate visualisation of the liver hilum [(12-14)] and should be performed consistently in all patients.

Figure 15 Slightly dilated MBD (10.6 mm, labelled as Ductus hepatocholedochus, DHC). next to the duodenal papilla (DP: Pancreatic duct) in a patient several years after cholecystectomy.



Imaging the intra-hepatic biliary tree is described in the liver chapter of this European course book [http://www.efsumb.org/ecb/ecb-ch02-ultrasoundliver.pdf]. Figure 16 gives an overview of the transducer positions for complete evaluation of the biliary tree.

Figure 16 Overview of transducer positions for complete evaluation of the biliary tree



Diagnostic criteria

An acronym has shown to be didactically helpful ["SSOTM"] when thinking about interpreting ultrasound images: Table 3.

Table 3 SSOTM algorithm to describe gallbladder

S	Size	The size of the gallbladder should be subjectively assessed. In a fasted state it should measure 10 x 2-4 x 2-4 cm, but this depends on the volume of bile present. Typical bile volume is normally 40 - 60 ml, measured by a rotating ellipsoid). However, gallbladder volume estimation is highly unreliable as it shows a wide intra and inter operator variability [(5, 6)].
S	Shape	The gallbladder is a saccular structure which has a pear or teardrop shape in long axis cross section when distended.
O	Outline	The normal gallbladder wall is very thin, smooth and mildly echogenic. Normal thickness is cited as measuring =/<3 mm in the fasted state [(figure 4)]. However, wall thickness is dependent on gallbladder distension, being thinner when distended, with pseudothickening due to lack of distension in the post-prandial state. There is no peri-cholic fluid around the normal gallbladder.
T	Texture	The normal gallbladder lumen contains bile and should not have any space occupying lesions [Figures 1, 3-5]. Normal bile appears anechoic (i.e. is completely black) and devoid of any internal echoes. However, slice-thickness and bow artifacts may mimic intraluminal structures [(15)]
M	Measurement	Measurements of the length/AP/transverse diameters and volume of the

		gallbladder are notoriously inaccurate as they depend upon the degree of gallbladder distension. Additionally, it is not possible to repeatedly freeze the same plane of the gallbladder to measure and there are no reproducible end-points for positioning of calipers. Consequently, the intra and inter-operator repeatability are poor and should be treated with caution for diagnostic interpretation.

Moreover, a systematic approach to ultrasound examination of the biliary system is required [(16)] [Table 4] [(16)].

Table 4 Standardised description of findings of the biliary system

Organ/ Finding	**Description**
1. Gallbladder	
Specific features	History of cholecystectomy, contraction state, tenderness on palpation
Dimensions	Two levels: longitudinal and transverse, compressibility
Content	Stones (maximum diameter, shadowing, floating, number: solitary, several, multiple), gas, sludge, mass
Wall pathology	Diffuse: (maximum) wall thickness, layering/ oedema, intramural findings (cysts, varices, echogenic spots), comet tail artifacts, vascularity Focal (e.g. defect, thickening, mass lesion, gas, calcification) : size, shape, echogenicity, cross of outer contour, comet tail artifacts, shadowing, vascularity
Perivesical findings	Free fluid, delimited fluid collections (size)
2. Bile ducts	
Dimensions	Intrahepatic: non-dilated/ dilated (“double-barrelled shotgun-sign“): maximum diameter (left and right liver lobe). Extrahepatic: maximum diameter, compressibility, sudden changes of diameter, level of dilatation
Content	Stones (maximum diameter, shadowing, number: solitary, several, multiple), other echogenic content, gas (aerobilia), mass lesion

Wall pathology	Diffuse: (maximum) wall thickness, echogenicity, (vascularity) Focal: site, shape, echogenicity, cross of outer contour, reverberating reflexes, shadowing, (vascularity)
3.Other related findings	
Main pancreatic duct	Non-dilated/ dilated (maximum diameter), pathological content (description)
Pancreatic parenchyma	Mass lesions (cystic, solid): size, location, relation to bile duct Oedema, peripancreatic fluid collections
Liver	Focal mass lesions related to intrahepatic ducts, abscess

Ultrasound has become widely accepted for the diagnosis of biliary system disease [(16)]. Typical examples of its use include (but not restricted to) are summarised in table 5.

Table 5 Definitions on hepatobiliary structures and terms and their explanations.

Definition	Explanation
Abdominal quadrant pain	Often right upper quadrant.
Aerobilia/ aerocholia	Echogenic reflexes with shadowing and/ or reverberations within bile ducts (aerobilia) or gallbladder (aerocholia), caused by gas with the biliary tree (e.g. following biliodigestive anastomosis or biliary sphincterotomy or stenting)
Cholelithiasis	Calculus disease of the biliary tree.
Cholecystolithiasis	Calculus/i within the gallbladder.
Choledochocystolithiasis	Calculus/i within the intra/extrahepatic biliary tree
Acute/chronic cholecystitis	Wide spectra of disease may be seen
Gallbladder carcinomas	Only usually detected by ultrasound at a late stage, often when the liver is already infiltrated by metastatic spread. This is a consequence of the disease presenting in older age with few early symptoms. In recent years, ultrasound contrast agents have proven to be useful for clarification of suspected biliary tumours.
Gallbladder polyps	Typically, easily demonstrated using B-mode ultrasound, > 95% are cholesterol polyps (no neoplasia).
Jaundice	Obstructive vs non-obstructive disease. Site and extent of dilatation of bile ducts in obstructive disease. Clarifying the aetiology of bile

	duct dilatation can be difficult using ultrasound. Careful evaluation of the clinical presentation, together with the level and extent of bile duct obstruction can assist in determining the cause using ultrasound.

Thickening of the gallbladder wall

Diffuse gallbladder wall thickening can be a diagnostic problem, as it occurs in symptomatic and asymptomatic patients. It can occur in patients who do not have primary gallbladder disease, but those where the gallbladder is secondarily involved in an extrinsic pathological condition. Examples include: liver cirrhosis, acute and chronic hepatitis, sinusoidal obstruction syndrome, hypalbuminemia and pancreatitis. In this condition, gallbladder wall thickening is often caused by congestion and oedema. In portal hypertension, gallbladder varices may be the reason for wall thickening.

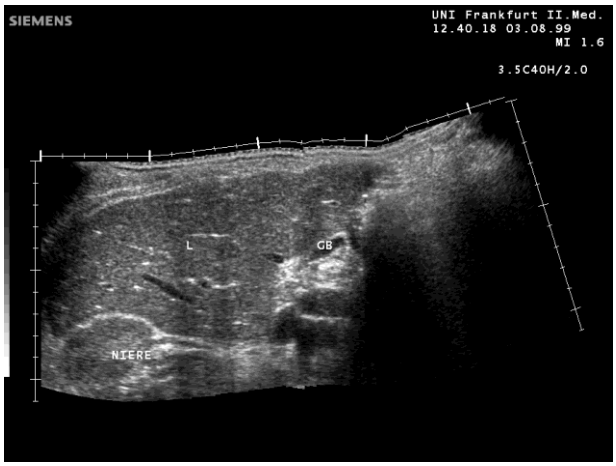
Congenital Anomalies of the Gallbladder

Congenital anomalies are rare in adults and can often also affect the bile ducts and local vasculature that can be difficult to assess using ultrasound. There is a wide variety of such abnormalities and they are more predominant in the paediatric setting. If congenital abnormalities are found during routine ultrasound examination, the findings should be highlighted in the clinical context of being mainly without consequences to patient management.

Agenesis, hypoplasia and microgallbladder

Agenesis (absence) of the gallbladder is rare and is normally without any clinical significance. About 50 % of gallbladder agenesis cases are discovered at autopsy and it is often associated with duodenal atresia and other congenital anomalies. Hypoplasia is associated with extrahepatic biliary atresia. Microgallbladder is defined as less than 2 - 3 cm long, 0.5 - 1.5 cm wide and regarded as a typical finding of cystic fibrosis; but, is also associated with idiopathic neonatal hepatitis and alpha-1-antitrypsin disease [(17)] [Figure 17].

Figure 17 Panoramic ultrasound image showing a microgallbladder; a congenital anomaly in a patient with cystic fibrosis. Microgallbladder is one of the typical findings in these patients. GB: Gallbladder. Niere = kidney [(17)].



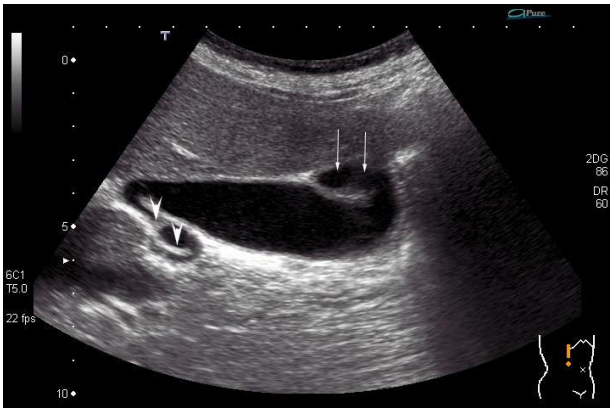
Abnormal position of the gallbladder

Abnormal positions of the gallbladder are rare. Left sided (with or without situs inversus), intrahepatic (< 5 %), suprahepatic, lesser sac or abdominal wall and retroperitoneal sites have been described. However, it should be remembered that there are normal variants with the four body habitus defined earlier in this chapter.

Other anomalies of the gallbladder

Variations of the gallbladder shape are more frequently encountered but are rarely of any clinical importance, for example the “Phrygian cap“ [Figure 18] [(18-22)]. Phrygian cap is an inversion of the distal fundus into the body, to which it may become adherent. It is either an anatomical variant or an acquired abnormality and is present in up to 5% of sonograms. Gallbladder diverticula and volvulus are also very rare [(8)].

Figure 18 Phrygian cap (arrows), which is a variation of the shape of the gallbladder. Note also the echogenic structures of the spiralic Heister`s valve in the gallbladder infundibulum (arrowheads).



Congenital anomalies of the gallbladder include duplication (2 gallbladders), bilobed gallbladder due to transverse (more common) or longitudinal septum and hypoplastic narrowing of biliary channels (true biliary atresia). Multiseptate gallbladder may be congenital or acquired and reveals three or more communicating compartments lined by columnar epithelium. In adults, cholecystolithiasis is often present. Heterotopia of the gallbladder, typically an incidentally finding, is also called ectopia or choristoma and is defined by normal tissue in an abnormal location. Liver parenchymal, pancreatic or gastric heterotopia have also been observed with ultrasound. An “hourglass gallbladder” is divided by a central constriction and is regarded as a variant of transverse septated gallbladder. Pathogenetically, “hourglass gallbladder” is usually acquired due to septum of inflamed fibrous tissue or adenomyomatous hyperplasia. Aberrant bile ducts (ducts of Lushka) are rarely identified by ultrasound, but are present in 10% of cholecystectomy specimens. They can be buried in the gallbladder wall and may communicate with intrahepatic bile ducts, larger accessory bile ducts or join with the cystic duct. Solitary congenital diverticula have a wide range of sizes (from 5 mm up to 10 cm), presenting all 3 layers of gallbladder wall.

Wandering gallbladder is caused by a long mesentery or no firm attachment to liver and is regarded at risk for torsion. The described findings are rarely encountered during routinely performed ultrasound but are important to know when it comes to a differential diagnosis.

Cholelithiasis

The term cholelithiasis describes the presence of calculi in the biliary tract. Depending on the location of the concrement, a further distinction between cholecystolithiasis (calculi in gallbladder) [Figures 19-20] and choledocholithiasis (calculi in bile duct) is used. In 5 - 15% of patients, a combination of both conditions has to be expected.

Figure 19 **Typical cholecystolithiasis on grey scale ultrasound. There is a large, isolated calculus in the gallbladder lumen. The gallbladder is otherwise normal in size and shape, with a thin wall. SS: acoustic shadowing which is typically seen deep to a calculus due to reflection of the ultrasound beam back towards the transducer from the proximal surface of the calculus, with resultant lack of echoes deep to the calculus.**

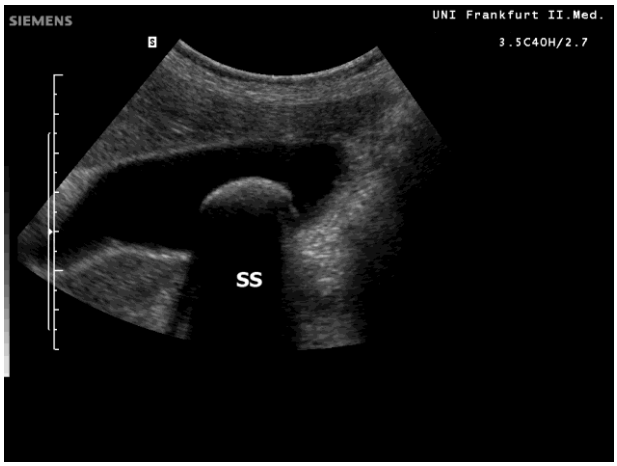
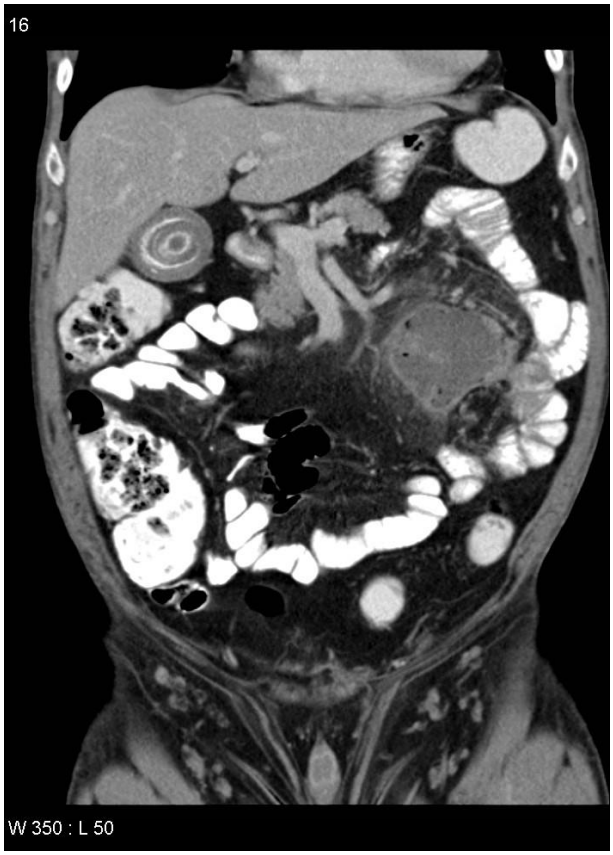


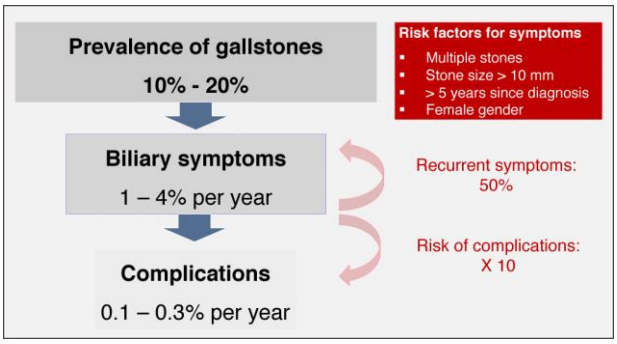
Figure 20 Cholecystolithiasis. The image shows cholecystolithiasis by computed tomography (please note the layering of the stone. Due to complete reflexion at the surface, regularly layering is not visible with ultrasound) [courtesy Dr. Baum, Bad Mergentheim].



Aetiology

Cholecystolithiasis is the most frequent disease of the biliary system. There are many risk factors for gallbladder calculi including: increasing age, female gender, obesity, ethnicity, family history and genetic predisposition. It is estimated that >10% of the adult European population have gallbladder stones. In females over 70 years of age cholecystolithiasis has a frequency of over 30% [(3)]. It is reported that 35% of the patients with gallstones will subsequently become symptomatic, requiring surgery [(23)] [Figure 21]. The increasing incidence of adult and childhood obesity is likely to increase the future incidence of gallstones, increasing the economic burden on healthcare provision.

Figure 21 Prevalence of gallstone disease and related complications



Role of Ultrasound

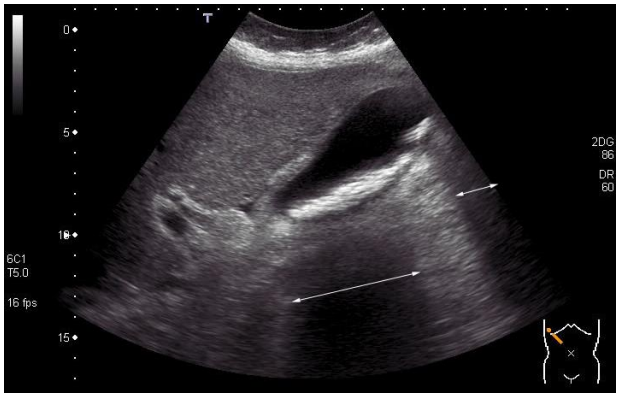
Cholecystolithiasis can be detected by transabdominal ultrasound with high sensitivity [(4)], whereas choledocholithiasis especially in undilated ducts is more difficult to detect [(24, 25)]. Many gallbladder calculi are asymptomatic and are only detected incidentally when scanning for other reasons. The literature has been recently summarized [(26)] and transabdominal ultrasound is the first line imaging method of choice for diagnosis of gallbladder stones. The accuracy of ultrasonography for the diagnosis of gallstones is up to 96 % for an experienced operator [(16)]. Ultrasound has the additional benefit of not using ionizing radiation and is relatively cheap and safe.

Ultrasound appearances of gallbladder calculi

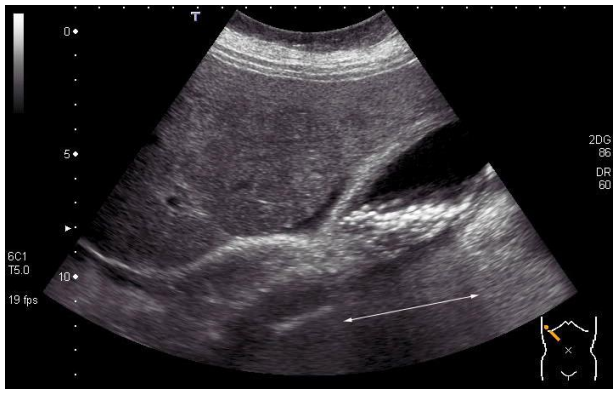
The number, size, echo texture, acoustic shadowing and mobility of gallbladder stones should be analyzed and recorded. The classical ultrasound appearance of the gallbladder stone is a hyperechoic/echogenic structure located within the gallbladder lumen with distal acoustic shadowing [Figure 19]. Mobile calculi typically lie on the dependent wall of the gallbladder under the influence of gravity, but this is related to the density of bile and the composition of calculi. To optimise acoustic shadowing and detection of small calculi, it is essential to insonate the dependent wall of the gallbladder at 90 degrees and to use different patient positions. A multitude of very small stones may cause a “sum shadow” [Figure 22].

Figure 22 "Sum shadows" (marked with double-head arrows) caused by a multitude of very small stones, which appear as one large stone echo at the first glance (a), but may be differentiated by slight change of the scanning angle (b). Note a small amount of free fluid between the echogenic liver and the gallbladder (with thickened wall).

a



b



To date, sonographically determined diagnosis of stone composition is not possible. Non-calcified cholesterin/cholesterol derived stones typically do not show acoustic shadowing [Figures 23] and may "float" in the gallbladder lumen in contrast to calcified stones. Usually, gallstones demonstrate mobility in response to movement of the patient, (the "rolling stone" sign) [Figure 24]. However, some gallstones become adherent to the gallbladder wall and do not move when the patient is moved. Differentials include polyps and neoplasm. Sensitive Doppler (usually power Doppler rather than colour flow imaging) and contrast-enhanced ultrasound can be used to exclude flow in adherent stones, as opposed to the

'stalk-like vessel' often seen feeding true solid lesions. However, gallbladder stones may cause a "twinkling phenomenon" with Doppler techniques [Figure 25].

Figure 23 **Small "soft" gallbladder stone (between calipers: 3.4 mm) without acoustic shadow (cholesterol based stones without any calcium component). To differentiate these small stones from small gallbladder polyps, it is important to move the patient to assess mobility of these stones**

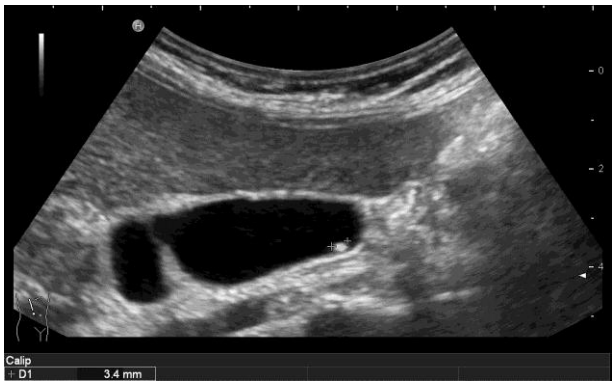


Figure 24 **The "rolling stones sign": changing patients position results in movement of small stones with the gallbladder, facilitating differentiation from gallbladder polyps.**

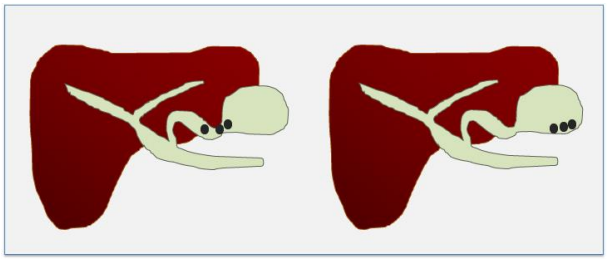
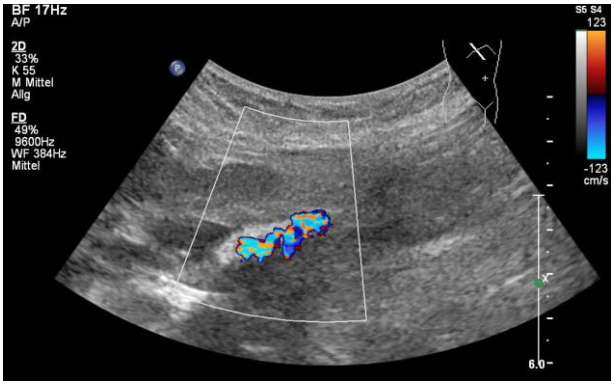


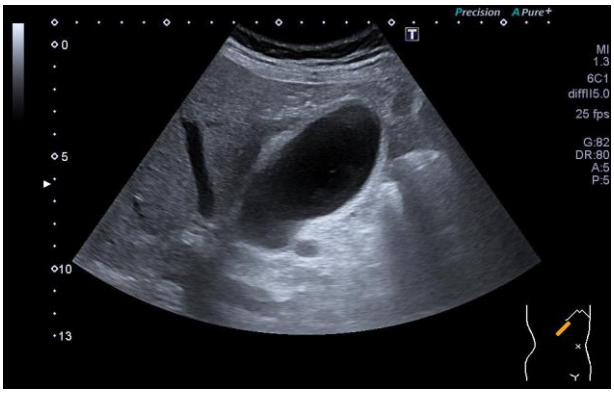
Figure 25 Twinkling caused by colour Doppler imaging of gallbladder stones. Note the high pulse repetition frequency.



So called pigment stones, rarely found in Europe (< 10 %), often are multiple with dense acoustic shadowing [(24)]. Very small stones (2-3 mm) may be overlooked, but the operator can optimize their detection by ensuring that they scan with the ultrasound beam perpendicular to the dependent wall of the gallbladder, with use of highest frequency and best use of focusing controls to enhance likelihood of generating an acoustic shadow from small stones. Additionally, routine use of the left lateral decubitus and standing position for all ultrasound examinations of the gallbladder improves the detection rate to almost 100% for an experienced operator. Use of high quality ultrasound systems, with improved resolution can also increase detection of small calculi. In cases with a high clinical suspicion of gallstone disease and negative findings in abdominal ultrasound endoscopic ultrasound should be used to detect very small stones (1-3 mm, microlithiasis) of the gallbladder [Figures 26 - 27].

Figure 26 Microlithiasis of the gallbladder detected by endoscopic ultrasound: In a patient with right upper quadrant pain transabdominal ultrasound shows a large gallbladder, visualisation of the infundibulum is poor, and no stones are visible (a). Longitudinal endoscopic ultrasound in the same patients reveals multiple very small stones (< 3 mm) in the gallbladder infundibulum (b).

a



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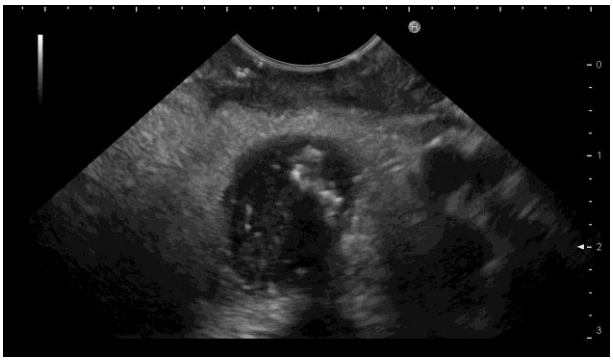
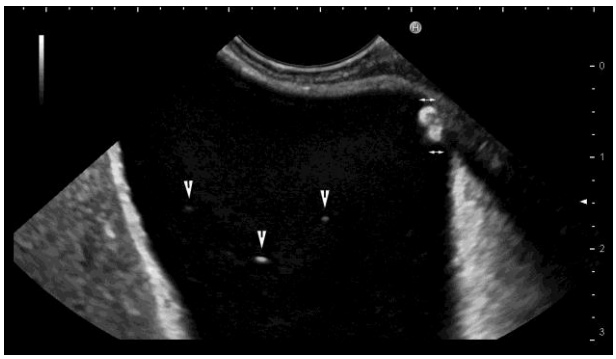
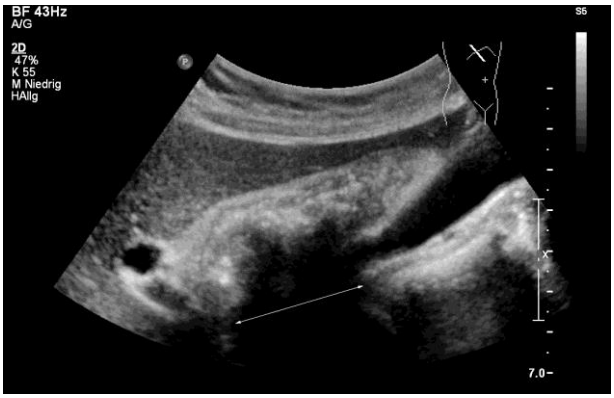


Figure 27 Another example of gallbladder microlithiasis, which was detected only using endoscopic ultrasound (two small stones of 2 mm diameter with shadowing marked with double-head arrows). Note the echogenic reflexes (diameter below 1 mm) without shadowing representing small agglomerates of cholesterol crystals (arrow heads) – a sign of lithogenic bile.



A gallbladder filled with stones (the “shell sign”) can be easily confused with gas in the GI tract, if the practitioner is not sufficiently experienced [Figure 28].

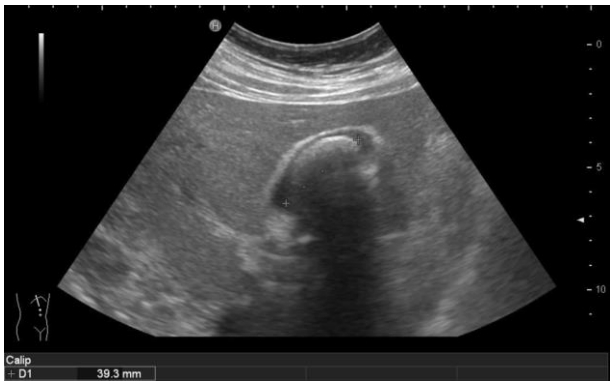
Figure 28 A gallbladder completely filled with stones (“shell sign”). Note the acoustic “sum shadow”.



To differentiate between the two, the transducer should be kept still over the region of interest to observe whether any peristalsis is evident, hence confirming bowel. Additionally, still water can be given to the patient orally to try to disrupt the appearances within the lumen if the structure is bowel. Occasionally, stones become impacted in the gallbladder infundibulum creating a hydrops. This is not always an easy diagnosis and stones can sometimes be missed as this region can be more difficult to visualise in some patients. Furthermore, the close anatomical relation to the gas containing GI tract can cause difficulties in imaging this region.

Size and number of gallbladder stones both are clinically relevant. In one recent study, multiple small stones (in women) were associated with a higher incidence of complications (mainly choledocholithiasis and biliary pancreatitis) than solitary larger stones (in men, mainly associated with acute cholecystitis) [(27)]. Very large gallbladder stones (> 30 mm) [Figure 29] are thought to be a risk factor for gallbladder cancer, and cholecystectomy is recommended also in asymptomatic patients [(16)].

Figure 29 Large gallbladder stone (between markers: 39 mm, note acoustic shadowing). Remaining fluid-filled gallbladder lumen is small. Gallbladder stones ≥ 30 mm are regarded a precancerous condition.



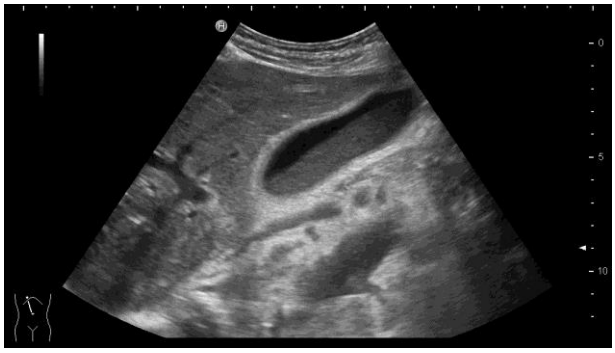
Biliary sludge

Biliary sludge represents a variety of precipitates formed from bile, which are most commonly calcium salts or cholesterol crystals. It has been associated with a number of conditions including: fasting, rapid weight loss, post solid organ transplantation etc. Various amounts of sludge have also been observed in fasting patients with or without motility disorders of the gallbladder. It is also often seen in intensive care unit patients (25 % – 47 %), total parenteral nutrition, stenosis in the extrahepatic bile duct and pregnancy [(23, 26)]. In most patient's, sludge is asymptomatic and is an incidental finding on ultrasound. Occasionally, patients can present with pain, nausea and vomiting. Sludge is sometimes the precursor of gallstones. More serious complications such as cholecystitis/pancreatitis have been reported.

The ultrasound appearance is of homogenous echogenic material in the gallbladder lumen, with no distal acoustic shadowing. It typically forms a straight horizontal line with the sludge normally collecting on the dependent wall of the gallbladder due to its density and gravity; the 'black'/anechoic bile without sludge lies above [Figure 30].

Figure 30 Shows a long axis (a) and short axis (b) section of a gallbladder containing dense, mobile echogenic sludge. Note there is no acoustic shadowing. There is a clear line delineating the boundary between the bile and the sludge, latter being more echogenic, hence settling to dependent wall of the gallbladder.

a



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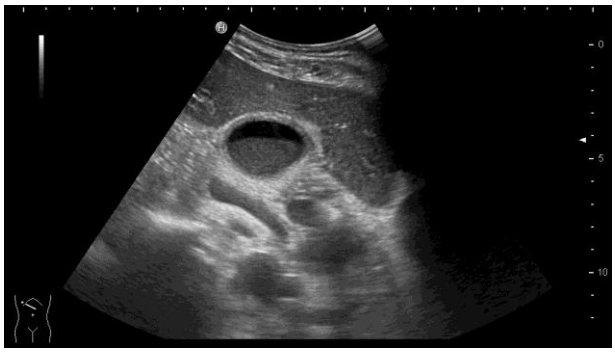
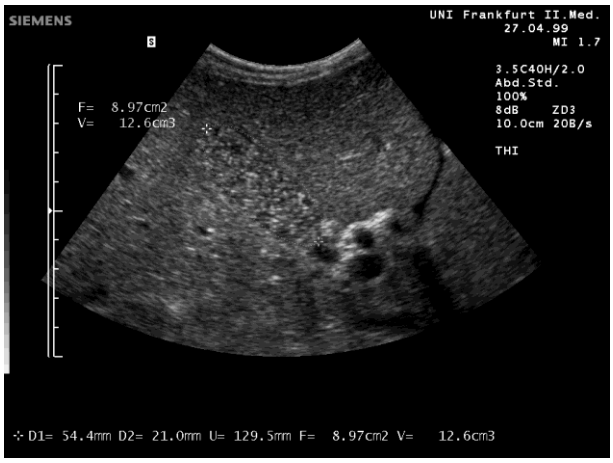


Sludge moves slowly with a change in patient position and it is recommended that the patient is moved during the scan to demonstrate this motion of the sludge. If the sludge completely fills the gallbladder, it may be difficult to distinguish from the adjacent liver parenchyma [Figures 31 - 32]. Sometimes the sludge is organized in a round shape, is hypoechoic, with no acoustic shadowing and is often called “ball like” or “tumour like” sludge. Occasionally, sludge becomes localized and can mimic a polyp [Figures 33 - 34].

Figure 31 Biliary Sludge, incidental finding. Gallbladder sludge completely filling the gallbladder lumen (GB), seen between the calipers. Small, punctate areas of

calcium can be seen and the structure is difficult to distinguish from the adjacent liver parenchyma (a, b).

a



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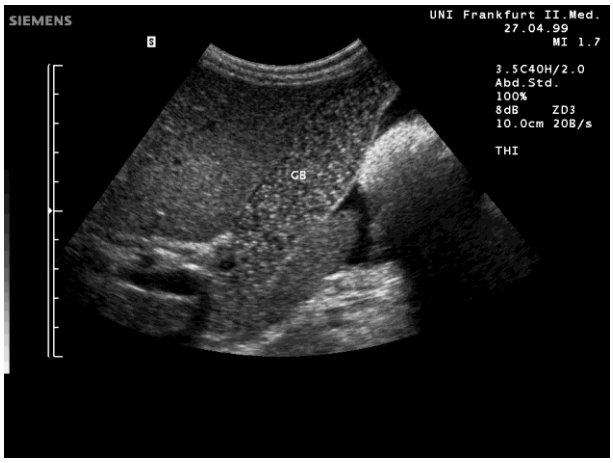


Figure 32 Another example of a gallbladder completely filled with sludge – there is almost no difference of echogenicity compared to adjacent liver parenchyma.

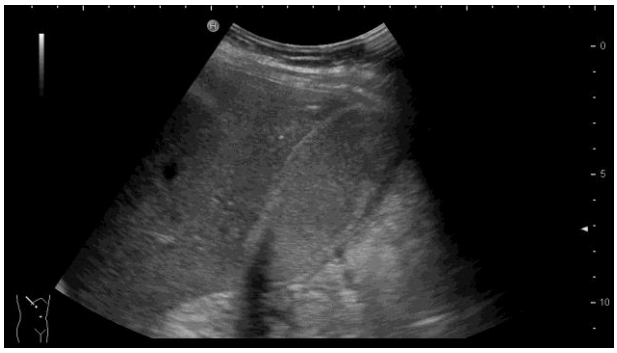
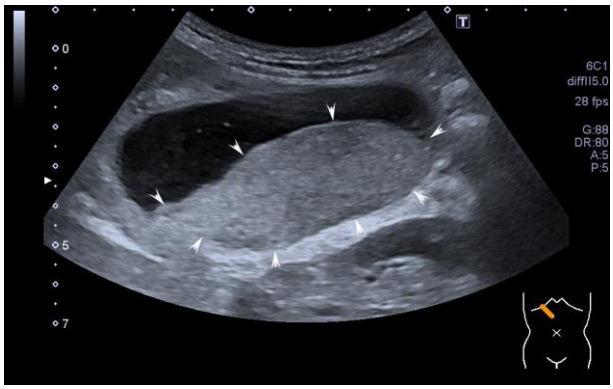


Figure 33 "Tumour like" sludge: A large, well-defined echogenic mass-like structure within the gallbladder lumen mimicking a large neoplastic lesion. To differentiate "tumour like" sludge from truly solid mass lesions, change patients position, cause pressure with the transducer or perform contrast-enhanced ultrasound.

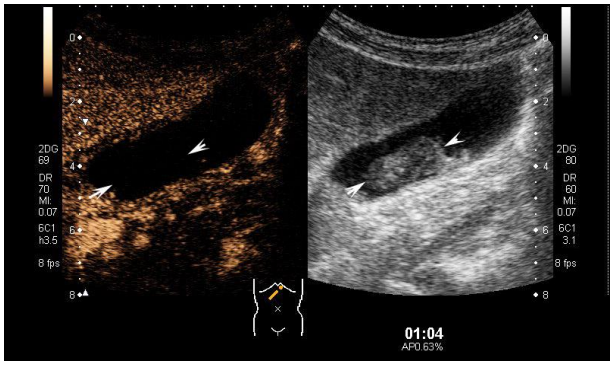


Differential diagnosis of sludge includes neoplasia, empyema and haemorrhage (clot). Contrast enhanced ultrasound is useful for the differentiation of localized and "tumour like" sludge from gallbladder neoplasia [Figure 34].

Figure 34 Differentiation of "tumour like" sludge and gallbladder polyps using contrast enhanced ultrasound: An echogenic polypoid structure within the gallbladder lumen (between arrow heads). Contrast-enhanced ultrasound shows lack of enhancement within the structure which therefore is diagnosed to be polypoid-

structured sludge (a). A very similar finding of an echogenic polypoid structure (16.5 mm x 7 mm; between arrow heads) was found in the gallbladder infundibulum of another patient (b). This lesion is demonstrated to be an enhancing solid polyp using contrast-enhanced ultrasound (c) and endoscopic ultrasound (d).

a



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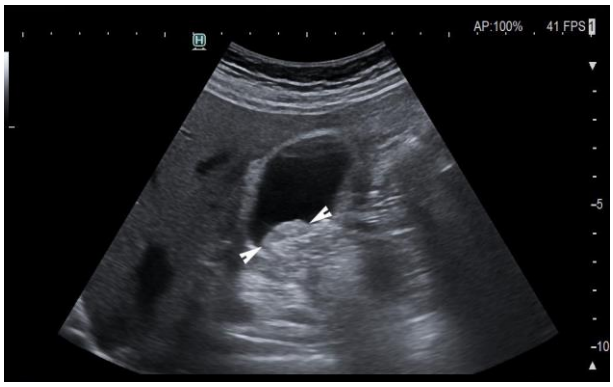
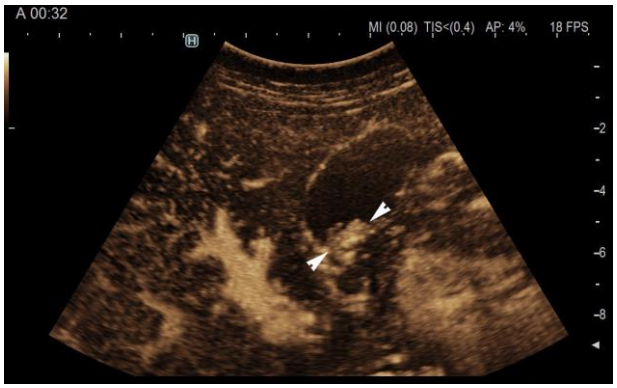
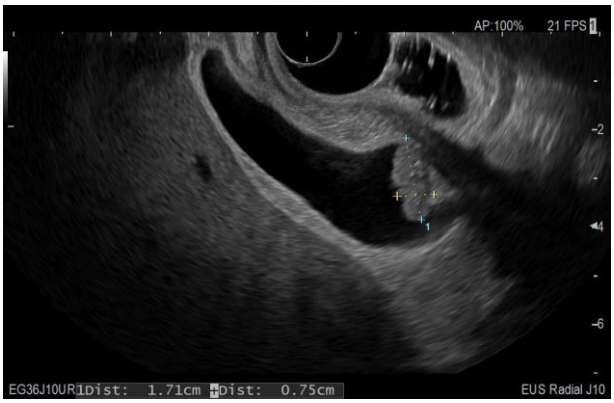


c



d



Cholecystitis

Cholecystitis is defined as inflammation of the gallbladder and is frequently classified as acute or chronic.

Acute cholecystitis

This is the most frequent complication of cholecystolithiasis and occurs in almost 1/3 of the patients with gallstones. Acute cholecystitis can be divided into either gallstone associated (acute calculous cholecystitis) or non-gallstone associated (acute acalculous cholecystitis). 95% of the cases are due to calculous obstruction of the gallbladder neck or cystic duct. 50% have bacterial infection (E. coli, Enterobacter, Enterococcus, Klebsiella, Clostridium, Peptostreptococcus, Bacteroides). More than 10% of affected gallbladders perforate without cholecystectomy.

Acute calculous cholecystitis

Sonographic appearances are of an enlarged, distended gallbladder with a thickened wall and evidence of gallbladder calculus. The thickened, multi-layered wall is a constant finding and is caused by oedema, haemorrhage, ulcers and pus [Figures 35 - 36].

Colour Doppler or contrast-enhanced imaging reveals hypervascularisation of the wall (“angry red colour”), which represents the typically pathoanatomically described congested vessels. Sometimes a hypoechoic inflammatory fluid collection is seen around the gallbladder (a hypoechoic “eye-brow”). Hyperechoicity of pericholic fat is also sometimes

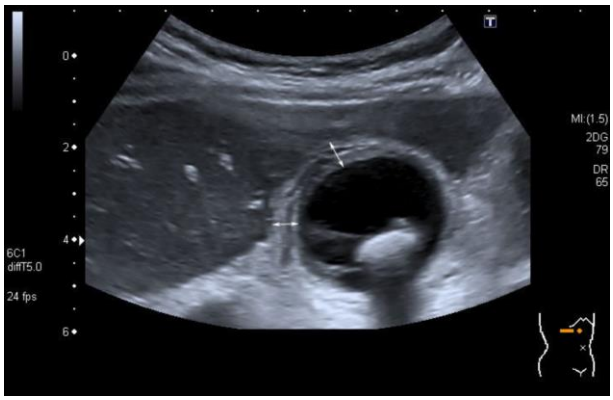
seen. The presence of gallstones on ultrasound examination combined with positive ultrasound Murphy's sign (pain elicited when pressure is applied using the ultrasound transducer over the inflamed gallbladder) has a positive predictive value of 92% for the diagnosis of acute cholecystitis [(28)].

Gangrenous cholecystitis occurs in 15% of acute cholecystitis cases with mural infarction, and with perforation in more than 25%. Typically, gas can be found in the gallbladder wall and sometimes in the gallbladder lumen (pneumobilia) [Figure 41]. Clostridium perfringes seems to be of pathophysiological importance.

In the majority of cases, gallbladder perforation occurs in the region of the hepatic surface, resulting in abscesses in the adjacent liver parenchyma [Figure 37].

Figure 35 Acute calculous cholecystitis. Gallbladder wall is thickened and layered caused by inflammatory oedema (a: transverse section; wall between markers). Longitudinal section (b) shows multiple stones, wall thickening (between markers) and small amounts of fluid between gallbladder wall and liver (arrowheads).

a



b

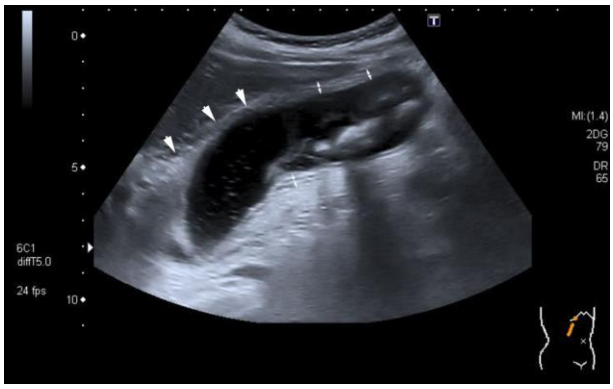
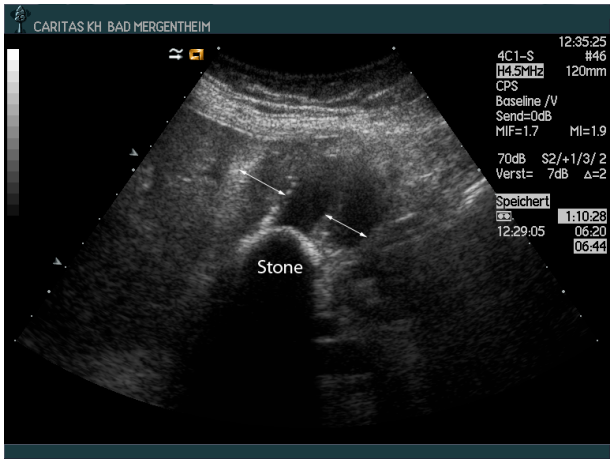


Figure 36 **Acute calculous cholecystitis. Cholecystitis might be confused with neoplasia using B-mode ultrasound. B-Mode image (a) demonstrates thickening of the wall of the gallbladder (marked with arrows) and presence of a calculous, with distal acoustic shadowing (stone), consistent with acute cholecystitis. Contrast enhanced ultrasound may be helpful for this differential diagnosis as shown in image (b), with better delineation of the thickened gallbladder wall.**

a



b

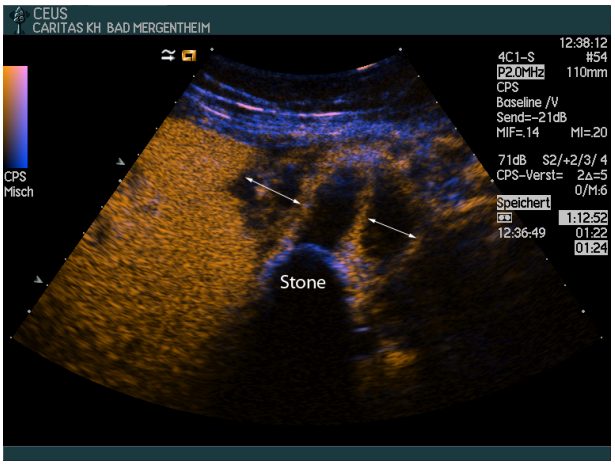
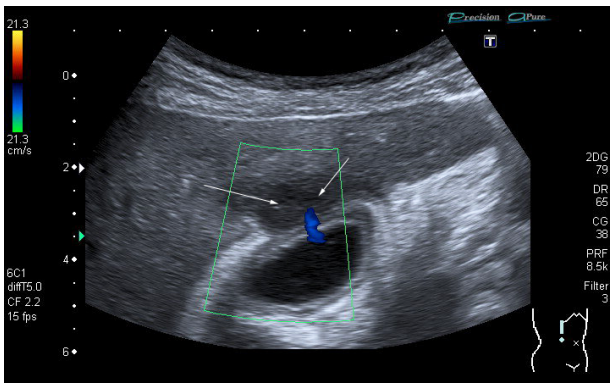
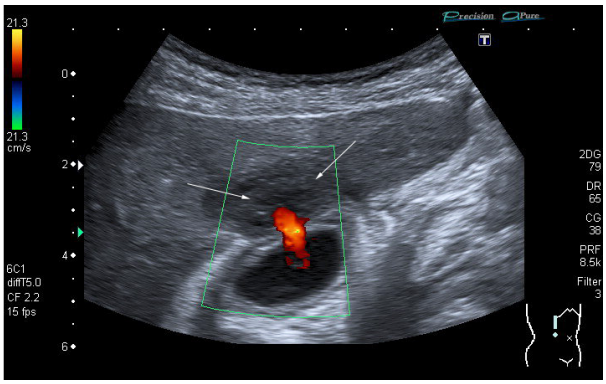


Figure 37 **Gallbladder perforation in acute cholecystitis: An ill-defined hypoechoic area is found in the liver parenchyma near the anterior gallbladder wall (arrows). Compression and decompression with the transducer shows flow signals between this liver abscess through the wall defect (caused by gall-bladder perforation into the liver) and gallbladder lumen (a: compression: flow from abscess into the gallbladder, coded blue; b: decompression: flow from the gallbladder into the liver abscess). Percutaneous aspiration of the liver abscess (c; arrowheads mark the course of the needle) and percutaneous drainage of the gallbladder were performed.**

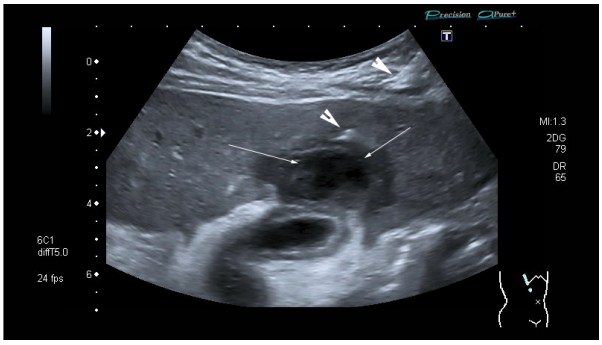
a



b



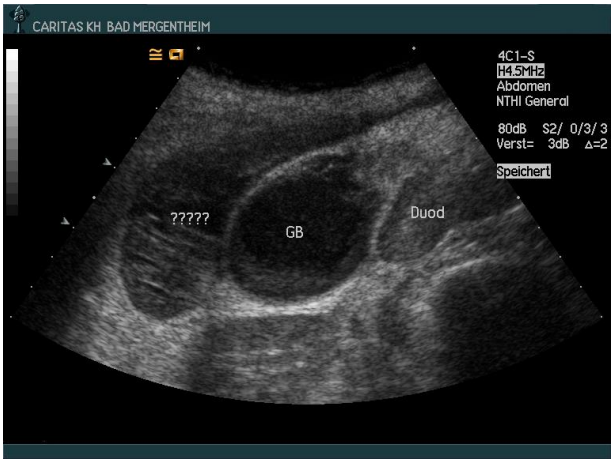
c



Acute acalculous cholecystitis

Acute acalculous cholecystitis represents only 5% - 10% of cases. Patients are usually severely debilitated, due to severe trauma, sepsis, shock, burns, cancer, diabetes, multiple blood transfusions, surgery or cystic duct obstruction from various causes. The mortality is extremely high (10 – 50%). A rare form of acute acalculous cholecystitis is cocaine related acute cholecystitis. The ultrasound appearances of acalculous cholecystitis are similar to those of the calculus form, with the obvious exclusion of presence of calculi in the gallbladder [Figure 38].

Figure 38 **Acute cholecystitis in a severely ill patient. Ultrasound can differentiate between either gallstone associated acute calculous cholecystitis or acute acalculous cholecystitis as shown in this case. (????? = free fluid. Duod: Duodenum. GB: gallbladder with some sludge evident).**



A very similar (transient) appearance of acute gallbladder wall oedema can be seen in patients with acute hepatitis in about 50% of patients [(29)] [Figure 39] as well as in patients with hypoalbuminemia [Figure 40].

Figure 39 **Acute Hepatitis. A similar (transient) appearance of gallbladder oedema resembling acute acalculous cholecystitis can be seen in patients with acute hepatitis. There is thickening of the gallbladder wall (oedema). LN: Lymph node. GB: Gallbladder lumen.**

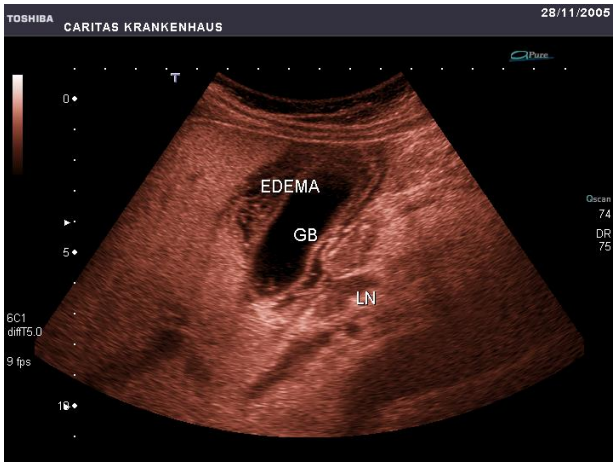
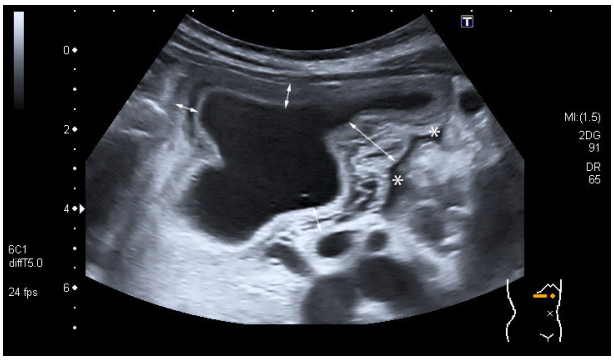


Figure 40 Gallbladder wall oedema in a patient with severe hypoalbuminemia in nephrotic syndrome (thickened gallbladder wall with oedema between double-headed arrows; * free fluid around the gallbladder)

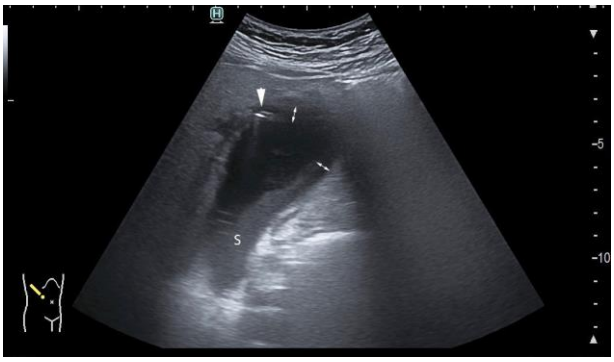


Emphysematous cholecystitis

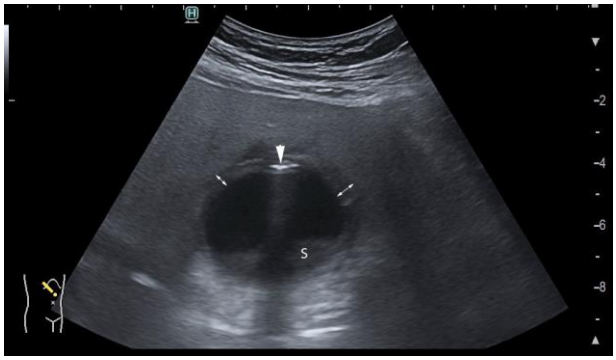
Emphysematous cholecystitis is a rare form of acute cholecystitis associated with diabetes and peripheral atherosclerotic disease. It typically results from infection of the gallbladder wall from gas forming organisms such as E-coli and Clostridium. Vascular compromise of the cystic artery has been described as the most important pathophysiological factor. Ultrasound reveals gas bubbles within the thickened gallbladder wall [Figure 41]. Gangrene and perforation are typical complications and mortality is high.

Figure 41 Emphysematous cholecystitis. Longitudinal (a) and traversal section (b) show an enlarged gallbladder containing sludge (S) with thickened wall (between markers) and an echogenic gas reflex with reverberation (arrow head).

a



b



Bouveret's syndrome

Gallbladder perforation due to a large stone (mostly > 25 mm) and stone passage into the bulb of the duodenum is called Bouveret's syndrome, which can easily be recognized with transabdominal ultrasound by identifying air bubbles from the duodenal bulb into the lumen of the gallbladder [Figure 42]. It is a rare condition, with a 0.3% incidence, associated with chronic cholelithiasis in 90% of the cases [(30)].

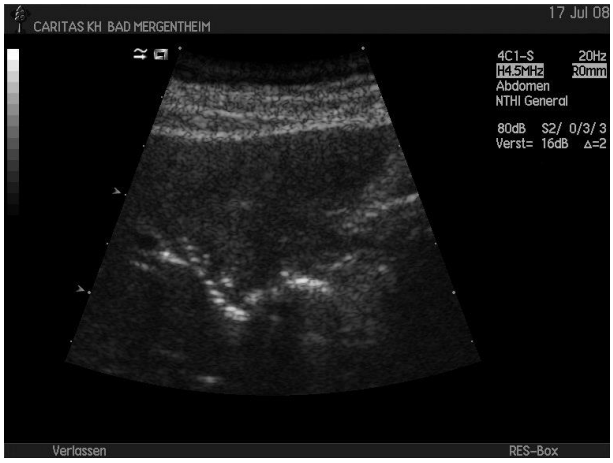
The first report of Bouveret's syndrome (1896) was published by Leon Bouveret who presented two patients with this disease [(31)]. Fistula formation is thought to occur as a result of adhesions between the gallbladder and the bowel wall due to chronic inflammation, impaired arterial blood supply and decreased venous drainage [(32)].

Secondarily, the stone lodges in the digestive tube, most commonly in the distal ileum (90%), colon (3-8%) or duodenum (3%) and rarely in the proximal duodenum or pylorus, causing gastric outlet obstruction (Bouveret's syndrome) [(33)]. Patients typically present with nausea, vomiting, epigastric pain and abdominal distension. Less commonly, they can present with haematemesis, weight loss and anorexia.

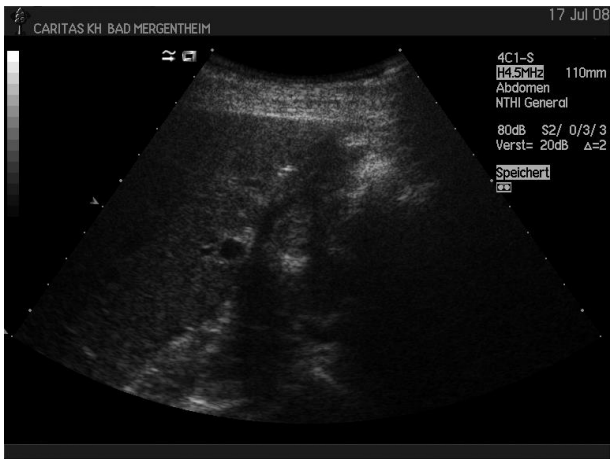
Abdominal ultrasound is a useful diagnostic tool because it will reveal aerobilia and gas bubbles in the gallbladder, and can frequently confirm presence of a stone in the duodenum. The diagnosis is completed by endoscopy [(34)]. In a review of 128 cases of Bouveret's syndrome, endoscopy revealed gastroduodenal obstruction in nearly all cases but identified the obstructing stone in only 69% of cases [(35)].

Figure 42 Bouveret's syndrome might be suspected in patients with unsuspected aerobilia. The syndrome is defined as gastric outlet obstruction caused by duodenal impaction of a large gallstone (white arrow) which passes into the duodenal bulb through a cholecystogastric or cholecystoduodenal fistula (a, b). Initial attempts at endoscopic retrieval, with or without mechanical or extracorporeal lithotripsy, should be performed as first-line treatment, though success rates with endoscopic treatment are variable.

a



b



Chronic cholecystitis

Aetiology

Chronic cholecystitis is typically associated with gallstones, with 95% of chronic cholecystitis cases associated with cholecystolithiasis or at least sludge. Other risk factors include, obesity, dietary factors, gallbladder activity/function and genetic predisposition. Repeated episodes of cholecystitis over time can result in a chronic inflammatory process of the gallbladder wall and it becomes thickened; consequently, the gallbladder fails to expand/contract properly and usually becomes small and shrunken.

Ultrasound Appearances

Chronic cholecystitis is sonographically characterised by an irregular thickened gallbladder wall, mainly caused by chronic inflammation and intermittent obstruction of gallbladder neck / cystic duct by gallstones, often causing biliary colic [Figures 43 - 44]. The gallbladder is frequently small and contracted, with a thickened wall due to fibrosis and often low-grade inflammation. Sometimes this condition may be misinterpreted as a bowel segment filled with gas and stool [Figure 45]. A pseudosolid appearance of the gallbladder may result in case of chronic cholecystitis with sludge-filled lumen [Figure 46].

Figure 43 Chronic calculous cholecystitis: note the thickened wall (between markers: 7.2 mm): no pain is caused by palpation.

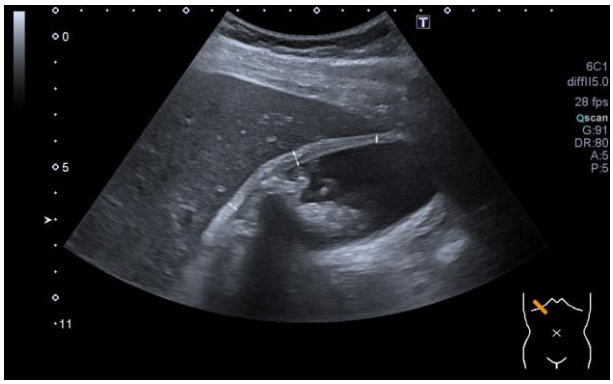


Figure 44 Chronic calculous cholecystitis: impressive thickening of the gallbladder wall (between markers: 7.7 mm). In this case differential diagnosis to gallbladder carcinoma is not possible.

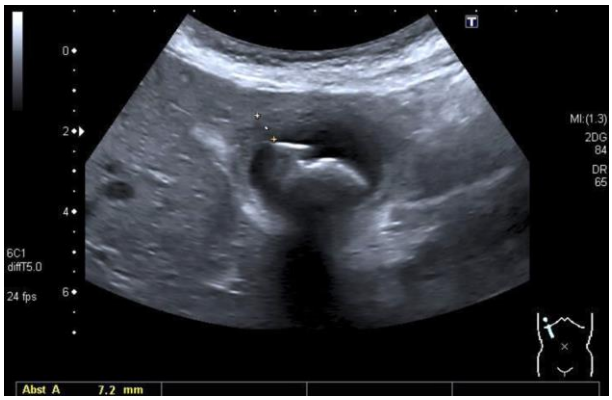
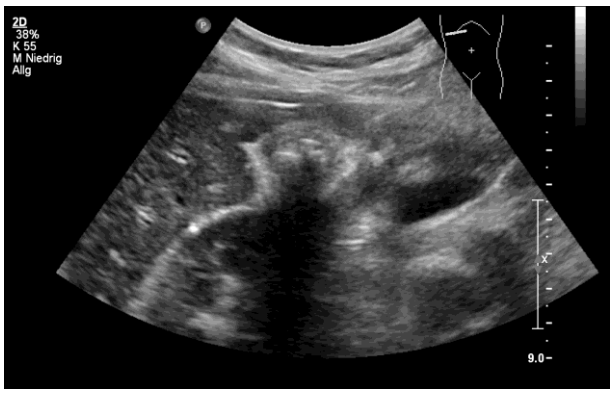


Figure 45 Chronic calculous cholecystitis without fluid-filled lumen: confusion with bowel is possible.

a



b

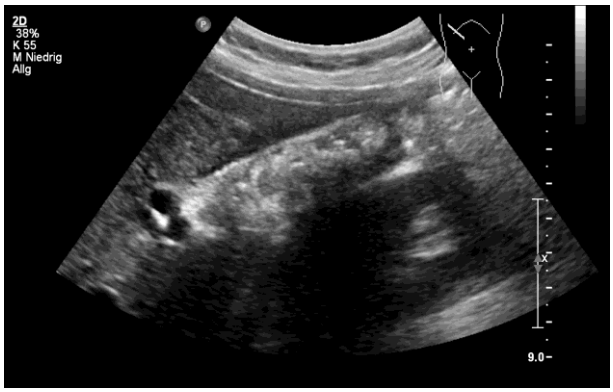
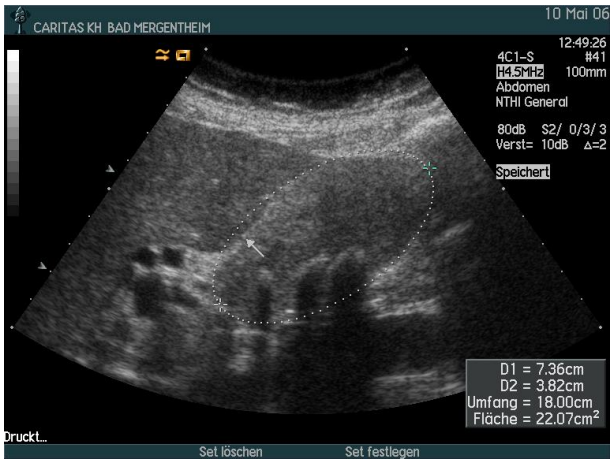
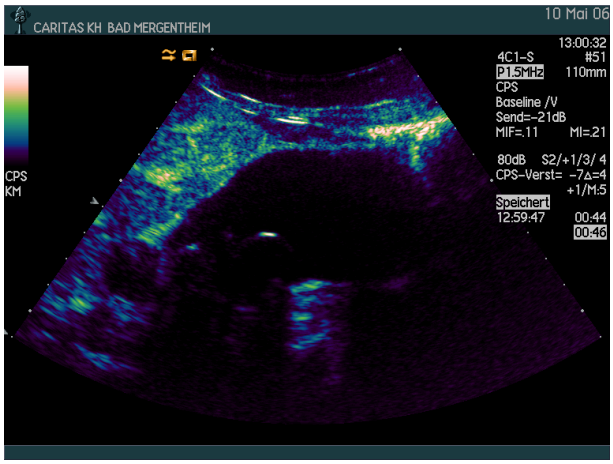


Figure 46 **Chronic cholecystitis: Sometimes a sludge filled gallbladder may present as a tumour like lesion using B-mode (white arrow) (a). The gallbladder is outlined using the on-screen calipers. Contrast enhanced ultrasound is helpful for the correct diagnosis (b).**

a



b

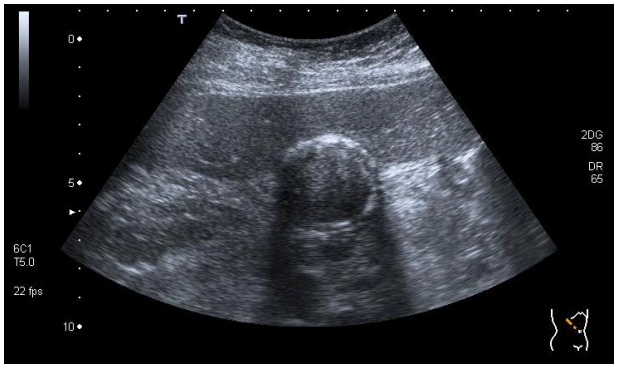


Additional types of Chronic Cholecystitis

There are many different forms of chronic cholecystitis that cannot be differentiated by ultrasound. “Diffuse lymphoplasmacytic acalculous cholecystitis” is a relatively sensitive sign for primary sclerosing cholangitis. An association with lymphoplasmacytic sclerosing pancreatitis has also been described. Other forms are AIDS related. Acalculous cholecystitis can be caused by opportunistic infections such as cryptosporidia, CMV and microsporidia. Eosinophilic cholecystitis is seen in Churg-Strauss syndrome. Another very rare type of acalculous cholecystitis is follicular cholecystitis (also called lymphoid polyp), which has been described in patients with typhoid fever. Other rare forms of cholecystitis include: granulomatous cholecystitis in patients with tuberculosis and xanthogranulomatous cholecystitis (due to rupture of Rokitansky-Aschoff sinuses with extravasation of bile or ulceration of gallbladder mucosa).

Porcelain gallbladder [Figure 47] is found in 0.5% of cholecystectomies. The association (> 20 %) with gallbladder carcinoma is well known [(26)]. Therefore, cholecystectomy is indicated when a porcelain gallbladder is diagnosed on ultrasound. Sonographically, the calcified wall can easily be detected. It is characterized by intramural shell-like calcification that may affect the entire wall or parts of it.

Figure 47 Porcelain gallbladder: circumferential echogenic calcifications of the gallbladder wall with shadowing.



“Limy bile”, in which there is a pathological accumulation of calcium carbonate in the gallbladder, is a very rare condition. The diagnosis is made on a plain abdominal X-ray, where the gallbladder is showed as an opaque pear shape structure.

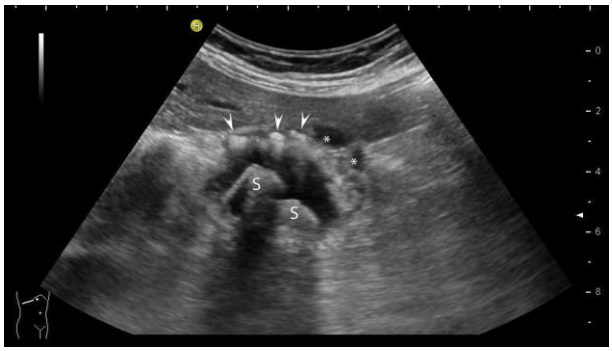
Miscellaneous non-neoplastic disorders

Adenomyoma and adenomyomatous hyperplasia

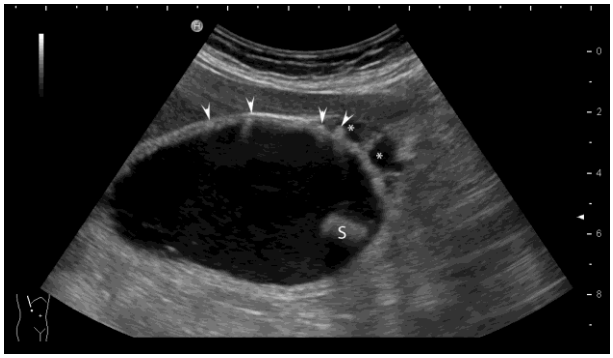
Adenomyoma and adenomyomatous hyperplasia are rare tumor-like benign lesions of the hepatobiliary and gastrointestinal tract, with most cases described in the gallbladder. They can present with a diverse range of symptoms including abdominal epigastric/ right upper quadrant pain, jaundice, cholestasis, cholangitis, abnormal biochemistry etc. However, the majority are detected as incidental findings when scanning for other conditions. Gallbladder adenomyomatosis is characterised by hyperplasia of all wall layers, resulting in gallbladder wall thickening and epithelial infolding within the underlying muscular layer (“acquired herniations”). These epithelium-lined pseudo-diverticular pouches are called Rokitansky-Aschoff sinuses and are found in 1% - 9% of cholecystectomies. They may show progressive occlusion of the communication with the gallbladder leading to cysts. Dehydratation of bile fluid within Rokitansky-Aschoff sinuses leads to precipitation of cholesterin crystals (cholesterolosis). Association with gallbladder stones and chronic cholecystitis is common. In abdominal ultrasound, adenomyomatosis of the gallbladder represents as focal (predominantly in the gastric fundus), segmental, or rarely diffuse wall thickening with small cystic intramural spaces and intramural echogenic reflexes with reverberation (cholesterolosis) or shadowing (calcification) [Figures 48 - 49]. Differential diagnosis to chronic cholecystitis and gallbladder cancer may be difficult [(36)].

Figure 48 Segmental adenomyomatosis of the gallbladder wall. Short axis (a) and long axis (b, c) sections of the gallbladder in the fundal region show segmental thickening of the wall with intramual echogenic reflexes with comet tail artefact (arrow heads), intramural cysts (Rokitansky-Aschoff sinuses, *) and gallbladder stones (S). The echogenic intramural cholesterol plugs cause an impressive “twinkling phenomenon” with Colour Doppler ultrasound (c) [(37)].

a



b



c

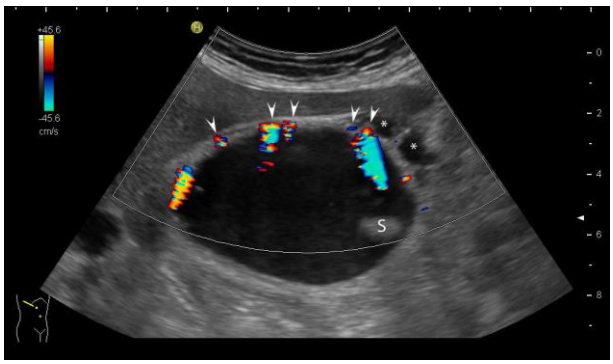
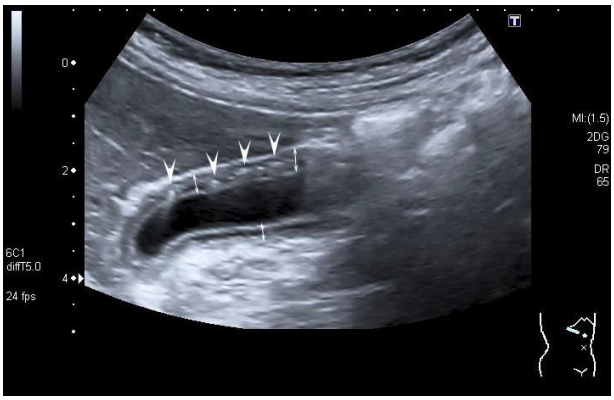
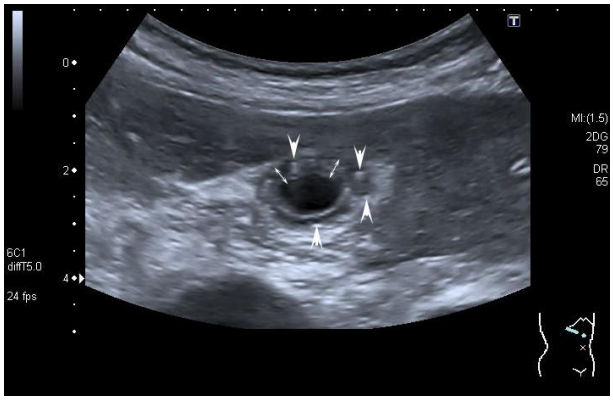


Figure 49 Diffuse adenomyomatosis of the gallbladder without gallbladder stones (long axis section, a and short axis section, b): Gallbladder wall is thickened in all segments and has a regular outline (between markers). A very small intramural anechoic (cystic) layer contains echogenic cholesterol plugs (Arrowheads; Please note the associated comet tail artefacts).

a



b



Asymptomatic cholesterolosis is mostly characterized by cholesterol infiltration (sonographically shown as comet tail artefacts) in an otherwise normal gallbladder wall [Figures 50 - 51]. Cholesterolosis is present in up to 20 % of cholecystectomy specimens, usually found in adult multiparous women. Cholesterolosis is associated with bile supersaturation with cholesterol, but not with increased serum cholesterol. Cholesterol infiltration is due to accumulation of cholesterol esters and triglycerides in subepithelial macrophages and gallbladder epithelium. Macroscopically focal or diffuse yellow, flat deposits are seen on mucosal surface which may have speckled appearance (“strawberry gallbladder”). Association with cholesterol polyps is reported in 20% of cases. A similar (unspecific) irregular gallbladder wall can be seen in amyloidosis [Figure 52] [(38)].

Figure 50 **Cholesterolosis of gallbladder wall: three echogenic reflexes within the gallbladder wall (arrowheads; approximately 1 mm diameter) cause echogenic fir tree-like reflections or comet tail artefacts (reverberation).**

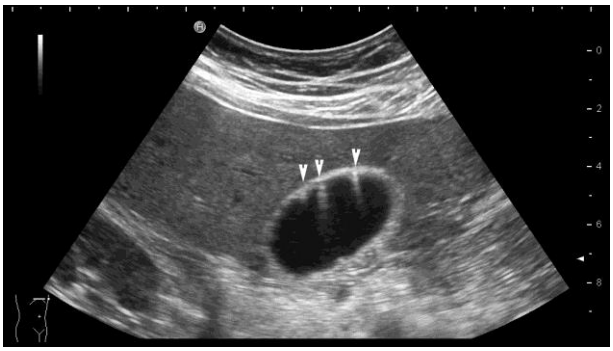


Figure 51 **A more pronounced case of cholesterolosis of gallbladder wall: numerous echogenic gallbladder wall reflexes with comet tail artefacts.**

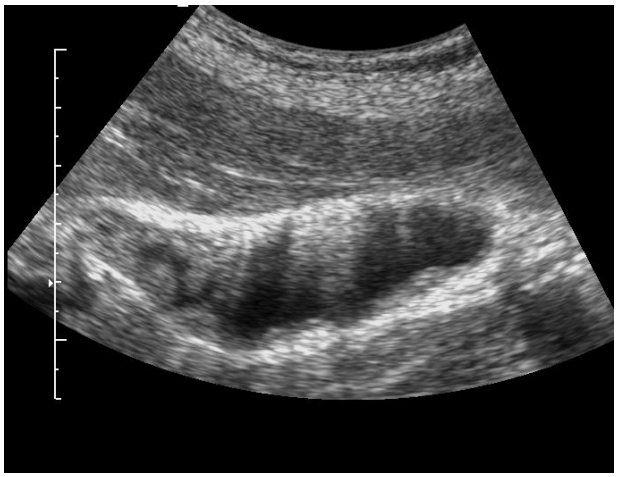
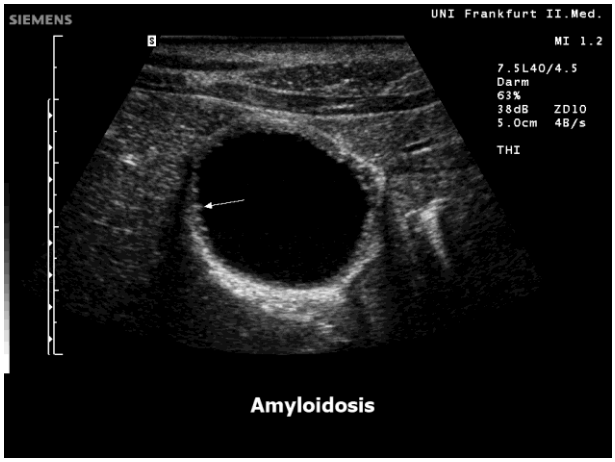


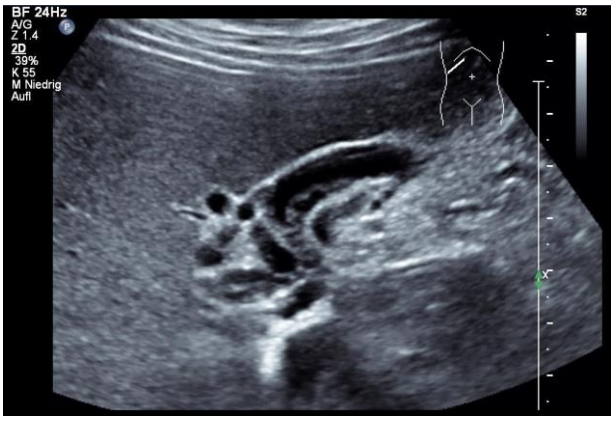
Figure 52 Amyloidosis of the gallbladder may show irregular deposits in the gallbladder wall (white arrow) [(38)].



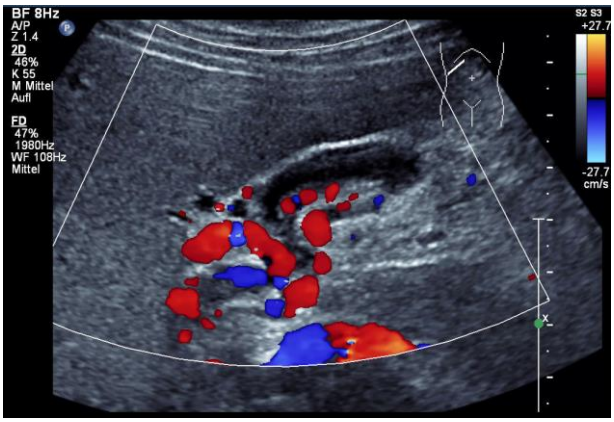
Gallbladder varices as a cause of gallbladder thickening [Figure 53] can be diagnosed or excluded using colour Doppler imaging.

Figure 53 Gallbladder varices: anechoic structures within the gallbladder wall (a), diagnosed to be intramural varices by colour Doppler ultrasound (b)

a



b



Gallbladder polyps

Lesions that protrude into the gallbladder lumen are known as polyps. Gallbladder polyps are observed in up to 7% of asymptomatic persons [(39, 40)]. Ultrasonically, they are polypoid lesions, with no acoustic shadowing that do not move with patient movement unless the 'stalk' joining the lesion to the wall is long. The vast majority of gallbladder polyps are benign cholesterol polyps, characterised by a homogeneous echogenic appearance and distinct borders [Figures 54 - 55]. Very often multiple small polyps are detected [Figure 56]. Adenomatous polyps are rare premalignant lesions. Most of them are solitary lesions [Figure 57]. Risk factors for malignancy are: size ≥ 10 mm, sessile and single polyp, concomitant gallbladder stones, age > 50 years, rapid increase in size. Polyps < 6 mm nearly never are malignant [(41)]. However, differentiation between benign and malignant lesions can be challenging [(42)]. Patient age, polyp size, number and rapid growth on serial scans can help in discrimination. Larger lesions > 6-10mm require at least yearly serial follow-up. Gallbladder polyps that are growing on serial scans or polyps larger than 10 mm should be surgically removed due to potential malignant transformation [(16, 43)].

Figure 54 A typical benign cholesterol polyp: homogeneous and echogenic with smooth borders (marked with arrow)

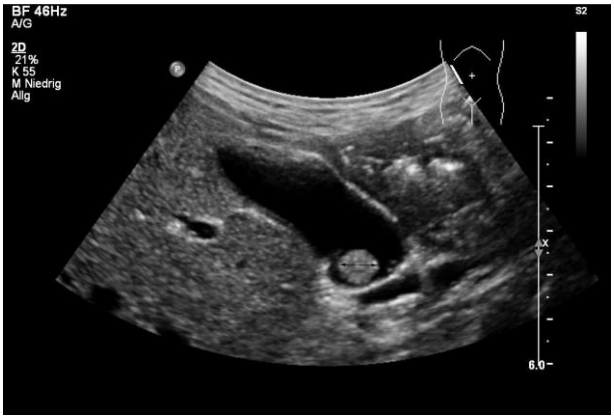
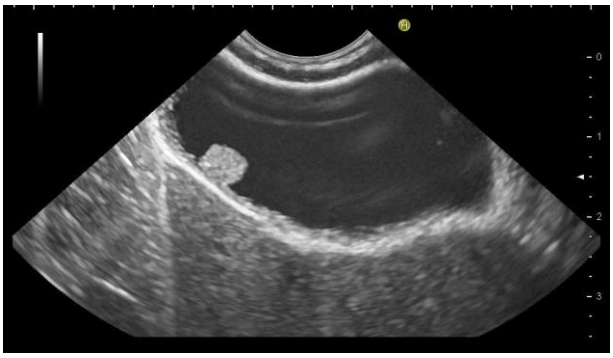


Figure 55 Endosonographic image of a typical cholesterol polyp measuring 5 mm (a). Colour Doppler imaging delineates a vessel inside the polyp (b). Detection of a vessel is not a sign of neoplastic character of gallbladder polyps.

a



b

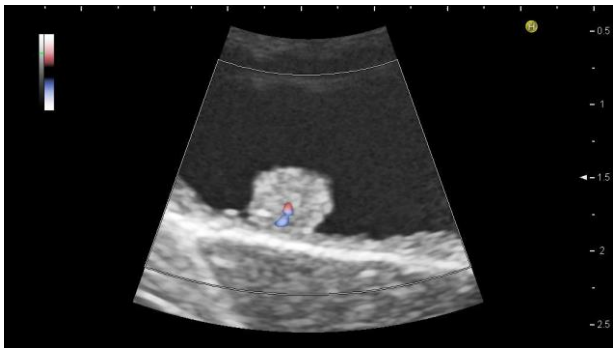


Figure 56 Multiple cholesterol polyps of the gallbladder, seen as multiple, small, smooth walled lesions, with no acoustic shadowing, in various sites, largest example (6 mm) shown between callipers +-----+.

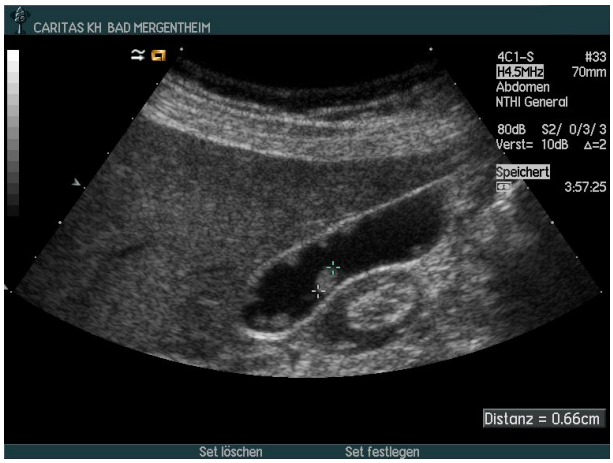


Figure 57 Adenoma (7 mm) of the gallbladder. Compared to cholesterol polyps, echogenicity is lower in neoplastic polyps. Often neoplastic polyps are solitary A central vessels penetrating the polyp is demonstrated (in red) using color Doppler imaging. Note the sludge filled lumen of the gallbladder.

Gallbladder carcinoma

Gallbladder carcinoma is a rare but highly fatal malignancy, associated in almost 100 % of

cases with cholecystolithiasis and is more frequent in patients older than 60 years. The risk of developing gallbladder cancer in a patient with gallbladder stones is 0.3 % over 30 years and the published data suggest a much higher cancer risk in stones larger than 3 cm and in porcelain gallbladder [(44)]. It is the 5th most common gastrointestinal cancer and the most common tumour of the biliary system worldwide. Incidence varies geographically and with ethnicity. Additional risk factors include history of stones and inflammation of the gallbladder; 85 % patients with gallbladder cancer have a history of stones. Increased incidence in cases of porcelain gallbladder is also seen. Female gender, multiparity, family history and obesity have also been reported. Links with smoking and working with metals and chemicals are noted [(45, 46)]. Symptoms of gallbladder carcinoma are often non-specific, vague and include abdominal pain (often RUQ), bloating, weight loss, jaundice, nausea and vomiting, hence its frequent late presentation, with advanced disease (a so called 'silent tumour'). 85 % arise from the glandular epithelium and are adenocarcinomas, the remaining 15 % being squamous cell, lymphomas or sarcomas. It has a poor five year survival rate (≤ 5 %) due to the late presentation of the disease at an advanced due to vague symptoms, with a lack of serosa anatomically to minimize local spread to liver and adjacent structures or via blood - the cystic veins to the liver, lymphatics and peritoneum.

The incidence by percentage of anatomical sites of gallbladder cancers (adenocarcinomas) are fundus (60 %), body (30 %) and neck (10 %). Carcinomas of the gallbladder can be easily recognised using transabdominal ultrasound whereas correct staging is much more difficult and underestimation of the extent of the disease is possible. Complimentary imaging such as CT and/or MRI is often also required. The majority of cases are found incidentally in patients with cholelithiasis: in 1-2 % of these cases a gallbladder carcinoma can be found [(47)]. As with other tumours of the upper GI tract, a definite sonographic distinction between inflammatory and neoplastic alterations or changes in connective tissue is not possible. In some cases, a sonographic diagnosis of adenomyomatosis, cholesterol polyps and other pathologies of the gallbladder can be made.

Sonographically, gallbladder tumours can be described as 3 types:

1. Focal – focal, irregular wall thickening, a poorly defined polypoid mass protruding into the gallbladder lumen.
2. Diffuse – with diffuse, asymmetrical thickening of the gallbladder wall.

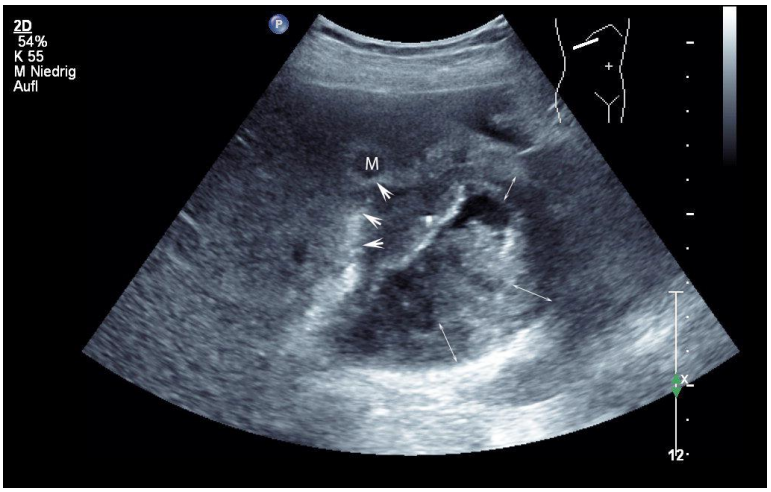
3. Complete replacement of gallbladder lumen with tumour - in more advanced disease, the replacement of the gallbladder lumen by a solid, normally hypoechoic, mass that actually completely fills the gallbladder is evident. The presence of a gallstone in relation to this mass suggests the diagnosis of gallbladder carcinoma.

Ultrasound has high sensitivity for detection of large tumours/ advanced disease [Figure 58], but is poor in early disease diagnosis and staging. Multi-modality imaging is important in these situations. Contrast enhanced ultrasound can be useful for the diagnosis of gallbladder carcinoma and can help in the differentiation of normal and infiltrated areas [Figure 59]. It can also help in the assessment of liver metastases.

Figure 58 Two examples of advanced gallbladder cancer: hypoechoic thickening of gallbladder wall (arrows) with infiltration of the liver parenchyma (arrowheads) and adjacent liver metastases (M). The gallbladder lumen is filled with echogenic content (sludge, a) or fluid and a stone with shadowing (b), respectively

a

b



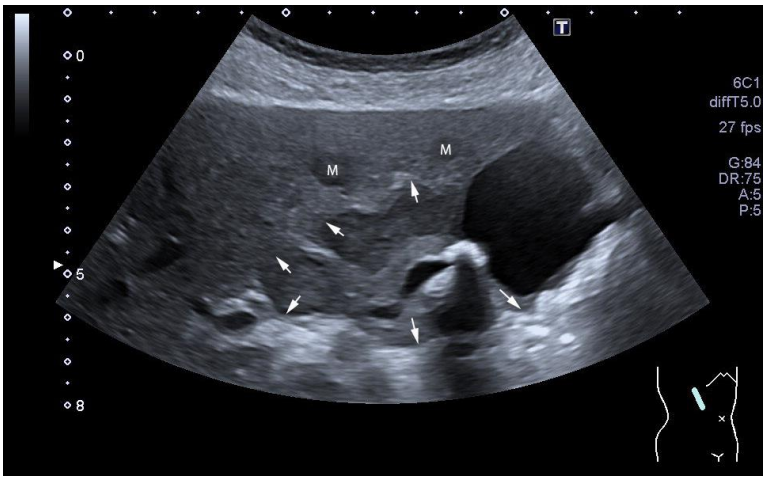
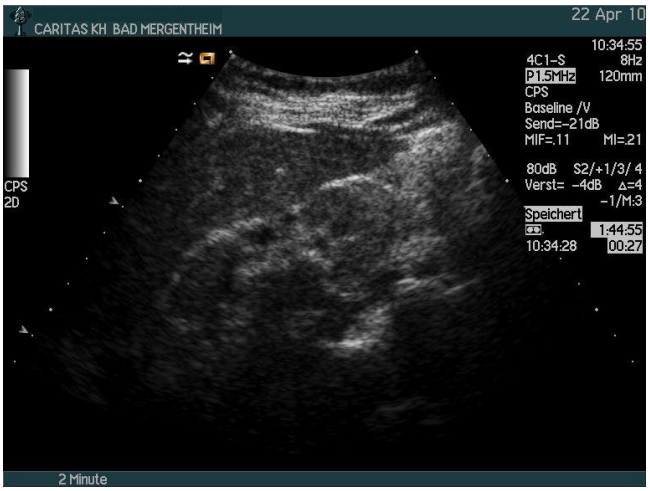
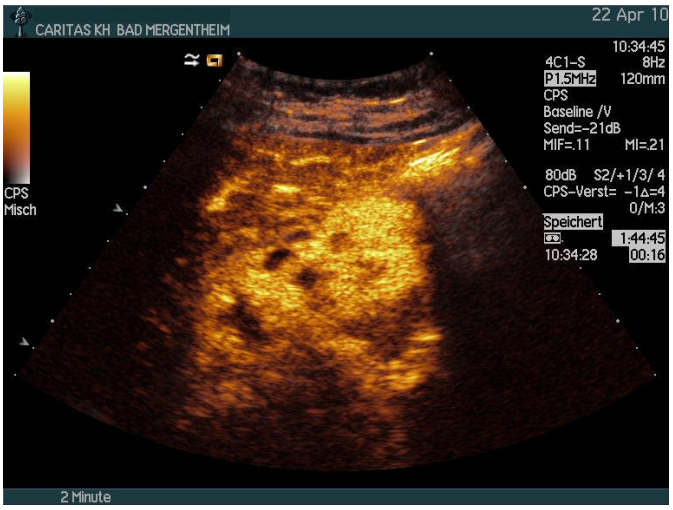


Figure 59 **Gallbladder carcinoma. Role of conventional grey-scale ultrasound imaging is often limited in the reliable detection of these tumours, particularly when small, diffuse and there is a lack of bile in the gallbladder lumen. An example of detection of a gallbladder tumour using this modality is shown as a diffuse thickening of the gallbladder wall with a focal solid lesion, causing irregular outline of the gallbladder (white arrow). The gallbaldder is not distended (a). Contrast enhanced ultrasound is helpful in delineating tumour infiltration (b) (white arrow).**

a



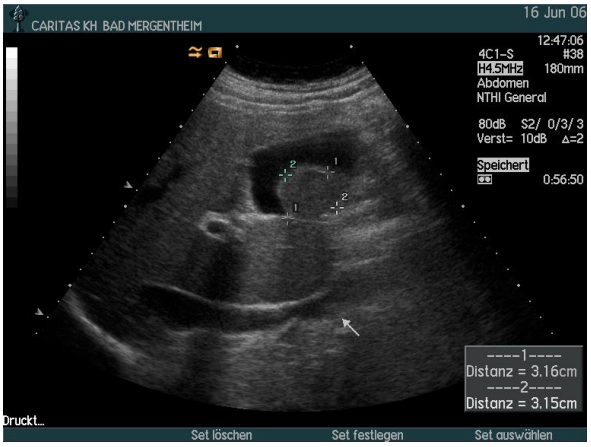
b



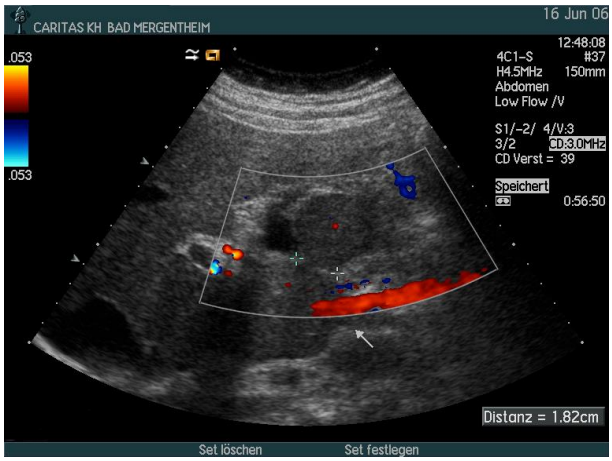
Sometimes other morphology may imitate gallbladder neoplasia, e.g. hyperregenerative nodules in liver cirrhosis [Figure 60] or even polyps.

Figure 60 Differential diagnosis of gallbladder neoplasia (between callipers +---+) might be atypical liver appearance (a). Demonstration in two anatomical levels is helpful (b) for the correct diagnosis.

a



b



Patients with jaundice

Patients with jaundice should be examined sonographically as early as possible, if possible immediately when they present. In some cases, it is better to scan the patient without fasting to assess the case and then repeat after fasting if necessary. For example, dilated intrahepatic bile ducts may be seen without fasting, since the liver acts as an acoustic window, and this may account for an initial presentation of jaundice.

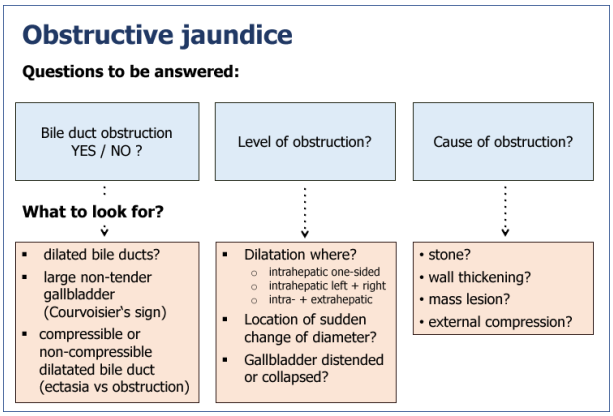
Ultrasound can differentiate jaundice caused by obstructive and hepatocellular origin in almost all patients by focusing and analysing the diameter of the main bile duct (Table 5 for bile duct measurements). In obstructive disease, the ultrasound practitioner should evaluate distribution of the dilated ducts in order to define the level of obstruction. In considering the cause – it is useful to think of the obstruction being:

- **Within the lumen**. Examples – stones, tumour invasion.
- **Arising in the wall**. Examples – tumour (primary such as CCC or invasion from other local tumours), stricture (primary or post-surgery).
- **External to the wall causing compression of the duct**. Examples – tumours of the papilla and of the pancreas, hilar lymph nodes, cysts.

A detailed sonographical analysis of the cause and level of obstruction may help guide treatment decisions and potentially avoid more invasive or expensive (e.g. endoscopic ultrasound; magnetic resonance cholangio-pancreaticography, MRCP) examination [Figure

61, table 6]. The left lateral decubitus position is helpful for adequate visualisation of the liver hilum [(12-14)] and should be performed consistently in all patients. The papilla of Vater can be less reliably displayed using the transabdominal approach.

Figure 61 Role of ultrasound in diagnosis of obstructive jaundice



Ultrasound has a very high accuracy in determining the cause of obstructive jaundice (sensitivity 83%, specificity 95%) [(48)].

Table 6 Levels of bile duct obstruction and typical sonographic features

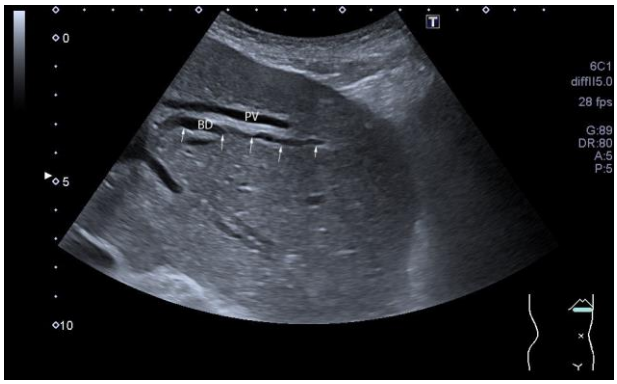
Level of obstruction	Sonographic features
Intrahepatic level	• Segmental or one-sided dilatation of intrahepatic bile ducts • Normal diameter of extrahepatic bile duct • Normal-sized gallbladder
Hilar level	• Bilateral or unilateral dilatation of intrahepatic bile ducts • Normal diameter of extrahepatic bile duct • Small or normal-sized gallbladder
Subhilar level [(49)]	• Bilateral dilatation of intrahepatic bile ducts • Normal diameter of CBD • Small or normal-sized gallbladder
Distal level (CBD,	• Bilateral dilatation of intrahepatic bile ducts

papilla)	• Dilatation of the MBD • Distended gallbladder (Curvoisier's sign)

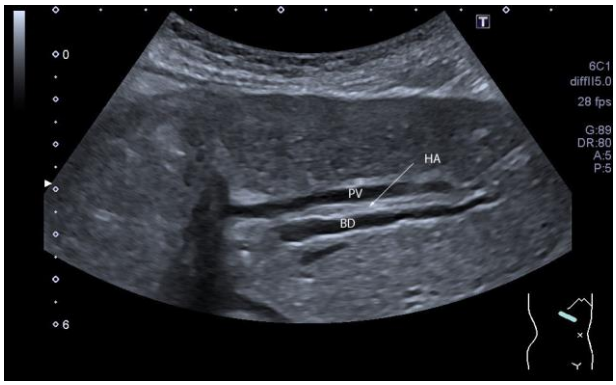
A typical sign of obstructive jaundice is the "double-barrelled shotgun" sign, caused by the parallel course of dilated intrahepatic bile ducts and portal vessels; Colour Doppler is helpful to differentiate between dilated intrahepatic bile ducts and vessels [Figure 62]. In patients with preserved gallbladder and distal obstruction of the biliary tree (CBD, papilla) a large non-tender gallbladder is typical (first described in 1890 by the Swiss surgeon L.G. Curvoisier) [Figure 63]. Hepatopetal parabiliary collateralization of portal vein thrombosis ("gallbladder varices", "cavernous transformation" of portal vein) may cause confusion with dilated extrahepatic bile ducts. Again, colour Doppler should be used to differentiate between main bile duct and vessels [Figure 64]. Segmental intrahepatic bile duct obstruction may be caused by intrahepatic masses [Figure 65] or by intrahepatic bile duct stones [Figure 72 - 73].

Figure 62 "Double-barrelled shotgun" sign, caused by slight dilatation of the intrahepatic bile ducts in the left liver lobe, running parallel to the portal vein branches (a: overview; b: detail; c: colour Doppler, characterizing the intrahepatic portal vein branch which is anterior to the dilated segmental bile duct; PV: portal vein branch; BD: dilated intrahepatic segmental bile duct; HA: segmental hepatic artery branch)

a



b



c

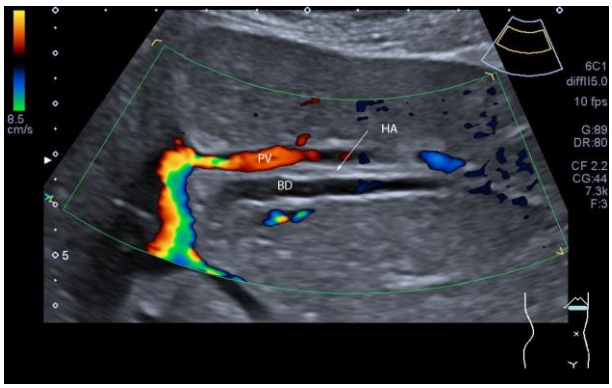
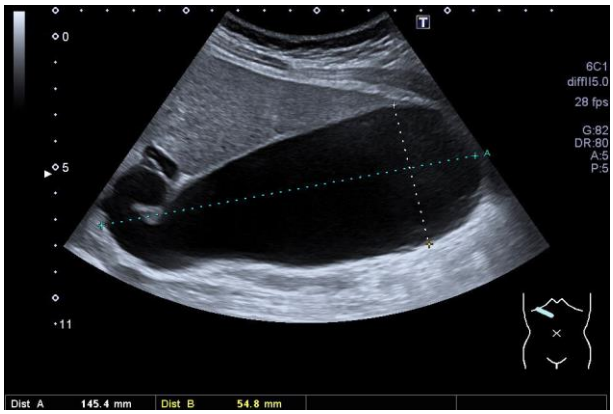


Figure 63 Distal bile duct obstruction by a pancreatic head tumor: large nontender Gallbladder (a, Courvoisier's sign) without stones and dilated extrahepatic MBD (b) with echogenic material within the lumen (sludge). Ah: *: hepatic artery; CHD: common hepatic duct; Gb: Gallbladder; PV: portal vein; Tm: tumour)

a



b

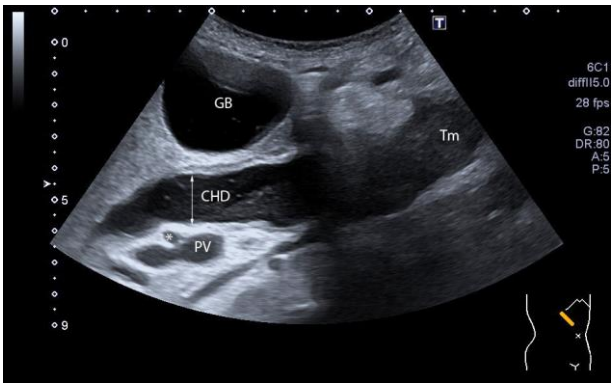
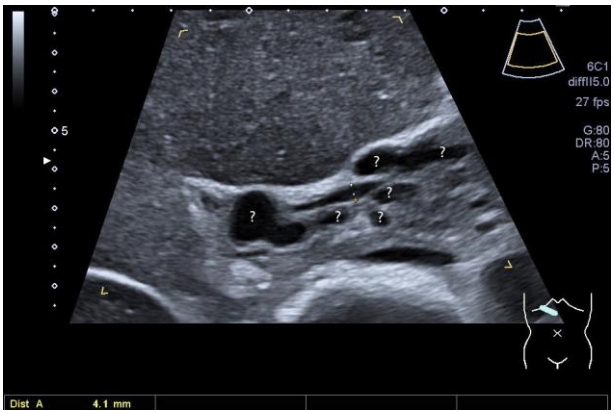


Figure 64 **Bile duct varices (cavernous transformation of portal vein) following portal vein thrombosis: with B-Mode image alone confusion of parabiliary collateral vessels (?) with dilated bile ducts is possible (a; between callipers: main hepatic duct). Colour Doppler delineates nicely hepatopetal porto-.portal collaterals (C) surrounding the normal sized main bile duct (b; marked with double-head arrows).**

a



b

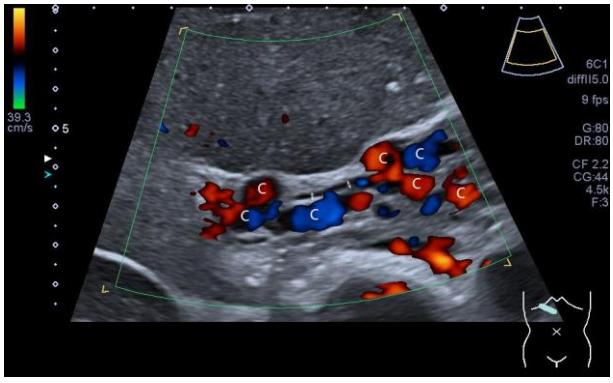
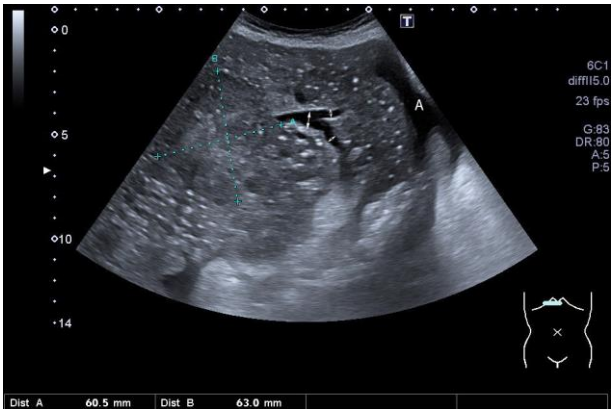


Figure 65 Segmental intrahepatic bile duct obstruction due to a liver metastasis (between calipers: left lobe; A: ascites; dilated intrahepatic ducts marked with arrows)



Choledocholithiasis

Cholecystolithiasis (gallbladder stones) can be detected by transabdominal ultrasound with high sensitivity [Table 7], whereas choledocholithiasis (bile duct stones) is more difficult to detect [Table 8]. The literature has been recently summarized [(50)]. In contrast to the diagnostically helpful acoustic shadowing exhibited by gallbladder stones, bile duct stones do not always show acoustic shadowing, especially when the stones are very small [Figures 66 - 69]. Even with the most modern ultrasound equipment, the sensitivity for choledocholithiasis is still largely dependent on the expertise of the ultrasound practitioner and has a large difference in detection rates (25 - 100 %).

In contrast to the transabdominal approach, endoscopic ultrasound (EUS) and miniprobe endosonography (extraductal (endoscopic) ultrasound, EDUS) are more efficient [Figures 70 - 71], but are not so readily available as they are obviously more invasive and require trained specially operators. EUS shows a detection rate of 94 - 100 % and EDUS diagnosis of choledocholithiasis was confirmed to be correct in 33 out of 34 patients (97 %). As expected, EDUS failed to detect peripheral lesions due to its limited depth penetration [(51)]. Parasites

have also to be considered, for example, Ascarias particularly in the accordant geographical regions [(52, 53)].

Table 7 Detection of cholecystolithiasis by transabdominal ultrasound – review of the literature [(50)]

Sensitivity (%)	Specificity (%)	Reference
98	94 – 98	(24)
70	100	(36)
97	92	(37)
91	99	(38)
98	Nm	(54)
91	100	(55)
87	93	(41)

Notes: nm: not mentioned

Table 8 Detection of choledocholithiasis by transabdominal ultrasound – review of the literature [(50)].

Patients (n)	Sensitivity (%)	Specificity (%)	NPV (%)	PPV (%)	Gold standard
62	25	100	56	100	ERCP with or without EST or IOC
52	80	94	nm	nm	ERCP/EST or surg. expl.
nm	38	100	nm	nm	No results
35	47	90	nm	nm	ERCP/EST
142	63	95	nm	nm	ERCP with or without EST or surg. expl.
36	50	100	74	100	ERCP/EST
50	100	97	92	100	ERCP/PTC
132	68	nm	nm	nm	ERCP/EST
29	38	100	nm	nm	ERCP

Notes: nm: not mentioned; NPV: negative predictive value; PPV: positive predictive value; ERCP: Endoscopic retrograde cholangiopancreaticography; EST: Endoscopic sphincterotomy; Surg. expl.: Surgical exploration; IOC: Intraoperative cholangiography; PTC: Percutaneous transhepatic cholangiography.

ERCP (endoscopic retrograde cholangiopancreatography) was considered the diagnostic gold standard with a reported success rate of 90 - 96 %. However, the value of diagnostic ERCP might be grossly overestimated, as the rate of correctly diagnosed choledocholithiasis seems to be much lower, especially since small gallstones (<3 mm) with normal or even dilated bile ducts are easily overlooked with all diagnostic techniques, even ERCP.

The combination of ERCP with endoscopic spincterotomy (EST), including stone extraction using the dormia basket or balloon, is nowadays the therapeutic method of choice in patients with choledocholithiasis, but it is an invasive technique with a significant risk of complications for the patient [(51)]. The reported results using magnetic resonance MRCP and computed tomography (56) are less convincing especially in small stones without main bile duct dilatation. However, these imaging techniques are improving and it is quite probable that these methods will become more important in the next few years, particularly due to the fact that they are non-invasive. However, the method of choice to exclude choledocholithiasis without sphincterotomy is endoscopic ultrasound [(4, 16, 57)].

Figure 66 Choledocholithiasis. This image shows dilatation of the bile ducts proximal to a stone in the bile duct (between callipers) causing obstruction to the flow of bile. Note, this large stone is insonated at 90 degrees to the ultrasound beam and distal acoustic shadowing is shown.

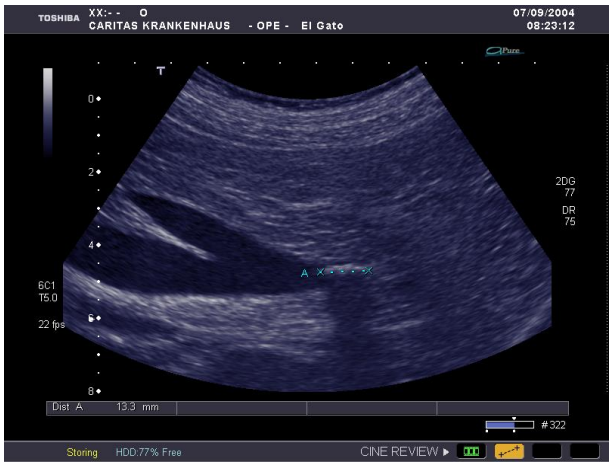
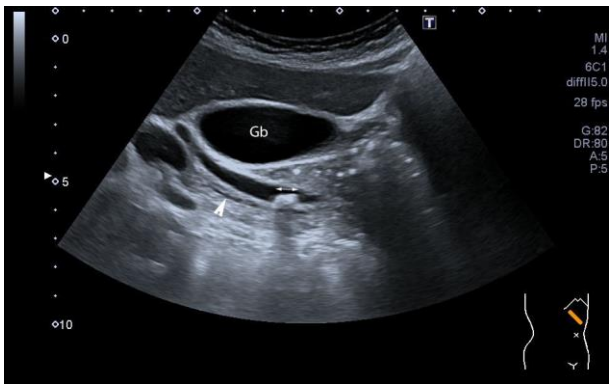


Figure 67 **Detection of a small stone in a non-dilated bile duct (a: hyperechoic intraductal structure with shadowing: arrow; GB: gallbladder; arrowhead: main pancreatic duct). Endoscopic image of the extracted stone after biliary sphincterotomy (b).**

a



b

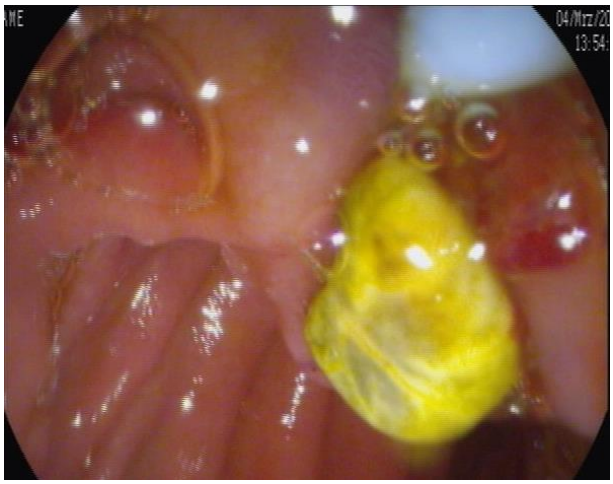
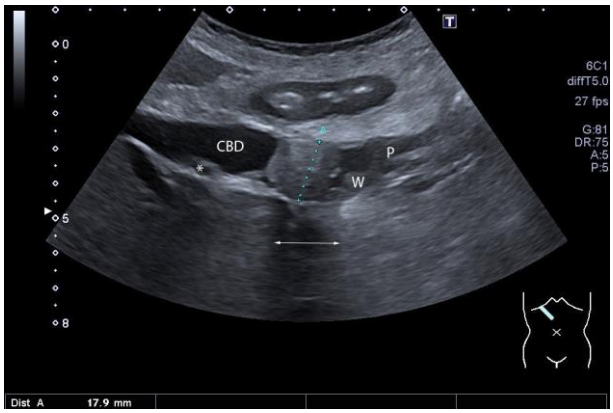


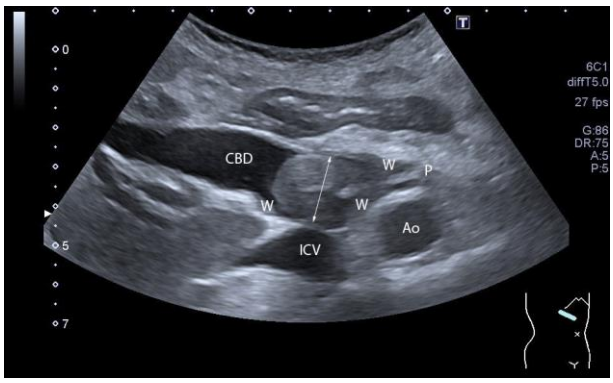
Figure 68 **Large bile duct stone in a patient with obstructive jaundice, B-Mode images (a, b) shows a markedly dilated common bile duct (CBD) containing a echogenic, well delineated solid structure (between callipers: 17.9 mm). Bile duct wall (W) near the papilla (P) is thickened. Minimal shadowing is inconsistently shown depending from insonation angle and echogenicity of structures "behind" the mass lesion (a: minimal shadowing marked with arrow; b due to minimal change of transducer position and anechoic ICV "behind" the mass lesion no shadowing may be observed; ICV: inferior caval vein; Ao: Aorta). Contrast-enhanced ultrasound (c) shows marked contrast enhancement of the thickened**

bile duct wall near the papilla, but no enhancement of the mass lesion, allowing differentiation from a neoplastic lesion.

a



b



c

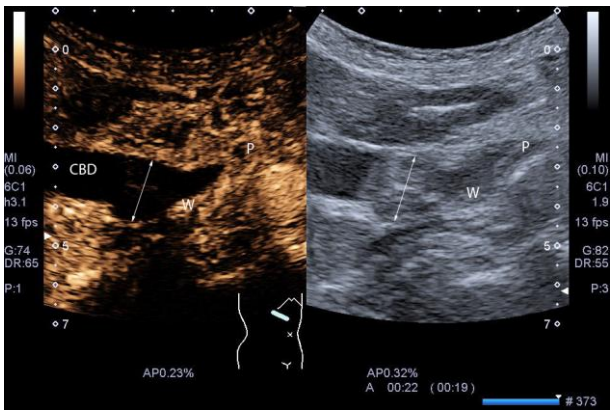


Figure 69 **Transverse section of common bile duct stone: the stone (marked with double-head arrrow) is translucent and no shadowing is observed (Ao: Aorta; Bulb: duodenal bulb; ICV: inferior caval vein)**

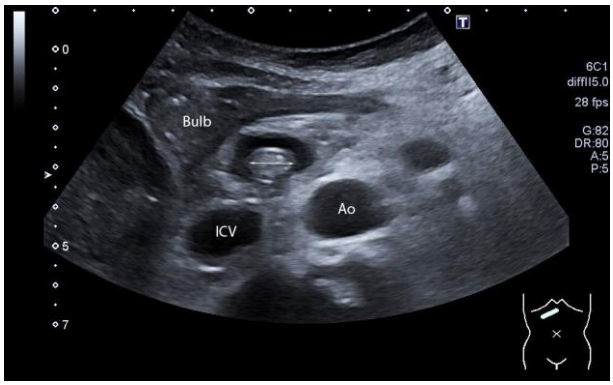


Figure 70 **Detection of a large bile duct stone in a normal diameter bile duct using radial endoscopic ultrasound (stone between callipers: 12.6 mm; CBD: common bile duct; P: papilla)**

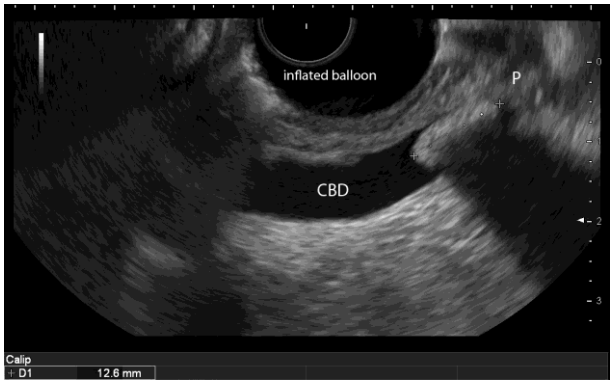
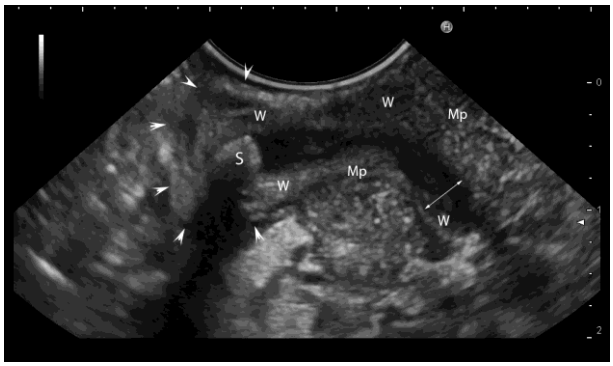


Figure 71 **Obstruction of the papilla by a bile duct stone. Longitudinal EUS (a) shows a swollen papilla protruding into the duodenal lumen (circumference marked with arrowheads). The papilla is obstructed by a small stone (S), the distal bile duct (lumen marked with double-head arrow) has echogenic content and a thickened wall (W) and may be followed from the pancreatic head through the duodenal wall (Mp: Muscularis propria). Compare the ERCP image (b) with the**

dark-coloured stone (S) and the swollen and protruding papilla (circumference marked with arrowheads).

a



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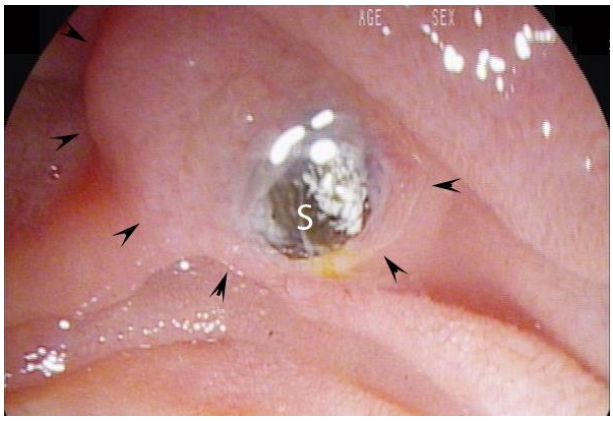


Hepaticolithiasis

Intrahepatic stones (hepaticolithiasis) are rare. They are much more common in Asia than in Europe. Congenital anomalies and parasitoses are the leading causes. Ultrasound appearances are hyperechoic structures with posterior acoustic shadowing inside the intrahepatic biliary ducts (sometimes with dilated intrahepatic biliary tree above the site of the stones) [Figures 72 - 73].

Figure 72 Hepaticolithiasis: an echogenic structure with shadowing (between markers: 8.3 mm) is seen within a slightly dilated intrahepatic duct.

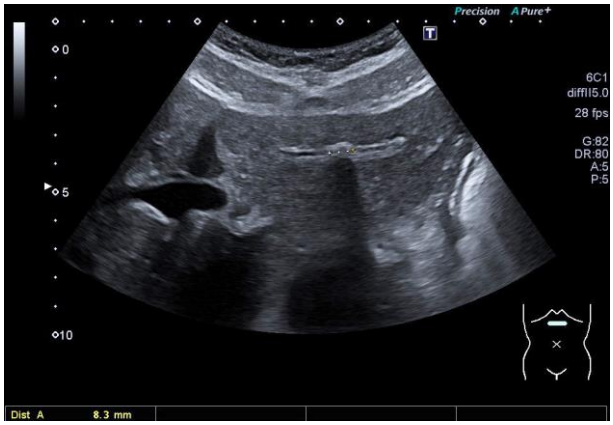
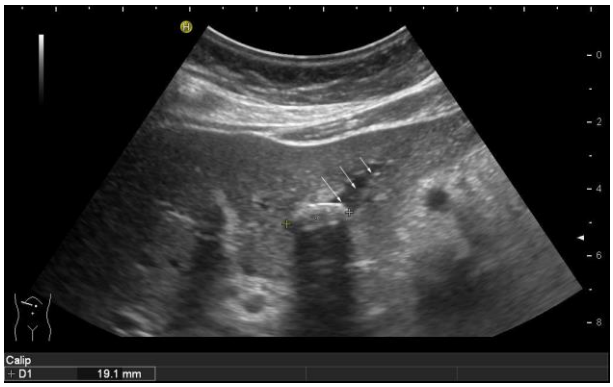


Figure 73 Large intrahepatic bile duct stone (between markers: 19.1 mm) causing upstream dilatation of the left hepatic duct (arrows)



Purulent Cholangitis

Sonographic features of cholangitis are enlarged extrahepatic bile ducts with typically symmetrical thickening of the wall [Figures 63b, 74 - 75]. Sometimes echogenic content of the duct may be observed. With CEUS, the thickened wall shows hyperenhancement [Figures 68c, 75b]. One important complication of purulent cholangitis is liver abscess [Figures 75 c - d].

Figure 74 Cholangitis. Image shows thickened wall of bile duct (between callipers +---+) with extrahepatic bile duct dilatation (CBD).

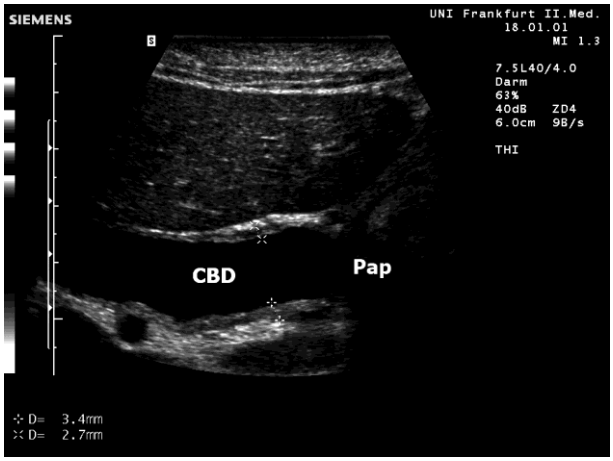
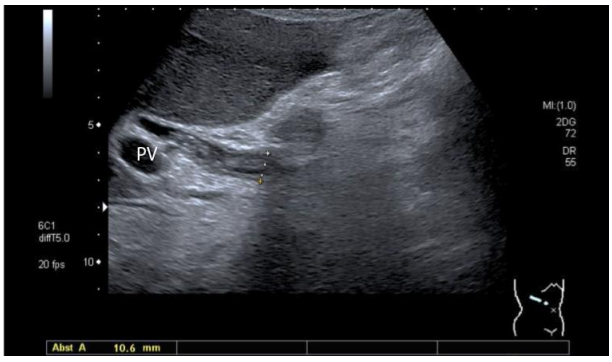


Figure 75 Purulent cholangitis in a patient with bile duct stones. B-Mode image (a) shows a slightly dilated main bile duct (between callipers: 10.6 mm) with thickened wall and non-anechoic content (58). With contrast-enhanced imaging hyperenhancement of the bile duct wall is demonstrated (b). In the same patient a biliary liver abscess (between callipers/ arrowheads: 43.8 x 38.5 mm) is detected using B-Mode ultrasound (c) and contrast –enhanced imaging (d; note the hyperenhancement of the liver parenchyma surrounding the abscess in the arterial phase).

a



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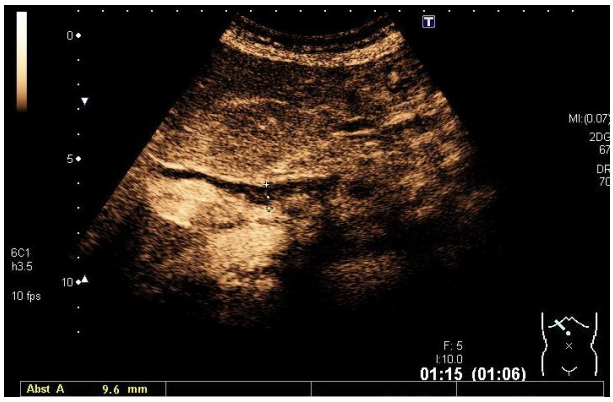

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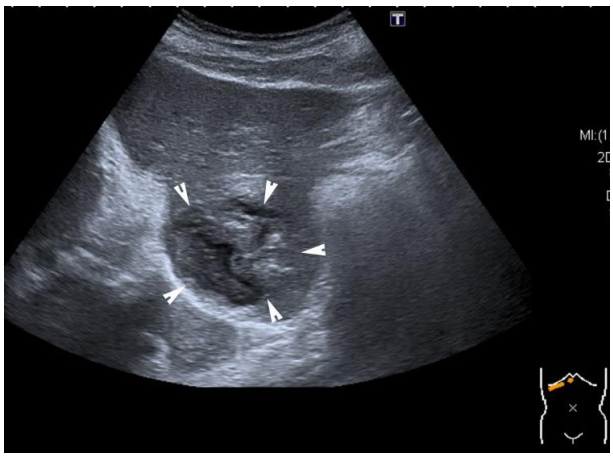
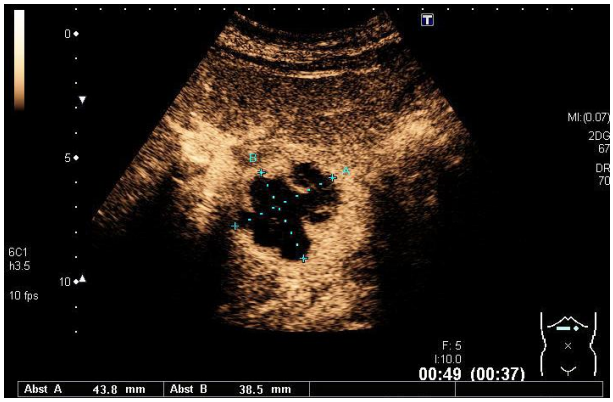


d



Primary sclerosing cholangitis

Primary sclerosing cholangitits (PSC) is a chronic inflammatory liver disease characterized by progressive fibrosis and destruction of the intra- and extrahepatic biliary tree leading to stricturing of the intrahepatic and/or extrahepatic bile ducts. The aetiology and pathogenesis

of PSC are not well understood. It has a clear association with inflammatory bowel disease (especially with ulcerative colitis) and is often progressive, leading to liver cirrhosis and end-stage liver failure. Primary sclerosing cholangitis (benign strictures) is a precancerous condition, and up to 20 % of patients with PSC develop cholangiocarcinoma. On ultrasound examination, enlarged perihepatic lymph nodes can be visualized in > 90 % of cases [(59, 60)] and asymmetric thickening of the bile duct walls with (benign) strictures and alternating dilatations can be found in 70 % [Figures 76 - 77] [(59)]. Cholangiocarcinoma in PSC is often detected at an advanced stage. Patients typically present with jaundice, weight loss and abdominal pain. Screening strategies are used, including regularly performed transabdominal ultrasound to detect the malignant tumour at an early stage permitting more timely treatment options. However, differentiation of inflammatory strictures from bile duct obstruction caused by cholangiocarcinoma is very difficult.

Figure 76 Primary sclerosing cholangitis (PSC). Asymmetric thickening of the bile duct walls is shown (between calipers). Benign strictures and alternating dilatations are typical sonographic findings in patients with PSC that can be found in more than 70 % of cases.

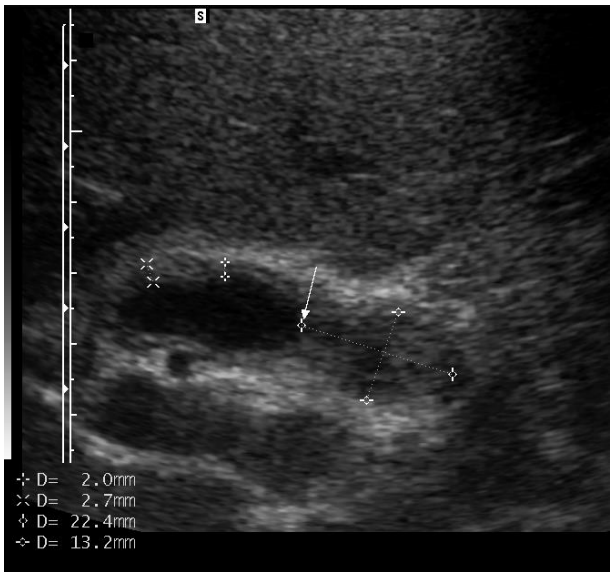
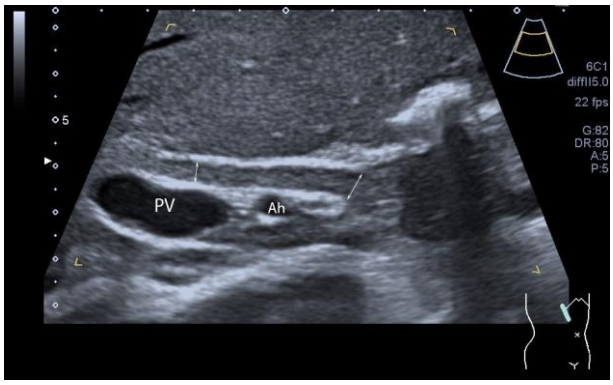


Figure 77 **Primary sclerosing cholangitis. In the hepatic hilum thickening of the common hepatic duct (a; marked with double-headed arrows, no anechoic lumen is visible; Ah: hepatic artery; PV: portal vein) is demonstrated. Upstream right hepatic duct (Rhd) is slightly dilated (b; stricture is marked with double-headed arrows). The ERC image correspondingly shows the long stricture of the common hepatic duct and right hepatic duct (marked with arrows) as shown sonographically (a, b) and the slight dilatation of the right hepatic duct (Rhd) (compare with the sonographic image in b).**

a



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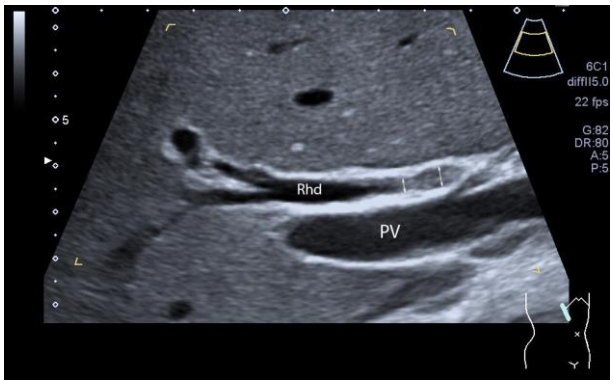

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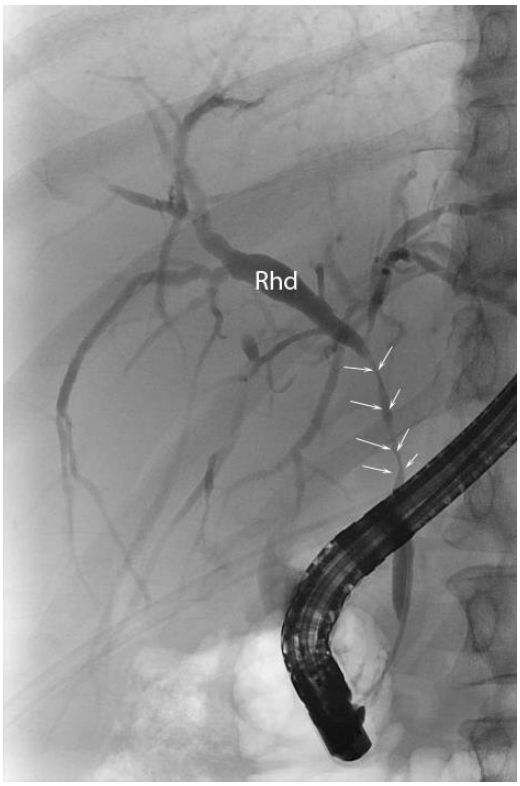


Secondary sclerosing cholangitis

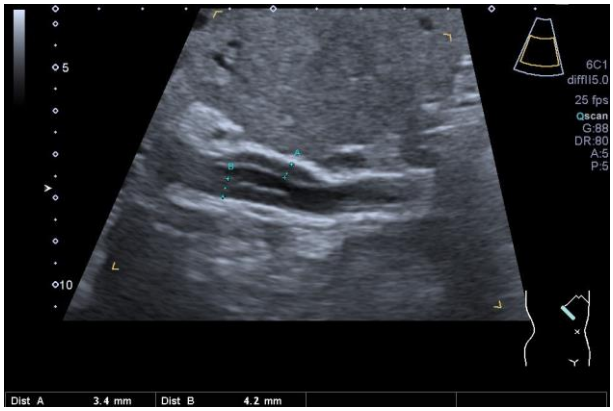
Decades ago secondary sclerosing cholangitis (SSC) was much more common than PSC, but has become a rare diagnosis due to the advent of endoscopic and surgical treatment of biliary obstruction. Typical causes are biliary obstruction caused by choledocholithiasis, post-operatively after insufficient drainage, chronic pancreatitis, choledochal cyst(s) and extrahepatic biliary atresia. However, infections in immunodeficient patients have also been reported causes, as well as toxins, ischaemia and malignancy. The most important complications of SSC, for example, hepatic lobar atrophy, could be reduced. Typical sonographic findings in these patients are enlarged extrahepatic bile ducts with more or less symmetrical thickening of the bile duct wall in contrast to the asymmetric thickening typically seen in PSC. However, the diagnosis of SSC is not made by ultrasound; rather, the gold standard is endoscopic retrograde cholangiography (ERC) in combination with patients' history.

Autoimmune cholangitis

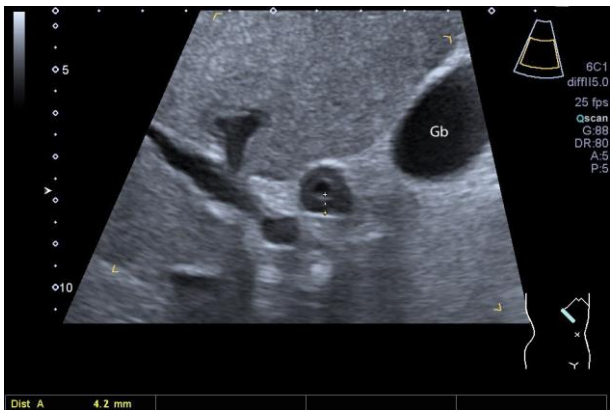
A rare condition is autoimmune cholangitis, in most cases a IgG4-related disease and sometimes observed together with autoimmune pancreatitis. Sonographic features are very similar to PSC, and differential diagnosis is possible only using serological markers (IgG4, ANCA) and by histology [Figure 78].

Figure 78 IgG4-related autoimmune cholangitis: segmental hypoechoic wall thickening of the common and right hepatic duct (between callipers) shown in longitudinal (a) and transverse (b) section (Gb: Gallbladder).

a



b



Parasitic infections

In Asia, a notable risk factor for cholangiocarcinoma of the intrahepatic bile ducts is infection with liver flukes like Clonorchis and Opisthorchis [(61)]. Patients are typically infected by eating non- or undercooked fish with the adult worms inhabiting and laying eggs in the biliary tree. This leads to a chronic biliary inflammation with a subsequent malignant transformation of the epithelium. Other parasites are encountered as well [(62-69)].

Cholangiocellular carcinoma (including Klatskin tumours)

95 % of extrahepatic bile ducts tumour are adenocarcinomas such as bile duct carcinoma and cholangiocarcinoma. TNM staging for extrahepatic bile duct carcinoma applies to carcinomas arising above ampulla of Vater, including carcinomas in congenital choledochal cysts and intrapancreatic portion of the common bile duct. The classification excludes sarcomas and carcinoid tumours. Features to report also from a surgical point of view are obstruction, bile duct wall thickness (as a sign of infection), stones, tumour location and size, depth of invasion, tumour extension to adjacent structures and regional lymph nodes.

Cholangiocellular carcinomas (CCC) can be more frequently detected using transabdominal ultrasound with the newer high-resolution ultrasound systems. However, the practitioner must appreciate its limitations and the role of CT and more specifically MRI (MRCP) in the evaluation of CCC must be understood. They arise from the epithelial cells of the intrahepatic, hilar and extrahepatic bile ducts. 95 % are adenocarcinomas. Carcinomas of the bile duct are much more common extrahepatically but can be found also intrahepatically (< 10 %). Incidence increases with age (> 65 years), history of intraductual stones, Caroli's disease and smoking. Risk factors for the development are primary sclerosing cholangitits (PSC), infection of the hepatobiliary tract with liver fluke (e.g. Clonorchis sinensis) and congenital abnormalities of the hepatobiliary tract (e.g. biliary atresia, choledochal cysts) [(70, 71)]. Bile duct adenoma are rarely encountered [(72)].

Cholangiocellular carcinomas (CCC) can be found extrahepatically, intrahepatically in the hilum [so called Klatskin tumours, comprising approximately 70% of CCC] or more peripherally in the liver parenchyma. For unclear reasons, the incidence of intrahepatic cholangiocarcinoma has been rising in the past decades all over the world, while rates of extrahepatic cholangiocarcinoma are declining [(73, 74)].

Sonographically dilated bile ducts proximal to the stenosis, is the typical finding of bile duct tumors. Delineation of the (often initial small) tumour is more difficult. Contrast enhanced ultrasound has improved the detection and characterisation of cholangiocellular carcinoma.
Common presentation of hilar and extrahepatic CCC include signs of biliary obstruction, notably jaundice, pale stools, dark urine and pruritus. However, the disease often presents late with symptoms seen commonly in malignancy such as lethargy, weight loss etc. Diagnosis of intrahepatic disease is often delayed due to a lack of early symptoms. Occasionally, they are identified as an incidental finding on abdominal ultrasound. Perihilar CCC of the bile ducts are called Klatskin tumours and are classified by Bismuth-Corlette I - IV depending on the localisation of the tumour and involvement of the hepatic ducts [Figure 79 and table 9].

Figure 79 Bismuth-Corlette classification of extrahepatic cholangiocarcinoma

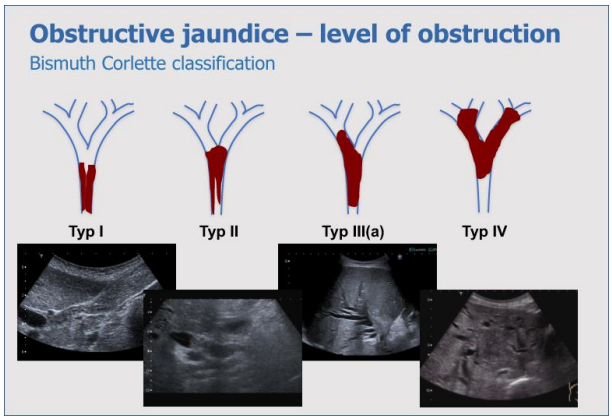


Table 9 Bismuth-Corlette classification of extrahepatic cholangiocarcinoma [(75, 76)].

Bismuth-Corlette classification I	Tumours below the confluence of the right and left hepatic ducts.
Bismuth-Corlette classification II	Tumours reaching the confluence but without involvement of the right or left hapatic ducts.

Bismuth-Corlette classification III	Tumours occluding the common hepatic duct and either the right (IIIa) or left hepatic duct (IIIb).
Bismuth-Corlette classification IV	Tumours that are multicentric, or involve the confluence and both the right or left hepatic ducts.

Typical appearances of cholangiocarcinomas on ultrasound show dilated bile ducts proximal to the stenosis caused by the tumour obstructing the lumen, hence, back-up of bile drainage causes the bile ducts proximal to the lesion to become dilated [Figures 80 - 82]. Delineation of the actual tumour is more difficult. Greyscale ultrasound has poor sensitivity in the hilar region of the liver. The majority of circumscribed cholangiocellular carcinomas are slightly hypervascular compared to the surrounding tissue by colour Doppler but imaging findings vary widely. Contrast enhanced ultrasound has improved the detection and characterisation of cholangiocellular carcinoma [Figure 82]. Enhancement patterns in the arterial phase vary, in most cases hyperenhancement may be observed; in the late portal venous phase, intrahepatic CCC typically are contrasted as ‘punched-out’ defects. This behaviour is not always easy to demonstrate in the case of the Klatskin tumours, which often exhibit an appreciable pericholangitic component. As far as differential diagnoses are concerned, in the case of the hilar type of CCC, inflammatory bile duct alterations should be considered, for example, cholangitis. Stratification of the bile ducts is then, however, preserved, and may actually be accentuated in the ultrasound image. For the detection of cholangiocellular carcinomas, the examination technique in the liver specific late phase has also proved to be diagnostically useful in patients who underwent normal CT, MRI, and MRCP results. However, also using contrast-enhanced ultrasound, the differential diagnosis of (primary) sclerosing cholangitis and cholangiocellular carcinomas is not possible.

Figure 80 **Dilated bile ducts proximal to a soft tissue lesion in the region of the ampulla (arrow). Diagnosis was distal cholangiocarcinoma (Bismuth-Corlette type 1)**

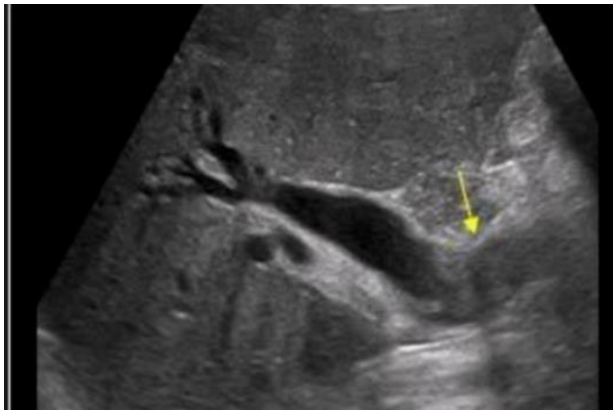


Figure 81 **Cholangiocellular carcinoma. Adenoma of the papilla and extrahepatic cholangiocellular carcinoma are drained by stents, which can be easily displayed by ultrasound. This patient who had severe deficits after stroke (and refusing surgery) had an adenoma of the papilla treated by endoscopic papillectomy and followed up for more than 8 years finally developing carcinoma.**

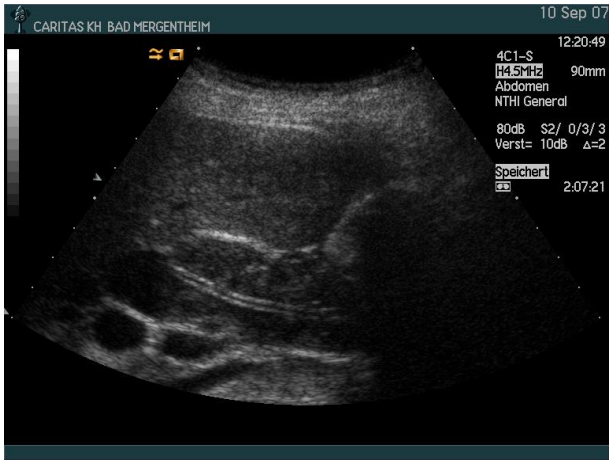
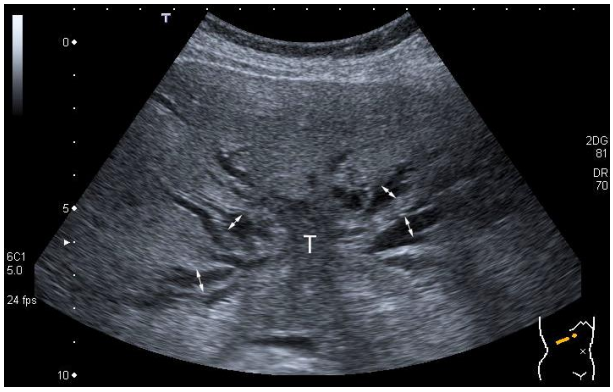


Figure 82 **Klatskin tumor: the ill-defined hypoechoic tumor (T) is located centrally in the liver hilum and infiltrates the parenchyma of both liver lobes. Intrahepatic bile ducts both of the left and right liver lobe are dilated (a; marked with double-**

heas arrows). Contrast-enhanced ultrasound at the end of the portal phase shows minimal hypoenhancement of the tumor (b) with progressive hypoenhancement in the late phase (c).

a



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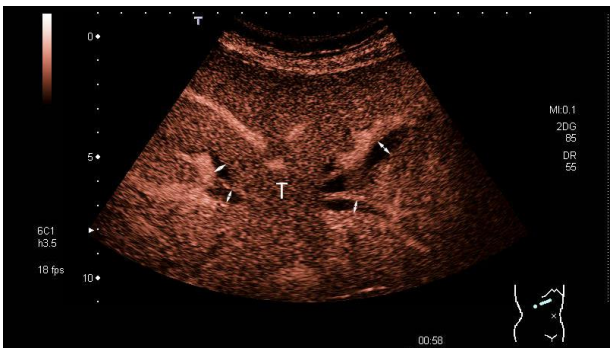
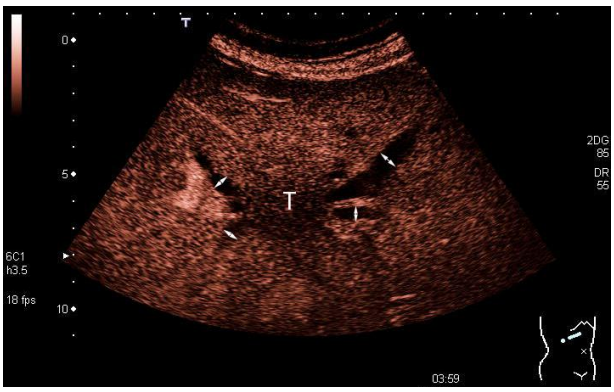


c



Intrahepatic CCC can be found often subcapsular, polygonal and are diffusely delineated. Typically the liver metastases of a peripheral CCC are situated like satellites around the primary focus. Ultrasound rarely demonstrates a mass and more commonly shows dilatation of the proximal intrahepatic ducts. Colour Doppler and contrast-enhanced imaging are useful

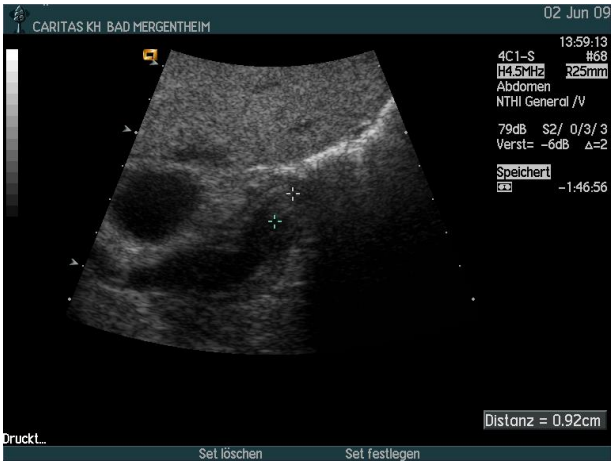
in differentiating tumour thrombus / compression of hepatic portal vein branches due to tumour thrombus. For further information on intrahepatic CCC see chapter 2 of the European coursebook) [http://www.efsumb.org/ecb/ecb-ch02-ultrasoundliver.pdf].

Other tumours of extrahepatic bile ducts

Adenomas represent only 10 % of the incidence of carcinoma and are much more common in the gallbladder than in the extrahepatic biliary tree [Figure 83]. Other forms of benign tumours of extrahepatic bile ducts are rare, for example carcinoid and show no pathognomonic ultrasound patterns. Even more rare, is the 'so called' benign hepatobiliary papillomatosis; nowadays described as intraductal papillary mucinous neoplasia of the bile ducts.

Figure 83 Adenoma of the papilla Vater (in between markers) demonstrated by ultrasound. This image sequence shows an adenoma using transabdominal B-mode ultrasound (a), transabdominal contrast-enhanced ultrasound (b), endoscopic elastography (c) [(77)] and endoscopic ultrasound using low mechanical index technique (CELMI EUS) [(78, 79)] (d). In contrast to adenoma, in [(80)] carcinoma infiltration of deeper layers can be delineated using elastography (e).

a



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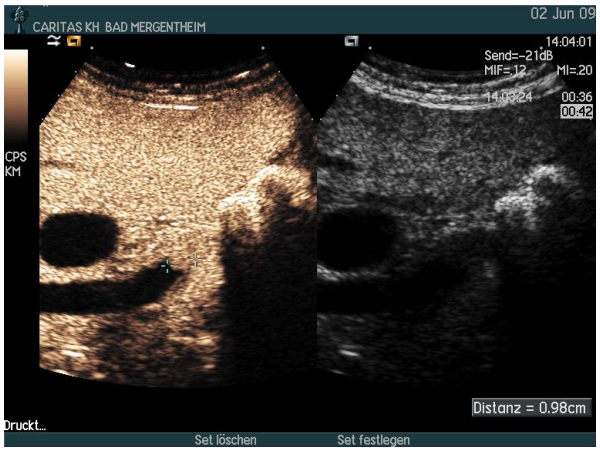
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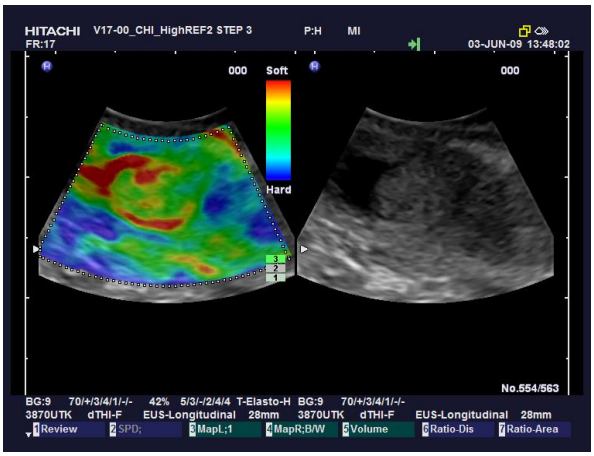
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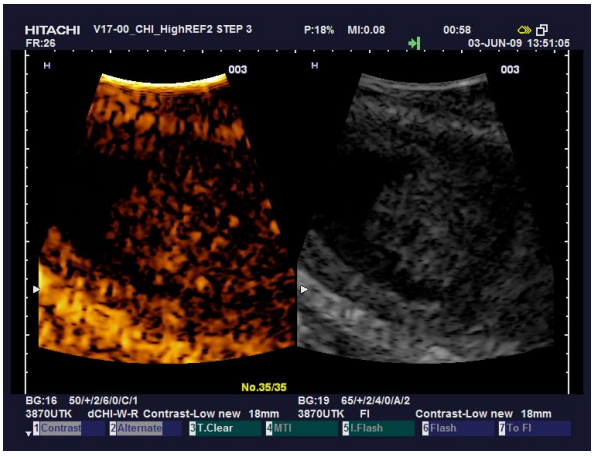
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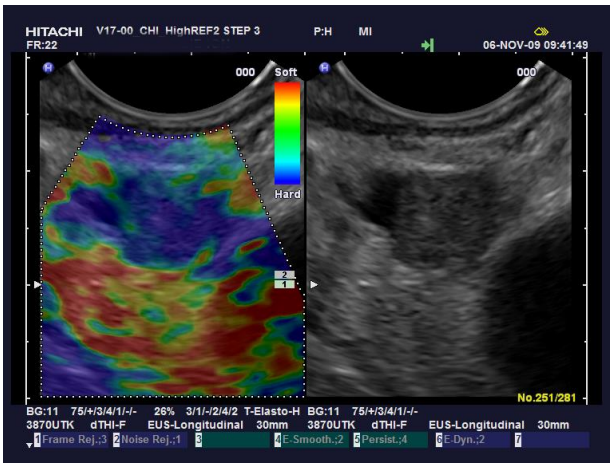
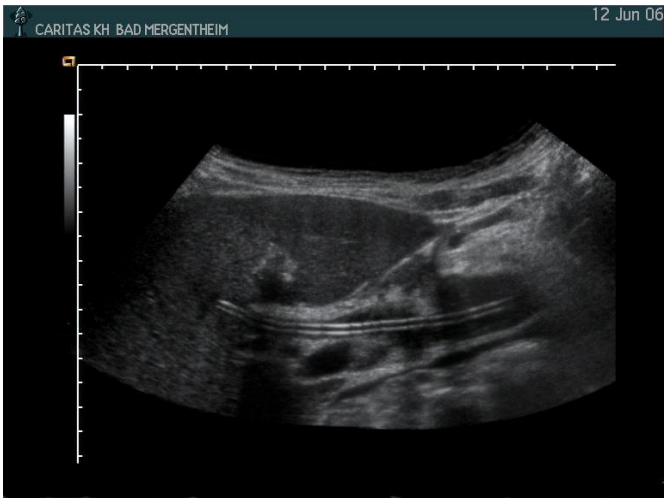


Findings following endoscopic treatment

After endoscopic therapy of a biliary obstruction with papillotomy and stent placement, the position of the stent can be controlled easily by ultrasound [Figure 84]. Other types of drainage also show a typical appearance, for example metal stents [Figure 85] and surgical drainage [Figure 86].

Figure 84 Bile duct carcinoma drained by stents can be easily displayed by grey scale ultrasound. A stent is shown using panoramic imaging (a) (white arrow). Stents can be sometimes better delineated using low mechanical index harmonic imaging techniques (b).

a



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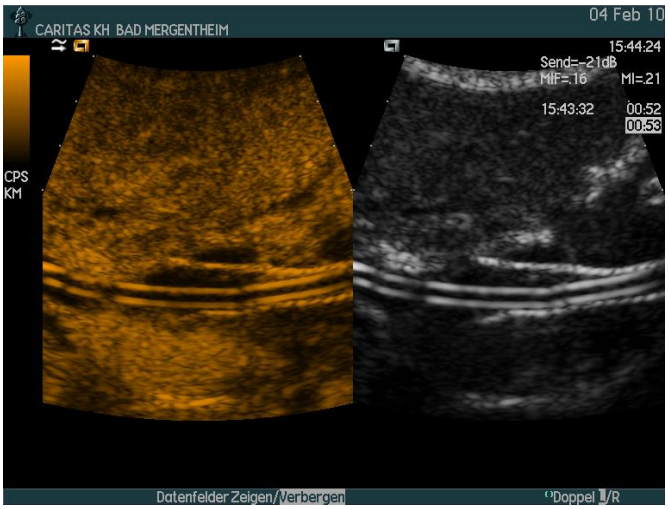


Figure 85 Metal stent in the distal bile duct (in between markers).

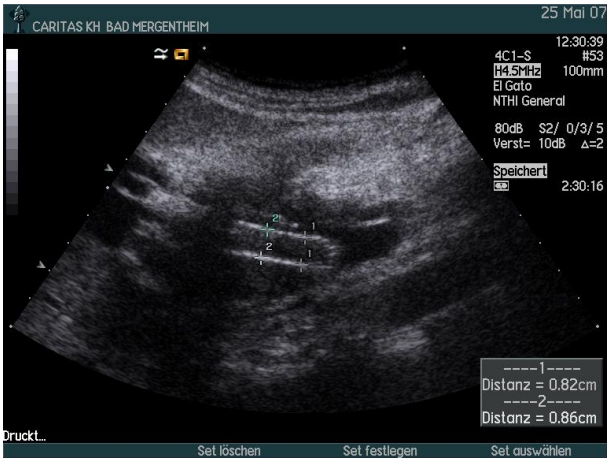
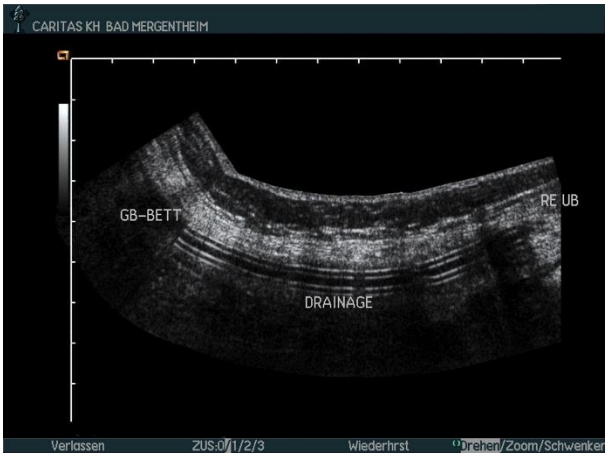


Figure 86 Surgical drainage displayed by panoramic ultrasound imaging [(81)]. GB-Bett: gallbladder fissure of the liver.



Aerobilia, Pneumobilia

Pneumobilia can be caused by a variety of diseases, for example perforation of stones of the bile duct system into the gastrointestinal tract. Most commonly, pneumobilia can be found after papillotomy, endoscopic stent drainage of the bile duct or surgical biliodigestive anastomosis. A very rare, but dreaded cause for pneumobilia, is a fulminant cholangitis with aerogenic bacteria. Characteristic signs that can be found in ultrasound examination are 'linear jerks' with typical reverberation ("ring-down-artefact"). In contrast to sessile calcifications, air is movable in the bile ducts if the patient position is altered [Figures 87 - 88].

Figure 87 Aerobilia after endoscopic biliary sphincterotomy: echogenic delineation of non-dilated intrahepatic bile ducts by luminal gas is considered an important criterion for successful biliary drainage.

a

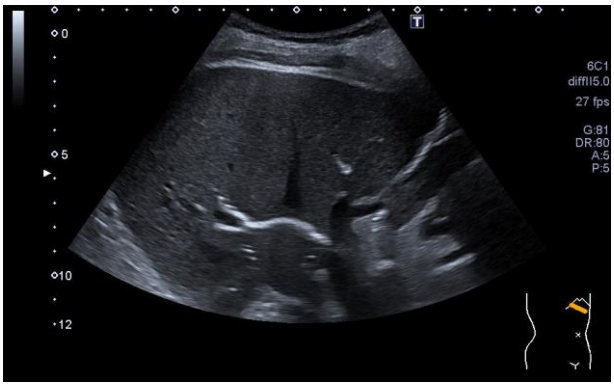
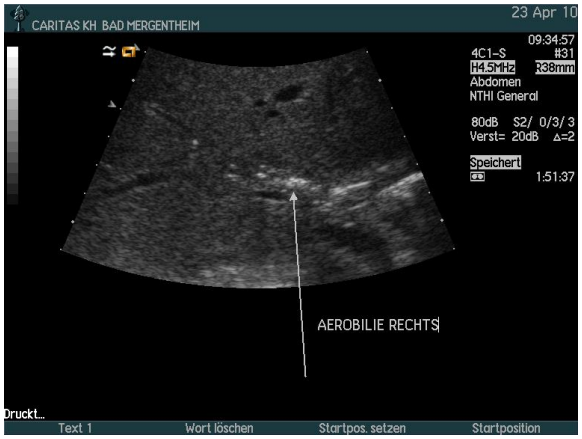


Figure 88 Aerobilia afollowing papillotomy and incomplete drainage in a case of Klatskins tumor. Aerobilia might be helpful in the differentiation of sufficient drainage (a, right liver lobe: aerobilia, intrahepatic ducts are not dilated) and insufficient drainage (b, left liver lobe: dilated intrahepatic ducts without aerobilia).

a



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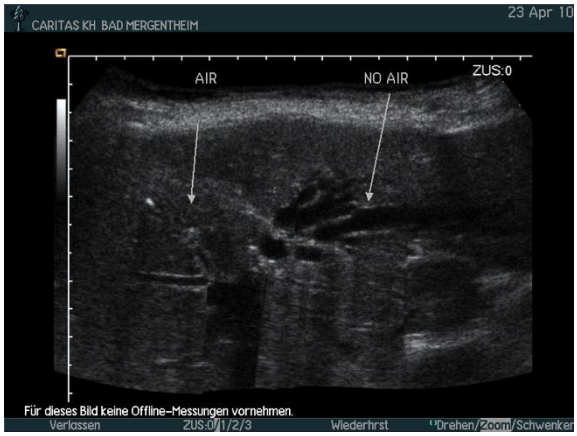


Congenital disorders

Choledochal cysts

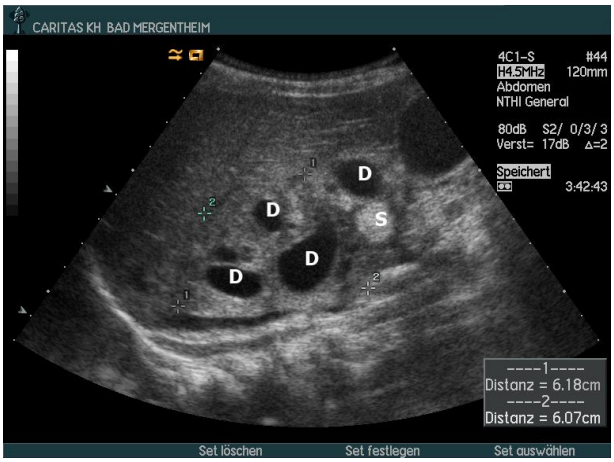
In infants, choledochal cysts are the most common cause of obstructive jaundice, but they may be found at any age. They are actually not cysts, but a dilatation of the common bile duct, which may cause secondary obstruction of other biliary ducts or the duodenum [Figure 89]. Choledochal cysts (table 10: classification of Todani Type 1 - 5) are often associated with other hepatobiliary tract abnormalities, for example anomalous pancreaticobiliary duct junction (APBDJ) [(82)]. Choledochal cysts may rupture spontaneously with potentially letal complications including cholangitis and sepsis [(83-85)].

Table 10 Todani classification for choledochal cysts [(82)].

Type 1	characterized by a segmental or diffuse fusiform dilation of common bile duct (50 - 90 %).
Type 2	diverticulum of common bile duct
Type 3	dilation of intraduodenal common bile duct (choledochocele)
Type 4	multiple cysts of extrahepatic bile ducts with (4A) or without (4B) cysts of intrahepatic ducts
Type 5	one or more cysts of intrahepatic ducts (Caroli's disease)

It is of importance that 2 – 10 % of the patients with choledochal cysts develop biliary tract carcinoma at a mean age of 35 years. Carcinomas may develop within the wall of the cyst, within the gallbladder or bile ducts. Therapeutically, complete cyst removal with biliary reconstruction, usually with Roux-en-Y hepaticojejunostomy, should be performed when a carcinoma is diagnosed in these patients. The role of ultrasound techniques is not yet fully determined, due to low incidence of this disease in adults and limited clinical experience. Magnetic resonance imaging (MRI) and endoscopic retrograde cholangiography (ERC) are the diagnostic methods of choice.

Figure 89 Choledochal cyst. Choledochal cysts are the most common cause of obstructive jaundice in infants and beyond infancy, but may be found at any age. This image shows tortuous distension of the main bile duct (D). Typically gallstones and sludge can be displayed (S).



New techniques

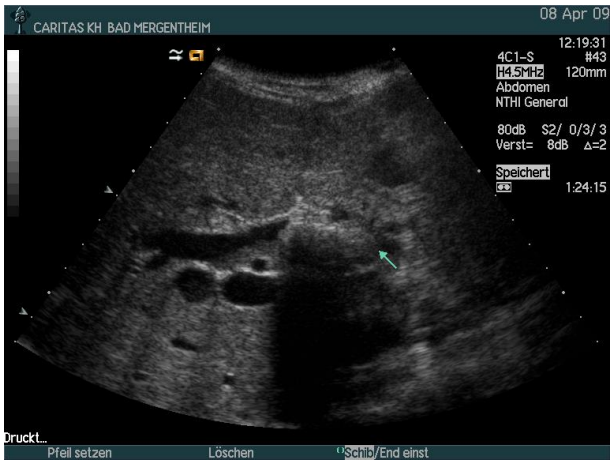
Contrast enhanced ultrasound has been introduced into routine practice for many presentations when imaging the liver, pancreas, kidneys, thyroid and for monitoring local ablative treatment, mainly of the liver, but also of other organs [(86-101)]. In biliary disease CEUS is helpful for the differentiation between “soft” stones or sludge and solid neoplastic lesions of the gallbladder or bile duct [Figures 34, 36, 46, 59, 68, 83, 90], for delineation of inflammatory lesions of the biliary system [Figures 68, 75], for diagnosis and staging of neoplastic disease of gallbladder and bile ducts [Figures 59, 82 - 83] and for guidance of treatment procedures [Figures 91 - 92]. However, its use varies throughout Europe with limitations in funding (e.g. UK NHS) precluding its regular use. New applications have also been introduced, for example, the application of BR1 (SonoVue®) into the bile ducts via a conventional endoscopic retrograde cholangiography (ERC) [(79, 102)]. Percutaneous transhepatic cholangiography and drainage (PTCD) is a procedure for diagnosis and treatment of dilated bile ducts in both malignant and benign biliary obstruction. PTCD has

some limitations due to the blind puncture technique of peripherally located intrahepatic bile ducts. Severe (major) complications have been described in about 2 % of cholangiography and up to 10 % of transcutaneous interventions, for example, sepsis, haemorrhage, abscesses, peritonitis and haematobilia. The latter is especially true when puncturing close to the liver hilum. Nevertheless, the complication rate varies with patients comorbidity and investigators experience. Ultrasound-guided PTCD (US-PTCD) has been described for dilated and non-dilated bile ducts and several studies have shown a reduction in complications and a faster access to the biliary ducts. CEUS-PTCD has recently been described in detail [(79, 102)].

Future studies in a larger numbers of patients are necessary to evaluate this new technique concerning (a) the optimal dosage, (b) the limitations and (c) additional indications [(79)]. Other hepatobiliary interventions have been recently summarized [(103, 104)].

Figure 90 Choledocholithiasis diagnosed by CEUS and contrast enhanced percutaneous cholangiography and treated by contrast enhanced ultrasound guided cholangiodrainage. Choledocholithiasis shown by B-mode may be confused with tumour like lesions (a), but contrast enhanced ultrasound may confirm this differential diagnosis since bile duct stones do not enhance (b).

a



b

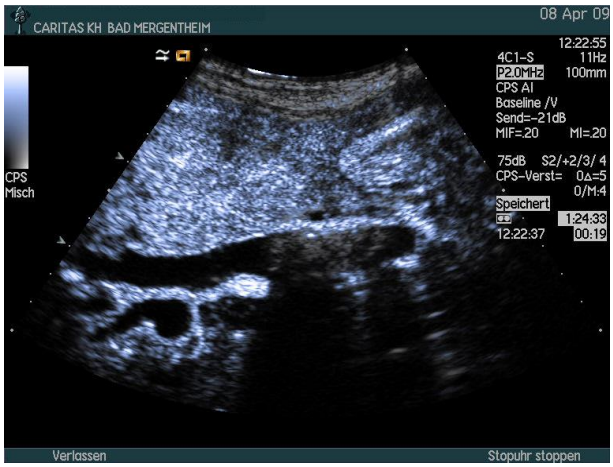


Figure 91 Intracavitary CEUS used for guidance of PTCD: the course of the drainage catheter and the intrahepatic bile ducts are enhanced after injection of the diluted ultrasound contrast enhancer into the drainage catheter.

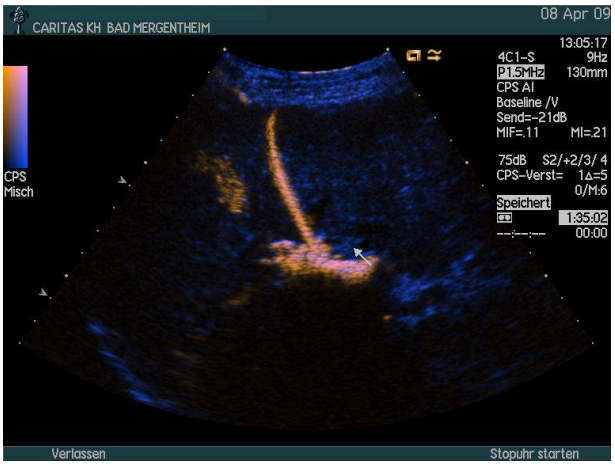
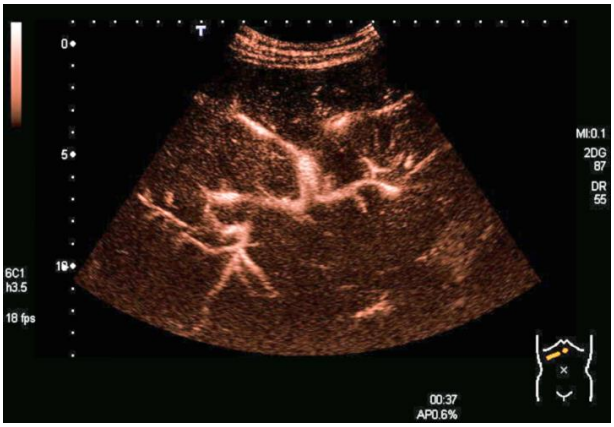


Figure 92 CEUS cholangiography after injection of the diluted ultrasound contrast enhancer into the percutaneous transhepatic cholangio-drainage catheter: non-dilated intrahepatic bile ducts are nicely delineated – complete biliary drainage is achieved.



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