Review

Ultrasound in the examination of the gallbladder – a holistic approach: grey scale, Doppler, CEUS, elastography, and 3D

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Abstract

Ultrasonography (US) is the essential imaging method in gallbladder examination being the most widespread and inexpensive technique. The method is indicated both in congenital and acquired disorders, inflammatory, tumoral, or degenerative pathology. Besides the basic technique (grey scale US), new sophisticated techniques exist: DopplerUS, i.v. contrast enhanced harmonic examination, tridimensional US, elastography. Each technique provides specific information, while their combination helps, in most cases, to establish the accurate non-invasive diagnosis. However, the US findings should be correlated with the patient's clinical exam and other imaging methods. This paper is a synthesis of literature combined with our own experience, aiming to present the US features of gallbladder pathology and the correlations within the clinical picture and other imaging methods. Relevant images for this integrative approach are presented. The final conclusion is the necessity for a correlation of all clinical and imaging data in order to obtain an accurate diagnosis.

Keywords: gallbladder, ultrasound, contrast enhanced ultrasound (CEUS), tridimensional ultrasound, elastography

Introduction

All cases suspected of biliary disorder benefit from ultrasound (US) examination as the first choice imaging method, performed right after the clinical examination. Using US the congenital anomalies, inflammatory conditions (acute, chronic cholecystitis), neoplasms (benign, malignant), cholecystosis (cholesterolosis, adenomyomatosis), gallstones, and associated complications are evidenced with high accuracy. Performed in emergency, US confirms or refutes the clinical diagnosis, at the same time assessing the severity of the disease [1].

The US techniques currently used are grey scale and Doppler. In the past years a number of new techniques have emerged, such as contrast-enhanced US (CEUS) or elastography, which proved to be very useful in the di-

agnostic process [2]. Tridimensional US also belongs to this category, but the technique is less used.

The aim of this paper is to review the ultrasound aspects in the main gallbladder (GB) diseases and to evidence the diagnostic value and limitations of i.v. CEUS in the light of the current state of knowledge. We also present information regarding the applications of elastography and 3D US. Emphasis is laid on the necessity to integrate the US findings with the clinical context and other imaging methods.

Ultrasound procedures

Grey scale two dimensional US (2DUS). It represents the basic procedure, bringing morphological information (evidences normal and pathological organs, liquid or solid structures, allows precise measurements) [3].

Doppler US. Its qualitative variant (Colour Flow Map- CFM) evidences the blood flow and its direction, while its quantitative variant (spectral Doppler) assess the blood flow velocity [4,5].

Intravenous contrast enhanced ultrasound (CEUS). The technique has entered in the current practice in the

last 10-15 years, its main application being liver tumoral pathology [6]. Taking into account that it depends on the operator and the type of equipment, in 2004 (with additions in 2008) CEUS guidelines were introduced for liver examinations and later on (2012) for extrahepatic structures, including the biliary system. Published data about CEUS for GB disorders are relatively scarce. The EF-SUMB guidelines of 2012 mention the role of the technique in the detection and/or exclusion of abscesses in acute cholecystitis and the evidence of gallbladder wall rupture in cases of associated perforation or to differentiate between GB tumours and biliary sediment [7].

Tridimensional ultrasound (3DUS). The technique is used for the assessment of the contours and the spatial representation of the organs enveloped in fluid, with applications in obstetrics. Information is gathered by uniform scanning performed by the examiner (free handed), or by a special transducer (mechanic or electronic) that scans in both directions concomitantly and fast enough to generate the impression of volume. The information obtained may be static or dynamic (4DUS). The 3D image results from the combination of two real planes perpendicular to a third reconstructed virtual plane. The device has special software, which uses the subtraction procedure in order to "uncover" the parenchyma around the liquid structures [8].

Elastography. It is a non-invasive technique for assessing the tissue stiffness. Several procedures exist, based on different physical principles and ways of representing data [3]. In broad lines, elastographic techniques may be classed as quantitative (output in kiloPascals or meters/sec) and qualitative (color coded). The examination technique differs according to the type of elastography applied or the equipment manufacturer. For data collection, either the transducer is placed over the ROI and there is a sequential compression at constant amplitude, or the transducer is kept still over the ROI for a few seconds.

Ultrasound examination technique. Normal aspect

The examination of the GB starts with a grey scale 2D ultrasound. The convex transducer (frequency 2.25 – 3.5 MHz for adults, 5MHz for children) is usually used. The optimal examination window is selected, which allows the visualization of the whole GB, followed by the selection of the region of interest (ROI). The examination is multidirectional and dynamic ("real time") and it assesses the aspect and size of the GB, wall thickness, content, pain at transducer palpation (US Murphy's sign). The Doppler examination used is CFM, applied along the walls, adjusted to low velocities of 2-10 cm/sec. The spectral technique is rarely used.
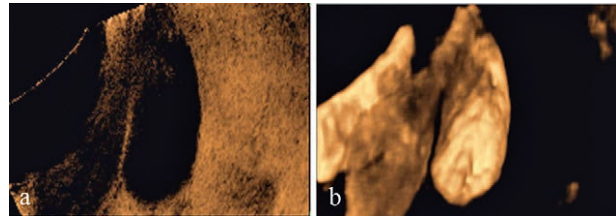

Fig 1. 3D ultrasonography of the gallbladder. Transparent mode visualizes the GB content (a). Surface mode visualizes the GB shape (b).

CEUS requires specific adjustment of the equipment for the "contrast" feature. The image is divided into two fields, focus is placed on the ROI, the mechanical index is lowered – IM (acoustic power) to an average of 0.10 [7]. The examination is continuous and starts at the moment of the contrast agent (CA) injection, marked as "0" second on the screen clock. The GB vascularization includes the cystic artery, therefore the examination has only two phases: the arterial phase (up to 20-30 seconds after CA injection), and the venous one (evidenced after up to 2-3 minutes). In the arterial phase the echogenicity of the GB wall increases. In the venous phase the wall seems to "melt" into the echogenic mass of the liver parenchyma [9]. Subsequently, an extensive examination of the liver is recommended, based on the patient's complaints and the clinical features. A recording in "avi" format is obtained. The result will be formulated for each time separately (arterial, venous, late). The image analysis will be qualitative and quantitative, using the analysis of the wash-out or time-intensity curves (TIC).

The 3D image of the GB may be represented in two modes: transparency mode – the GB appears transonic and the liver is more echogenic; the surface mode – the GB appears echogenic and the liver parenchyma is "extracted" from the image. In the transparency mode the GB content may be studied, while the surface mode provides information on its shape and position. Elastography for the normal GB is not relevant [10].

The normal GB aspect is that of a pear shaped structure, maximum dimensions 100/40 mm, with transonic content, no echogenic elements inside, thin walls, hardly visible, without vascular signal at the Doppler or CEUS examinations, and no perceivable rigidity (fig 1). We emphasize the absence of pain at transducer palpation.

Pathology

Acute cholecystitis (AC)
The GB wall inflammation is usually associated to lithiasis (about 6-11% of the patients with biliary complaints develop AC) [11]. AC without lithiasis is rare

(about 5-14% of all AC cases) [12], the most common causes being ischemia, hypotension, or a state of shock [13].

Ultrasound. Grey scale US is the first imaging examination performed after the clinical examination [14]. The method evidences: wall thickening > 4-5 mm, aspect of "double contour"; pain in the right hypochondrium at transducer palpation (US Murphy's sign, specificity 87%, positive predictive value 92% in AC with lithiasis) [15]; distension to hydrops of the GB lumen; fluid around the GB [16]. The sensitivity and specificity of US for the AC diagnosis reaches 88% (95% CI 0.74 − 1.00) and 80% (95% CI 0.62 – 0.98) respectively, while for the evidence of biliary lithiasis it is 84% (95% CI 0.76 – 0.92) and 99% (95% CI 0.97 – 1.00) respectively [17]. In experimented hands, the method can differentiate between catarrhal, phlegmonous, and gangrenous AC. The presence of air inside the GB is a sign of severity [fig 2]. Doppler examination evidences the arterial circulatory signal in the GB wall. The presence of a pulsating arterial signal increases the likelihood of the AC diagnosis. With the CEUS examination the GB wall will appear to take up the contrast agent quicker, intensely, and evenly during the arterial time. The washout is late. The echogenicity variation generated by the CA is assessed in relation to the liver parenchyma. CEUS consolidates the diagnosis of GB wall inflammation, evidences/excludes the wall perforation (interruption of the wall represented by the absence of the CA load at this site), the abscesses in the adjacent liver parenchyma, or the micro-abscesses associated with the pathological thickening of the GB walls. In addition, the method is useful in the differentiation from the portal venous disorders of the GB, in which the CA load occurs in the portal venous time (fig 3)[18]. The 3DUS and elastography do not bring additional benefits to the AC diagnosis.

Other imaging examinations. Magnetic resonance cholangio-pancreatography (MRCP) has a reduced sensitivity in evidencing GB wall oedema (~ 69%), but it is highly accurate in detecting gallstones (100% sensitivity) [14]. The use of MRCP in the AC diagnosis is reserved for clinical studies. Abdominal computed tomography (CT) evidences the oedema of the GB wall [19] but it may miss the presence of radio-transparent gallstones [20,21]. CT is not mandatory in the diagnosis of AC, but it is useful in detecting associated complications: emphysematous cholecystitis or perforation of the GB wall [22, 23]. GB scintigraphy with 99mTc or morphine (HIDA scan) may be indicated as a diagnostic method if the US diagnosis is still uncertain. The technique involves the i.v. injection of iminodiacetic acid traced with 99mTc or morphine, the substances being taken up by the liver and
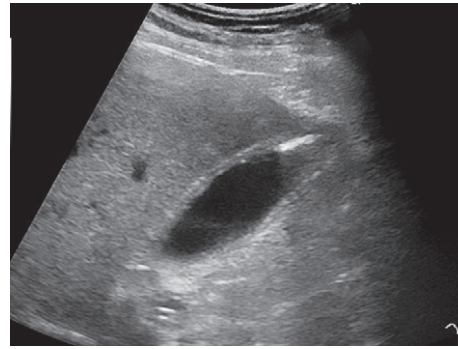

Fig 2. Severe acute cholecystitis (2D grey scale aspect). A diagnostic criterion is thickened GB wall. The presence of air in the GB lumen is a sign of severity.
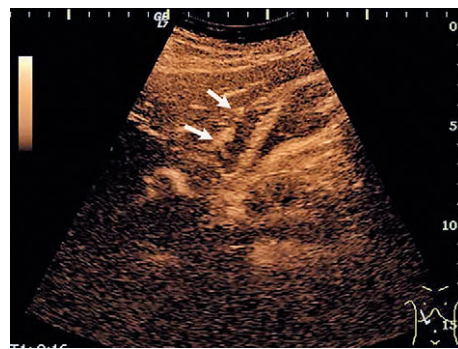

Fig 3. Gangrenous acute cholecystitis (CEUS examination). Abscesses in the GB wall. CEUS evidences gaps in the GB wall in the arterial phase (arrows)

excreted into the bile ducts, the objective being to assess the permeability of the cystic duct, the common bile duct, or the ampulla of Vater.

Chronic cholecystitis

The disease is a long-term, irreversible inflammation of the GB wall, often associated with biliary lithiasis including two entities: the porcelain gallbladder (diffuse or localized calcification of the wall) [24,25] and xantogranulomatour cholecystitis (about 2% of the cholecystectomy pieces; characterized by the presence of inflammatory infiltrate formed of lymphocytes, fibroblasts, polymorphonuclear cells and foamy histiocytes at the wall level) [26,27].

Ultrasound. 2DUS examination evidences focal or diffuse wall thickening and parietal nodules. The sign of the double arch may also be evidenced [28] (the first arch formed by the GB wall, the second by the intraluminal gallstones); an anechoic layer is also evidenced between the 2 structures. In the case of the porcelain GB the presence of the shadow cone that starts from the walls con-
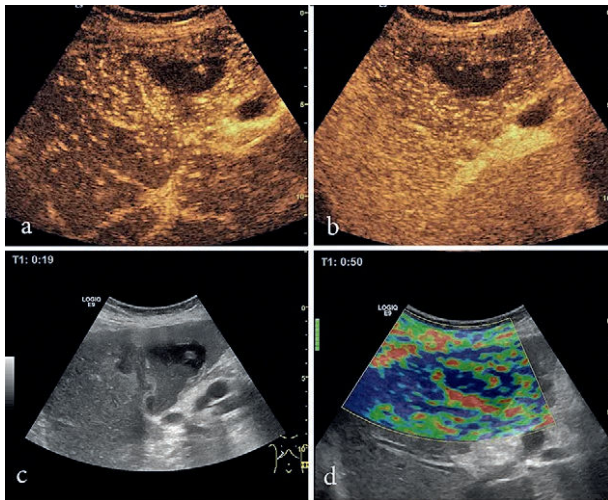
Fig 4. Xanto – granulomatous cholecystitis. Holistic aspect (2DUS, CEUS, elastography). The loading of the contrast agent is fast but uneven in the arterial phase (a), followed by moderate clearance (b). A marked thickening of the GB wall with the aspect of a pseudo-tumor may be seen (c). Elastography shows moderate stiffness around the galblader (d). The overall aspect cannot be different from a GB neoplasm, given the extent of the phenomenon.

Fig 5. Gallbladder cholesterolosis. a) Grey scale aspect; b) CEUS aspect. Even loading of the contrast agent in the arterial phase (20 sec after i.c. injection).

Fig 6. Gallbladder cholesterolosis, 3DUS aspect. Cholesterolosis is suggested by the polypoid structures disseminated on the inner surface of the GB wall.

stitutes the diagnostic element [29]. CEUS will evidence hyperloading at the wall level in the arterial phase [9]. There is no significant clearance of the CA in the late phase. Elastography may evidence increased stiffness in the cholecystic bed (fig 4).

Other imaging techniques. In the case of the porcelain GB, the abdominal X-ray and CT images have a typical aspect. In xantogranulomatous cholecystitis the alterations identified on the contrast CT scan refer to the marked wall thickening and the wiping out of the partition with the liver parenchyma. The infiltration of the parenchyma may lead to the false positive diagnosis of neoplasm.

GB cholesterolosis

The disorder is characterized by the infiltration of the GB wall (lamina propria) with lipid-loaded macrophages [25]. Two macroscopic forms are known: polypoid and diffuse. Cholesterolosis in association with gallstones represents one of the most frequently encountered conditions [30] being reported in 9-26% of the surgical cases [31]; the necrotic cases have a prevalence of 12%, 1/3 of them being the nodular polypoid form [32]. The disease is benign and the complications (pain, bile ducts obstruction with jaundice, acute pancreatitis) are secondary to a GB wall disjunction.

Ultrasound. 2DUS evidences the diffuse form with difficulty, while the polypoid form is distinguished by echogenic lesions, round or lobular, immobile. Doppler
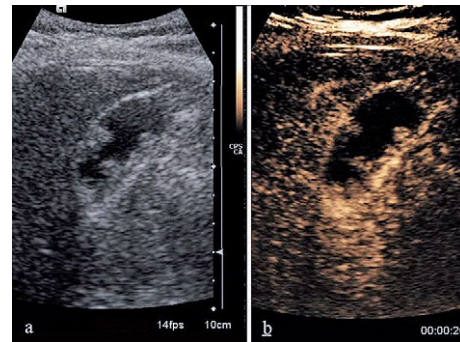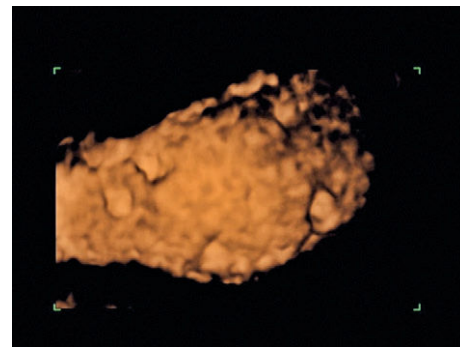
examination does not provide additional data. CEUS will evidence the GB wall and polyps loading during the arterial phase. Washout is slow, moderate and even. Cholesterolotic polyps are hyper-capturing in the arterial phase in 93% of the cases, and become hypo- (64%) or iso-capuring (36%) in the late phase [33] (fig 5). 3DUS may evidence filling defects at the level of the GB contour. Elastography is irrelevant for the diagnosis. As a rule, other imaging methods are not necessary, ultrasound being the gold standard for this disease (fig 6).

Other imaging procedures. Are not relevant and currently used for the diagnosis of GB colesterolosis

Adenomyomatosis

It is relatively frequent disorder (1-9% of the cholecystectomy pieces) [34,35], characterized by the presence of intramural diverticuli, associated or not with wall thickening. There is also intraluminal accumulation of cholesterol, with possible cholesterol crystals precipitated from the bile trapped inside the intraparietal diverticuli. It is not associated with adenomatous development
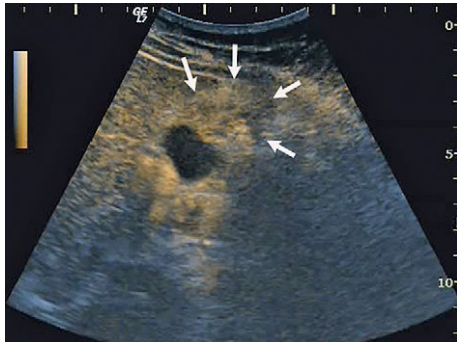
Fig 7. Gallbladder adenomyomatosis (CEUS). Enhancement of the lower part of the gallbladder in the arterial phase (arrows).
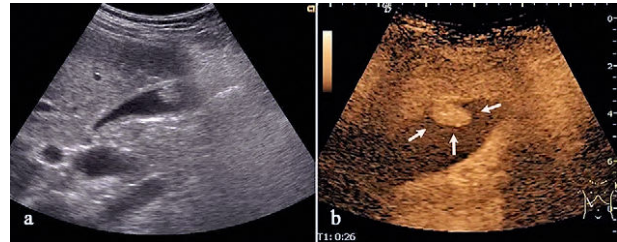

Fig 8. Adenomatous polyp. a) Greyscale ultrasonography. b) CEUS. During the arterial phase the polyp (arrows) is evenly loaded. In the venous phase the CA is discharged.
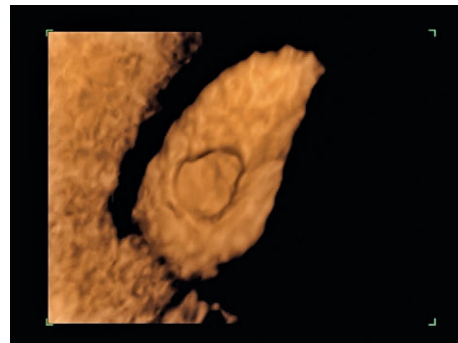

Fig 9. Adenomatous polyp (3DUS). The examination evidences (surface mode) a gap in the GB wall.

of the epithelial layer. It is considered a benign condition, though the conjectural association with GB cancer may plead for a premalignant status [36]. In a retrospective study of 4560 GB resection samples, Natabame et al evidenced GB cancer in 6.6% of the patients with adenomyomatosis [37].

Ultrasound. Grey scale US may detect echoic foci due to cholesterol deposits, with comet-tail artefacts – a highly specific sign [38, 39]. The GB wall thickening may be diffuse of localized, in which case the differentiation from a GB carcinoma is required. The Doppler examination does not provide additional information for the diagnosis. CEUS evidences an uneven, focal load of the GB wall, without washout in the venous phase (fig 7). 3DUS and elastography are not relevant for the diagnosis.

Other imaging procedures. CT scan may evidence GB wall thickening. However, it is not the choice examination for this condition.

Inflammatory polyps

They represent fibrous and granulation tissue proliferations inside the GB.

Ultrasound. With the 2DUS examination the polyps appear small, between 5-10 mm, sessile or pedicled. Polyps larger than 10 mm may be sometimes confused with malignant ones [40]. Doppler examination evidences vascularization inside the polyp. CEUS evidences focal arterial overload at the polyp level. No significant washout is evidenced in the venous phase. 3DUS detects a "gap" in the GB wall, well delimited. In practice no other imaging methods are used [41]. Elastography does not provide additional diagnostic information in this disease.

Other imaging procedures. There are no useful procedures used for the diagnosis of inflammatory polyps.

Adenomatous polyps

Adenomatous polyps are benign epithelial growths (tubular, papillary, tubule-papillary) with an incidence of

0.5% in the general population [42]. The premalignant condition is suggested by the large size, which may develop towards filling the GB lumen, and by the association with chronic cholecystitis. The incidence of carcinoma is 43-77% for polyps larger than 10 mm [43], and 100% for those over 20 mm [44]. Another risk factor is age between 50-60 years [45].

Ultrasound. Grey scale US evidences an echoic, pedicled structure, with a narrow implantation basis. It is differentiated from calculi by the absence of mobility at the patient's movement and the shadow cone.

The Doppler test may differentiate benign from malignant lesions. The assessment is based on the presence of the colour flow, vascularization patters, flow velocity, but with low sensitivity for small tumours due to the low flow velocities [46-48]. With CEUS the adenomatous polyps appear overloaded with CA in the arterial phase (78%), or iso-capturing (28%), while in the late phase they present lower (44%) or the same loading (56%) as the liver parenchyma (fig 8). 3DUS evidences a circumscribed deformation in the GB wall. Elastography does not bring diagnostic benefits [fig. 9].

Other imaging procedures. CT has a relatively small sensitivity as compared to 2DUS regarding the detection of small polyps [41]. Echoendoscopy has a histological

prediction rate of 96%, as compared to the 76% provided by transabdominal US [49]. Given the difficulty in establishing the presence of dysplasia or in situ cancer in the case of adenomatous polyps based solely on imaging methods, cholecystectomy is recommended for patients over 50 years old and polyps over 1 cm [50,51]. Another surgical indication is represented by the growth tendency evidenced by a systematic follow-up at 3-6 months.

Galbladder carcinoma (GBC)

It is a severe disease, with a reserved prognosis being asymptomatic or with very few symptoms until the late stages. Its incidence is 1-2 cases/100,000 population [52]. About 1-2 % of the GBC cases are detected by chance in patients submitted to GB resection for gallstones [53,54]. The risk factors of GBC include: biliary lithiasis (70-90%) [55]; porcelain GB; adenomatous polyps (especially>10 mm) [56], chronic infections (Salmonella typhi or Helicobacter billis) [57-59]; biliary cysts of the biliary canal (about 14.3% of the malignant GB tumours in patients over 20 years old) [60]; pancreato-biliary junction abnormalities [61,62]; exogenous carcinogenic agents; drugs (methyldopa and isoniazide). Pathology is mainly represented by adenocarcinoma (~90%), though squamous carcinoma, neuroendocrine tumours, lymphoma, or sarcoma have also been found.

Ultrasound. Grey scale US may evidence several macroscopic models, according to the tumour stage. In the initial polypoid stage, GBC have no characteristic aspect. The method evidences the tumoral structure, the malignancy criteria being represented by the wide implantation base, usually 10 mm, and the exacerbated erratic arterial Doppler signal. The infiltration of the GB wall layers represents another element of suspicion. In advanced stages, the GB carcinoma appears as a parenchymatous mass involving the GB bed, often centered by a gallstone image. Intrahepatic ducts dilation, in the context of the hilum invasion, is frequently associated. The Doppler US has a controversial diagnostic value. CEUS evidences hyper-capture of the CA in the arterial phase and hypo-capture in the late phase. The differential between benign and malignant lesions can be made with sensitivity and specificity of 88.2%, and of 78.7%, respectively using the arterial phase and of 100%, and of 87.2%, respectively using the venous phase (fig 10, fig 11) [33]. Lin Na Liu et al studied the role of CEUS in GB tumoral pathology in a multicenter study. They investigated the intratumoral vascularization, the relation tumour-wall, and the CEUS washout features. The diagnostic accuracy has been higher when an association of these elements has been used. During the arterial phase the vascular aspect was predominantly branched. It has been found that malignant tumors present a faster washout time (41.4 sec) than benign ones (58.2 sec). The evidence of parietal disruption and liver infiltration suggest malignancy [4]. The accuracy in the evaluation of the tumoral invasion of the liver as assessed by EUS-CE-US (contrast echoendoscopy), was 92.9% compared to 78.6% in conventional echoendoscopy. The destruction of the GB wall is highly predictive (84.8% sensitivity and 100% specificity) of malignancy [33]. In 2011 the non liver CEUS guidelines stated that the difference between benign and malignant is based mainly on clinical criteria and the polyp size over 10 mm representing an indication for cholecystectomy. CEUS has not been introduced yet in the current clinical guidelines and practice, its role in the benign/malignant differentiation of the GB polyps being still under evaluation [18]. The 3DUS examination may be useful as it evidences the tumoral mass. In the transparent mode the tumour may be assessed from the point of view of its extent and location. Elastography is useful only when the tumour is large and superficially located. The method evidences the increased stiffness, which may have an uneven distribution (fig 12).

Other imaging examinations. CT and MRI may be useful for detecting liver metastases and the invasion of the GB bed.

Neuroendocrine tumours of the GB (GBNET)

The neuroendocrine tumours of the GB are rare entities (about 0.5% of the total of human neuroendocrine tumours) [63]. Among the carcinoid tumours of the GB, almost 50% are carcinomas with endocrine cells [64]. While the classical carcinoid tumours of the GB rarely determine metastases, the atyipical variants are much more aggressive. Considering the difficulty to differentiate preoperatively the benign or malignant nature, any polypoid lesion over 1 cm is an indication for cholecystectomy. Prognosis is established based on the histopathological features, imaging, and intraoperative staging. In a study of 435 malignant tumours of GB, Duffy et al reported only 13 cases of such tumours [65]. Very rarely the diagnosis is established preoperatively, the symptoms being unspecific. The macroscopic aspect is of a solid mass, yellow, cauliflower-like, initially occurring in the lamina propria, then infiltrating the muscular and serous layers [66]. The evidence of neuroendocrine cells is mandatory for the diagnosis.

Ultrasound. Grey scale US evidences the tumour, but not its nature. In general the tumours are large. More rarely they may be polypoid, exophytic. As in the case of the GB carcinoma, the neuroendocrine tumour is detected when it goes beyond the GB walls and invades the liver parenchyma [66]. The Doppler US may evidence an arterial signal within the tumour. CEUS evidences a quick loading of the CA by the tumour and washout
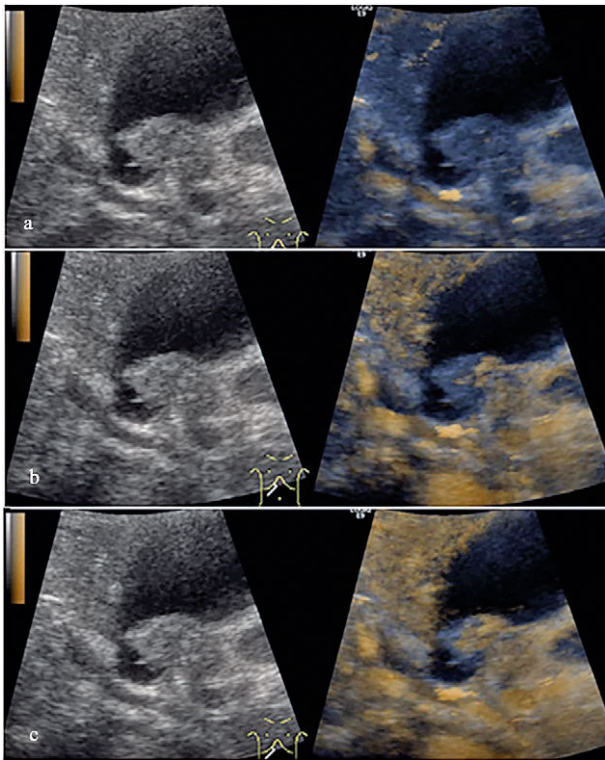
Fig 10. Early carcinoma of the gallbladder (polyp). CEUS evaluation. Progression of the contrast agent in arterial time into the tumor is represented (a,b,c).
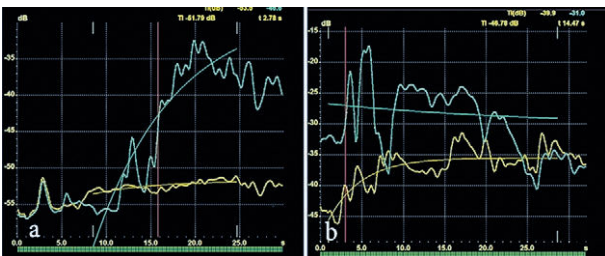

Fig 11. Carcinoma of the gallbladder (same case as fig 10). Time intensity curves representing income (a) and outcome (b) of the penetration of the contrast agent into the vascular bed.
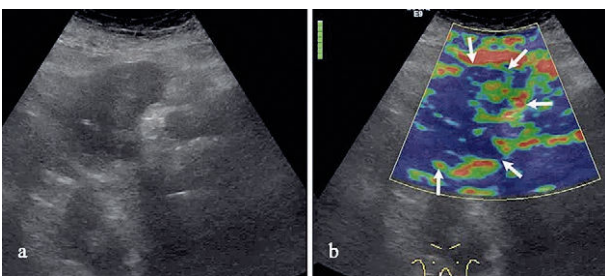

Fig 12. Advanced gallbladder carcinoma. a) Grey scale ultrasonography: a typical image of a gallbladder a tumor with blurred margins is represented; b) Elastographic examination. The invasion of the liver parenchyma by the tumor may be seen.
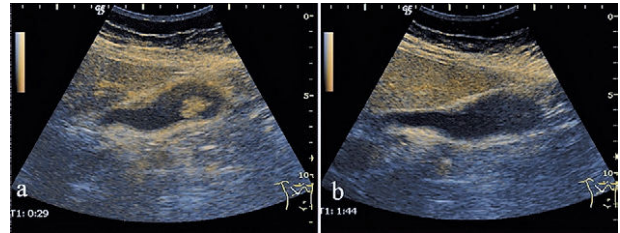

Fig 13. Neuroendocrine tumor of the gallbladder. CEUS: a) Arterial phase; b) Venous phase.

in the venous phase (fig 13). Elastography evidences rigidity when the tumour is large and invades the liver bed. Echoendoscopy is more sensitive and specific than 2DUS. In a study of 194 patients, 58 submitted to cholecystectomy, the EUS versus CEUS accuracy was 97% vs. 76% regarding the histological prediction [49]. EUS evidences the invasion at the level of the GB wall, and the dissemination to the local-regional lymph nodes (portal, peripancreatic) [67]. Echoendoscopy also allows the harvesting of the biliary fluid for cytological analysis (73% sensitivity) [68], while EUS fine needle aspiration biopsy is an accurate method, cumulated sensitivity 0.84 (95% CI: 0.78-0.88) and cumulated specificity 1.00 (95% CI: 0.94-1.00) in the exploration of gallbladder tumours [69].

Other imaging techniques. The role of CT, EUS-FNA, MRCP, ERCP is known in the assessment of the malignant character and the loco-regional extension. Some neuroendocrine tumours present receptors for somatostatin, which makes scintigraphy, PET-CT, and PET-MRI labeled with somatostatin complementary methods in their identification [70]. CT may evidence the tumoral mass, liver invasion and possible secondary determinations [71]. The CT scan combined with positron-emission tomography (PET-CT) is useful in evidencing postoperative tumour recurrence or advanced disease, thus avoiding a falsely curative surgical intervention. MRI, especially MRI cholangiography, are useful techniques in evidencing loco-regional invasion, the invasion of the hepato-duodenal ligament, portal vein, and lymph nodes [72]. ERCP is useful from a therapeutic point of view, providing the prosthesis for the biliary tree in the case of obstructive jaundice secondary to the common bile duct invasion.

Intracholecystic metastases

The GB metastases may have as its origin, the stomach, colon, rectum, liver, uterus, skin (melanoma), ovaries, or appendix, representing about 4.8% of all GB malignant tumours [73]. 2DUS evidences wall thickening and calcifications, parenchymatous masses adhering to the wall and protruding into the lumen and/or infiltrating the liver. The accuracy of local or distant staging is limit-
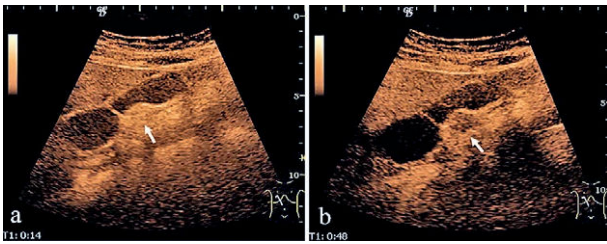
Fig 14. Metastasis into the gallbladder wall (arrows). CEUS: a) Arterial phase; b) Venous phase.
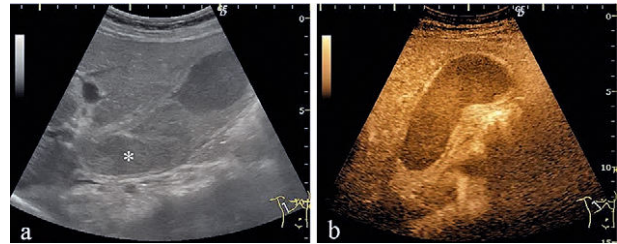

Fig 15. Pseudotumoral GB sediment. False tumor image at the level of the infundibulum. a) Grey scale ultrasonography (asterix); b) CEUS aspect with no vascularization (tumor is ruled out).
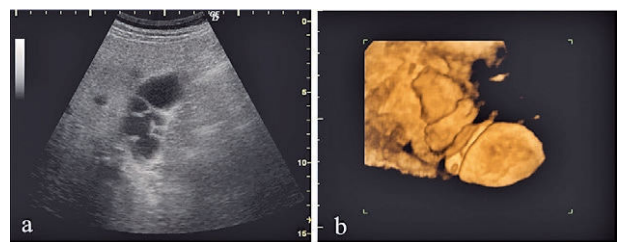

Fig 16. Malformation of the gallbladder: a) Grey scale ultrasonography; b) 3D ultrasonography.

ed. In a study of 26 patients, the sensitivity of evidencing liver infiltration or lymph node metastases was 50% [74].

Ultrasonography. Doppler examination is irrelevant in the diagnosis of intracholecystic metastases. CEUS evidences the metastases in the form of gaps situated in the GB lumen or wall, with marked load in the arterial phase and washout in the venous phase, distinct from that of the GB wall (fig 14). The 3DUS, surface mode, evidences tumoral masses. Elastography detects stiffness and is relevant within the large tumours.

Other imaging procedures. The use of CT is in relation to the detection of the primary site of the tumour.

Portal venous cholecystopathy

Together with portal cholangiopathy it is an integral part of the pathophysiological entity called portal hypertensive biliopathy, a cholangiopathy associated with portal hypertension or with portal cavernoma. Portal biliopathy is a late complication of portal hypertension and it is more frequently encountered in cases of extra-hepatic portal vein obstruction (81-100%) [75-77] or idiopathic portal hypertension, not induced by cirrhosis (9-40%) [78]. Two mechanisms are incriminated in its etiopathogenesis: external compression caused by the collateral veins and ischemic injuries of the biliary tree due to portal thrombosis. Symptoms, when present, include: jaundice, pruritus, or signs of angiocholitis. The treatment targets portal hypertension and the biliary obstruction, while in the refractory cases or advanced disease liver transplantation is recommended.

Ultrasound. 2DUS evidences the marked uniform wall thickening. Characteristic imaging features include small, elongated transonic gaps in the GB wall thickness. These alterations associated with the signs of portal hypertension are sufficient for establishing the diagnosis. The Doppler examination may sometimes evidence continuous portal venous flow. CEUS evidences loading of the walls in the portal venous phase in about 35-40% of patients with extrahepatic portal vein obstruction [79,80]. 3DUS and elastography are not useful in the diagnosis.

Other imaging procedures. MRI cholangio-portography and ERCP (in cases requiring endoscopic treatment)

are the main methods of investigation. High-resolution US and EUS are also useful for the diagnosis.

Cholecystic sediment

It represents a semi-fluid or viscous mixture resulted from the precipitation of bile salts and acids. It occurs in the prolonged absence of the GB contraction and may constitute a real risk factor for the development of non-lithiasis cholecystitis. The differentiation of the immobile GB sediment from the GB carcinoma may be difficult. CEUS makes the differentiation in 100% of the cases: due to the absence of vascularization at the level of the sediment, the CEUS aspect is without loading both in the arterial and late phases (fig 15).

Hemobilia

It is rare and difficult to assess clinically but sometimes is confirmed by endoscopy. Causes include: lithiasic cholecystitis, trauma (including iatrogenic), tumours (liver, extrahepatic biliary tree or GB), vascular abnormalities, coagulation disturbances. Laing et al identified traumatic etiology in 50% of the cases, spontaneous in 28%, inflammatory in 22%, coagulation disturbances being present in almost half of the patients [81]. The 2DUS shows echogenic content diffused in the GB lumen. Gallstones are difficult to be seen in such circumstances and so are the tumours. CEUS shows non-capturing hematoma or clots. In cases of active hemorrhage (arterial or venous) the CA extravasation from the vascular bed may be seen. CT uses the attenuation coefficient in establishing the diagnosis

Gallbladder malformations

These are rare conditions that have clinical manifestations immediately after birth. In the adult they represent shape abnormalities that may cause dyspeptic complaints. Grey scale US may suggest the condition. 3DUS is more relevant as it may evidence the anatomical features of the GB (fig 16).

Limitations of the ultrasound methods

The US examination of the GB is very valuable and useful in the diagnosis of the GB disorders. 2DUS is operator-dependent. Doppler is useful, but with an orientative value. CEUS is useful in the diagnosis of GB diseases. The limitations of CEUS in GB pathology overlap with the general ones. Among the lethal side effects are anaphylactic reactions. These are rare and reported in less than 0.002% [82]. CEUS also requires a high qualification in ultrasound interpretation. EFSUMB have established 3 hierarchical levels, recommending CEUS to be performed by highly experienced examiners [83]. Regarding the differentiation between benign and malignant polyps, the role of CEUS has not been established by practice guidelines as yet.

Conclusions

Ultrasound examination of the gallbladder remains the first-instance method for all gallbladder complaints. Current techniques are numerous, some focused on morphology (2DUS, 3DUS), some on circulation (Doppler, CEUS), other oriented on assessing rigidity. The combination of all these techniques leads to the establishment of an accurate diagnosis in most inflammatory or tumoral GB diseases. The patient's clinical picture remains an essential criterion. An appropriate selection of other imaging procedures is also very important for the final diagnosis.

Conflicts of interest: none

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