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REVIEW

Gallbladder reporting and data system (GB-RADS) for risk stratification of gallbladder wall thickening on ultrasonography: an international expert consensus

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Abstract

The Gallbladder Reporting and Data System (GB-RADS) ultrasound (US) risk stratification is proposed to improve consistency in US interpretations, reporting, and assessment of risk of malignancy in gallbladder wall thickening in non-acute setting. It was developed based on a systematic review of the literature and the consensus of an international multidisciplinary committee comprising expert radiologists, gastroenterologists, gastrointestinal surgeons, surgical oncologists, medical oncologists, and pathologists using modified Delphi method. For risk stratification, the GB-RADS system recommends six categories (GB-RADS 0–5) of gallbladder wall thickening with gradually increasing risk of malignancy. GB-RADS is based on gallbladder wall features on US including symmetry and extent (focal vs. circumferential) of involvement, layered appearance, intramural features (including intramural cysts and echogenic foci), and interface with the liver. GB-RADS represents the first collaborative effort at risk stratifying the gallbladder wall thickening. This concept is in line with the other US-based risk stratification systems which have been shown to increase the accuracy of detection of malignant lesions and improve management.

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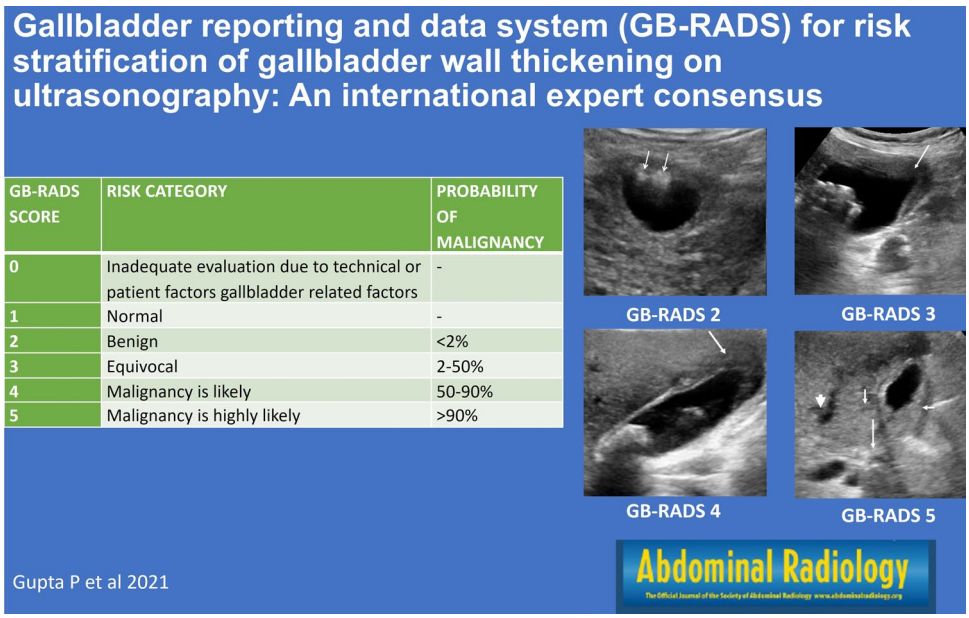
Graphical abstract



Keywords Gallbladder cancer · Ultrasound · Method · Scoring

Abbreviations

GB-RADS	Gallbladder reporting and data system
US	Ultrasound
GBC	Gallbladder cancer
RAS	Rokitansky-Aschoff sinuses
CBD	Common bile duct
CT	Computed tomography
MRI	Magnetic resonance imaging

Introduction

Pathologies affecting the gallbladder are among the most common encountered in day-to-day clinical practice. These present as a wide spectrum encompassing both benign and malignant diseases. Gallbladder cancer (GBC) is more common in certain regions of the world, including Mexico, Chile, Eastern Europe, North India, and South Pakistan [1]. Advanced GBC carries a dismal prognosis [2, 3]. This poor outcome associated with GBC is due to non-specific clinical features, leading to a delay in diagnosis at a stage when the disease is metastatic. GBC can present as gallbladder wall thickening, polypoid intraluminal lesions, or a mass [4]. The diagnosis of wall thickening type of GBC is challenging as gallbladder wall thickening can be encountered in both benign and malignant conditions [5]. The ability to appreciate the significance of wall thickening as being representative of GBC is low at preoperative evaluation, leading to 'incidental' GBC, or worse still, disease advancement and poor prognosis [6].

Transabdominal ultrasound (US) is a widely available, cost-effective, radiation-free modality, which is excellent for visualization of the gallbladder. It is the initial method of choice for screening and identification of gallbladder pathologies, based on which further investigations are directed [7]. With technical advances, the diagnostic accuracy of US has significantly improved over the years [8]. US is the best suited modality for screening and risk stratification of non-acute gallbladder wall thickening. If US findings are suggestive of a benign pathology, patients can be managed without further investigations, thus reducing the treatment cost, especially in resource poor countries. On the other hand, if US evaluation is inadequate or suspicious for GBC, further investigations can be planned to allow further characterization of the observed lesion.

We, thus, conducted an International Consensus for the proposal of a risk stratification system for gallbladder wall thickening (gallbladder reporting and data system: GB-RADS) in non-acute setting on US. This concept is in line with the existing reporting and data systems for other organs.

Data collection

Rationale and scope

Even though gallbladder wall thickening is a common finding on US, there are no existing reporting and risk stratification systems. This leads to significant variability in US reporting of gallbladder abnormalities [9]. This International Consensus was conducted to develop objective guidelines for reporting and risk stratification of gallbladder wall abnormalities in non-acute setting on US based on the existing literature and expert opinion. The goal is early detection and hence improved outcomes in patients with GBC. These recommendations are intended to guide practitioners who perform US assessment of gallbladder wall thickening. They should not be considered as standards.

Consensus process

GB-RADS encompassed several stages, aiming to systematically reach International Consensus on the US findings defining the risk of malignancy in non-acute gallbladder wall thickening. In the first instance, a systematic review of the literature using PubMed and Embase databases was performed (Supplementary material). The protocol was registered in PROSPERO (international register for systematic reviews with the registration number CRD42020204625). The data extracted from the systematic review guided the organization of the subtopics and informed subsequent literature selection. The GB-RADS was achieved through a Delphi-like consensus using multidisciplinary team members from Asia, Europe, Australia as well as North and South America, in a combination of electronic and web-based rounds. The consensus statements were formulated by a multidisciplinary panel comprising 40 international specialists in Radiology, Gastroenterology, (medical and surgical), Oncology (medical and surgical), and Pathology. Members of the panel were selected because of their experience, publication track-record, and knowledge in hepatobiliary diseases.

A core committee comprising nine experts developed the first draft of survey statements. These statements were sent via email to the panel of experts for voting. A statement was accepted if 80% of participants voted 3 (agree) or 4 (strongly agree) on a scale of 1–4 (with 1 and 2 indicating strongly disagree and disagree, respectively). Statements not achieving agreement were further revised and subjected to the second round of voting. Finally, a web meeting was conducted in January 2021 to discuss statements for which consensus was not reached after two rounds (Supplementary Tables S1–S5). Based on this web meeting, the GB-RADS working group has defined six categories for risk stratification. These include GB-RADS 0—incomplete evaluation; GB-RADS 1—normal appearance; GB-RADS 2—benign; GB-RADS 3—equivocal; GB-RADS 4—malignancy is likely; and GB-RADS 5—malignancy is highly likely. The probability of malignancy in each GB-RADS category was based on the literature review (as a part of systematic review discussed above) and expert consensus.

The manuscript was drafted by the core committee and was critically reviewed and approved by every author.

Technical aspects

US of the gallbladder should be done after at least 6 h of fasting [10]. Evaluation is preferably performed with a convex transducer (frequency range, 1–5 MHz). Additional evaluation with a higher frequency (6–12 MHz) linear transducer should be performed when the evaluation with the convex transducer is equivocal or in thin built patients where the abnormality falls in the near field. While performing US of the gallbladder, the patients' position should be changed to lateral decubitus, and if required to semi-recumbent or erect to visualize all parts of the gallbladder and demonstrate the mobile intraluminal contents [11, 12]. Different insonation angles should be utilized to evaluate the gallbladder completely. Gallbladder evaluation should be done in sagittal as well as axial planes. The focus and depth should be adjusted to allow accurate assessment of mural characteristics.

Gallbladder US lexicon (Table 1)

A. Gallbladder lumen

Gallbladder distension

The gallbladder distension is considered adequate if the lumen contains sufficient bile on visual assessment to permit a complete evaluation of the wall and lumen (Supplementary Fig. S2). The gallbladder should be defined as contracted when it is visibly small precluding complete assessment of the wall and/or lumen. Gallbladder is distended in the fasting state. In addition, there is reduced bowel gas in the fasting state which provides an optimal acoustic window [10]. A contracted gallbladder gives falsely higher values of the gallbladder wall thickness [13]. Also, there is a greater possibility of missing a malignancy on US in a contracted gallbladder [14].

Table 1 GB-RADS lexicon

Feature	Category	Definition
Intraluminal changes		
Distension	Adequate	Lumen contains enough bile on visual assessment to allow complete evaluation of the wall and the lumen
	Contracted	Visibly small gallbladder precluding the complete assessment of the wall and/or lumen
Intraluminal contents	Calculus	
	Sludge	
	Tumor	
Mural changes		
Symmetry of wall thickening	Symmetric	Entire wall is uniform in thickness
	Asymmetric	One part of the wall is thickened more than the rest of the wall
Extent of involvement	Focal	Limited to a part of the wall
	Diffuse	Entire wall is involved
Site of thickening	Neck	
	Body	
	Fundus	
	Peritoneal aspect	
	Hepatic aspect	
Mural layering	Present	Visualization of inner and outer layers
	Absent	
Intramural changes	Echogenic foci	Bright spot with or without comet tail artifact within the gallbladder wall
	Intramural cysts	Anechoic spaces in wall
Interface with liver	Distinct	Sharp transition from the gallbladder wall to the liver
	Indistinct	Transition from the gallbladder wall to the liver is not clearly seen

Luminal contents

The lumen of the gallbladder should be assessed for calculi, sludge, and tumor.

The presence of gallstones is associated with both benign and malignant pathologies of the gallbladder. Gallstones play an important role in the etiopathogenesis of various diseases and should be reported to advise appropriate management. Benign gallbladder diseases have been associated with a higher incidence of gallstones than GBC in a few studies [15, 16]. However, a few studies suggest a higher malignancy risk in the presence of gallstones [17–19]. Although the number of gallstones does not affect the chances of malignant disease, the size of the gallstone does, as larger stones have been associated with increased risk of malignancy [20, 21]. Furthermore, larger stones can get impacted leading to cholecystitis. Being highly reflective echogenic structures with associated posterior acoustic shadowing, gallstones (when large or numerous) can limit complete evaluation of the gallbladder wall. Biliary sludge is seen as homogeneous low-level echoes along the dependent lumen of the gallbladder. Sometimes there is impaction of the sludge giving the appearance of an intraluminal lesion which can mimic malignancy [22]. Color flow with Doppler waveform assessment may help confirm the lack of vascularity in cases of tumefactive sludge [22].

B. Gallbladder wall

Degree of wall thickness

The wall thickness should be measured from the inner aspect of mucosa (inner hyperechoic layer) to the outer aspect of outer connective tissue layer (outer hyperechoic layer). Wall thickness should be reported in millimeters. In symmetrical circumferential thickening, wall thickness can be measured at any point, whereas in cases of focal thickening, measurement should be obtained at the thickest point. The normal gallbladder wall is thin, smooth, and measures < 3 mm in thickness [23–25]. The degree of gallbladder wall thickening encountered in gallbladder pathologies is highly variable [26–28]. Other features of thickening including symmetry, intramural features, and interface with liver and other adjacent structures should be considered for risk stratification.

Extent and symmetry of wall thickening

Wall thickening should be categorized as either circumferential or focal. Circumferential thickening is defined as

the involvement of the entire wall of the gallbladder. Focal thickening refers to thickening limited to a portion of the wall. The entire gallbladder wall should be assessed for symmetry of the thickening. Wall thickening is considered symmetrical if the entire wall is uniform in thickness, while it is considered asymmetrical if one part of the wall is visibly more thickened than the rest of the wall. Symmetrical wall thickening is a common manifestation of benign diseases. However, it can sometimes be encountered in malignant diseases [29, 30].

Site of thickening

The site of thickening should be mentioned. The thickening can be present at the fundus, body, or neck of the gallbladder. The involvement of hepatic or peritoneal aspects should be reported. Fundal thickening is usually well appreciated. Often the thickening at the neck of the gallbladder can be overlooked if not carefully examined. Although there is no site predilection of benign or malignant thickening, infiltrative GBCs are more commonly located in the region of the neck [31]. Thickening at the neck is more likely to cause biliary obstruction due to its close approximation to the liver hilum. Involvement of the hepatic surface leads to early direct invasion of the adjacent liver parenchyma. In contrast, the involvement of the peritoneal surface leads to early peritoneal spread of the disease via peritoneal ligaments or lymphatics [32]. Also, the likelihood of involvement of adjacent organs including colon, duodenum, and stomach increases when disease occurs along the peritoneal surface [33, 34].

Gallbladder wall layered appearance

Layered appearance of the gallbladder wall thickening is defined as the visualization of the inner and outer layers of the gallbladder (Supplementary Fig. S1). Intact echogenic mucosal lining with an associated hypoechoic outer wall (predominantly due to associated edema in deeper layers) produces a layered appearance favoring benign pathology [35, 36]. Most of the gallbladder wall malignancies are epithelial in origin [37, 38]. The mucosa is disrupted with infiltration into deeper layers leading to loss of the layered appearance of the wall [8].

Intramural changes

Intramural changes including echogenic foci and/or cysts within the gallbladder wall should be assessed (Fig. 1). Echogenic foci are seen as a bright spot with, or without, comet tail artifact (triangular acoustic enhancement posterior to the echogenic focus-a form of reverberation artifact) within the gallbladder wall, while intramural cysts appear as anechoic spaces. Intramural cysts and echogenic foci are commonly encountered in benign gallbladder disease. Intramural cysts are sonographic evidence of Rokitansky-Aschoff sinuses (RAS), while the echogenic mural foci correspond to the cholesterol deposition/intramural calcification within the RAS [39, 40]. They can be seen in both circumferential as well as focal wall thickening.

Interface with liver

The interface of the gallbladder with the liver is said to be distinct when there is a sharp transition from the gallbladder wall to the liver (Fig. 2). At the hepatic surface of the gallbladder, there is a lack of peritoneal covering causing direct contact of the gallbladder wall with the adjacent liver parenchyma. However, the interface between the two structures is sharply demarcated on US. An indistinct interface between gallbladder wall and liver has significant association with malignancy [41, 42]. The presence of definitive extramural lesions within the liver parenchyma with adjacent

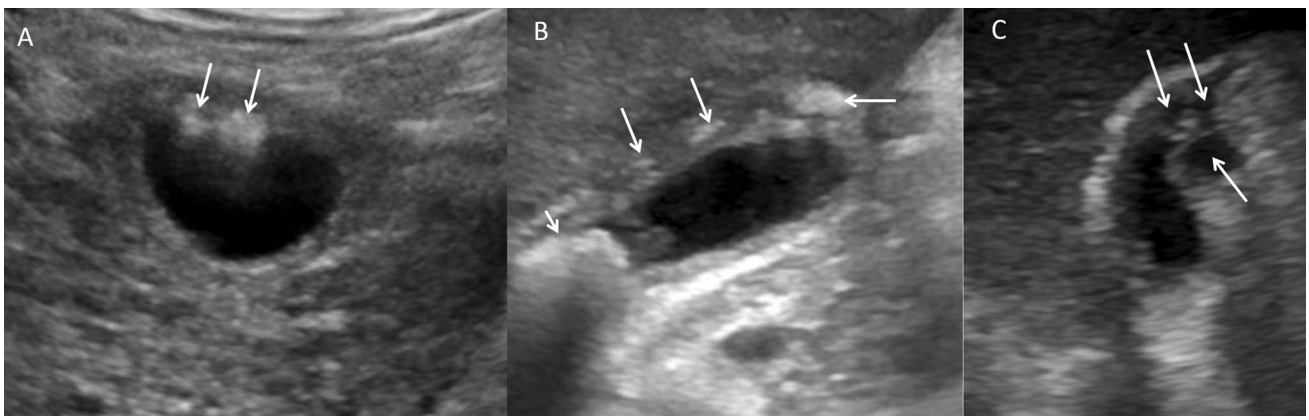


Fig. 1 Intramural echogenic foci and cysts. **a** Focal gallbladder wall thickening with intramural echogenic foci (arrows). **b** Diffuse gallbladder wall thickening with intramural echogenic foci (arrows). **c** Diffuse gallbladder wall thickening with intramural cysts (arrows)

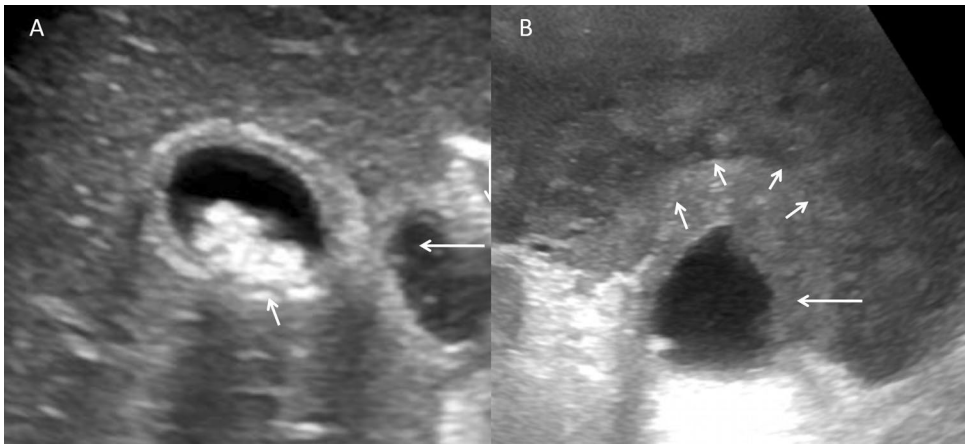


Fig. 2 Interface with liver. **a** Distinct interface. Gallbladder is distended with calculi in the lumen (short arrow) and layered gallbladder wall thickening (note that the inner and outer layers of the gallbladder are distinctly seen). The interface of the thickened gallbladder with liver and the duodenum (arrow) are distinct. **b** Indistinct interface. Asymmetric mural thickening (arrow) is showing indistinct interface with the liver (short arrows)

gallbladder wall thickening suggests locally advanced malignancy [2].

GB-RADS categories (Table 2)

GB-RADS should be applied after exclusion of acute cholecystitis, systemic, hepatic, and other extracholecystic causes of gallbladder wall thickening (including cardiac disease, chronic liver disease, hepatitis, viral illness). GB-RADS categorization is applicable to gallbladders with or without stones.

GB-RADS 0

Incomplete gallbladder evaluation due to technical, patient, or gallbladder-related factors.

Technical and patient-related factors include but are limited to morbid obesity, marked liver steatosis, recent upper abdominal surgery or chest wall abnormalities resulting in an inadequate acoustic window, and debilitated patients who cannot change position for adequate visualization of the entire gallbladder. Gallbladder evaluation may also be incomplete due to several gallbladder-related features. A contracted gallbladder can obscure as well as lead to false suspicion of abnormality. If a thickened contracted gallbladder is due to inadequate fasting, repeat evaluation after fasting should be performed. The wall-echo-shadow complex implies that a single large stone or multiple small stones have completely filled the gallbladder lumen and most of the gallbladder wall is obscured (Fig. 3). The other scenarios include but are not limited to air or hemorrhage within the gallbladder lumen (in the setting of emphysematous or gangrenous cholecystitis, post endoscopic retrograde cholangiopancreatography status, or other biliary interventions), porcelain gallbladder, and variations of gallbladder position.

Comments: It is important to identify and mention the factors related to the gallbladder which preclude complete US evaluation.

GB-RADS 1–4

GB-RADS 1–4 is based on gallbladder wall features on US including symmetry and extent (focal vs. circumferential) of involvement, layered appearance, intramural features (including intramural cysts and echogenic foci), and interface with the liver (Figs. 4, 5, 6).

GB-RADS 5

GB-RADS 5 is assigned to gallbladder wall thickening that shows definite extramural extension in addition to the features of GB-RADS 4 (Supplementary Fig. S3).

The definition, US features, probability of malignancy, and management based on GB-RADS categories is given in Table 2. A reporting format is proposed in Table 3.

Discussion

GB-RADS represents the first collaborative effort at risk stratification of non-acute gallbladder wall thickening. The multidisciplinary committee comprising experts from different specialties identified the key US features, based on available scientific literature and multiple rounds of discussion, that help to stratify the risk of malignancy in gallbladder wall thickening. Within each risk category, the committee proposed the probability of malignancy and management strategy. The risk stratification of gallbladder wall thickening represents an unmet need to manage patients with gallbladder diseases. Of particular interest to the experts involved in the care of patients with GBC is that almost one-third

Table 2 GB-RADS categories

GB-RADS score	Risk category	Lexicon descriptors	Probability of malignancy	Management
0	Inadequate evaluation due to technical or patient factors or gallbladder-related factors	*Few examples* Morbid obesity Wall-echo-shadow complex Porcelain gallbladder Gas in the gallbladder lumen	–	Repeat ultrasound in selected cases. Consider multiphasic contrast enhanced CT/MRI after multidisciplinary discussion
1	Normal	Adequate gallbladder distension Wall thickness ≤ 3 mm	–	No additional imaging or follow-up is needed
2	Benign	Symmetric circumferential thickening with or without intramural changes or focal thickening with intramural changes Layered appearance Preserved interface with liver	< 2%	No additional imaging or follow-up needed
3	Equivocal	Circumferential thickening without layered appearance Focal thickening without intramural features (cysts or echogenic foci) or layered appearance Distinct interface with liver	2–50%	Consider multiphasic contrast enhanced CT/MRI after multidisciplinary discussion
4	Malignancy is likely	Circumferential or focal thickening without layered appearance and with loss of interface with liver	50–90%	Multiphasic contrast enhanced CT/MRI
5	Malignancy is highly likely	Same as GB-RADS 4 with definite extramural invasion as suggested by one of the following: Biliary or vascular involvement by direct extension of mural thickening Liver mass in contiguity with the mural thickening	> 90%	Multiphasic contrast enhanced CT/MRI

CT computed tomography, *MRI* magnetic resonance imaging, *US* ultrasonography

of patients with GBC may present with gallbladder wall thickening that needs accurate risk categorization on initial imaging [33]. As US represents the initial imaging test of choice for patients with suspected gallbladder diseases, GB-RADS is a significant step towards improving objectivity and accuracy of reporting gallbladder wall abnormalities and identifying patients who are likely to harbor GBC and may benefit from further imaging.

The initial part of the document proposed the reporting lexicon for patients with gallbladder thickening. A wide array of terms has been used to describe the characteristics of the gallbladder in patients with gallbladder wall thickening. The existing literature uses terms that are often poorly defined and inconsistently applied. Furthermore, for the same US feature, multiple terms are often used. This inconsistency leads to confusion about recommendations for further management. The committee members identified the common terms that are already in use in the literature rather than proposing new terms. Concise definitions were proposed that can be used as a guide for practitioners. The committee recommended including the terms that would be reproducible and demonstrate consistency in diagnosing malignant gallbladder wall thickening. Several terms like echogenicity of the gallbladder wall, gallbladder wall continuity, hypoechoic intramural nodules, and degree of gallbladder wall thickening were not included for the same reasons. Although Doppler US features were proposed by some members, the committee did not recommend its inclusion based on limited literature about its value in differentiating cancer from benign gallbladder wall thickening [43, 44].

The second part of the document proposed the risk stratification based on the key US features, including symmetry and extent of involvement of the gallbladder wall, layered appearance, intramural features (including cysts and echogenic foci), and interface with the liver. To apply GB-RADS criteria, gallbladder must be adequately distended. Exclusion of acute cholecystitis, systemic, hepatic, and other extracholecystic causes of gallbladder wall thickening is critical

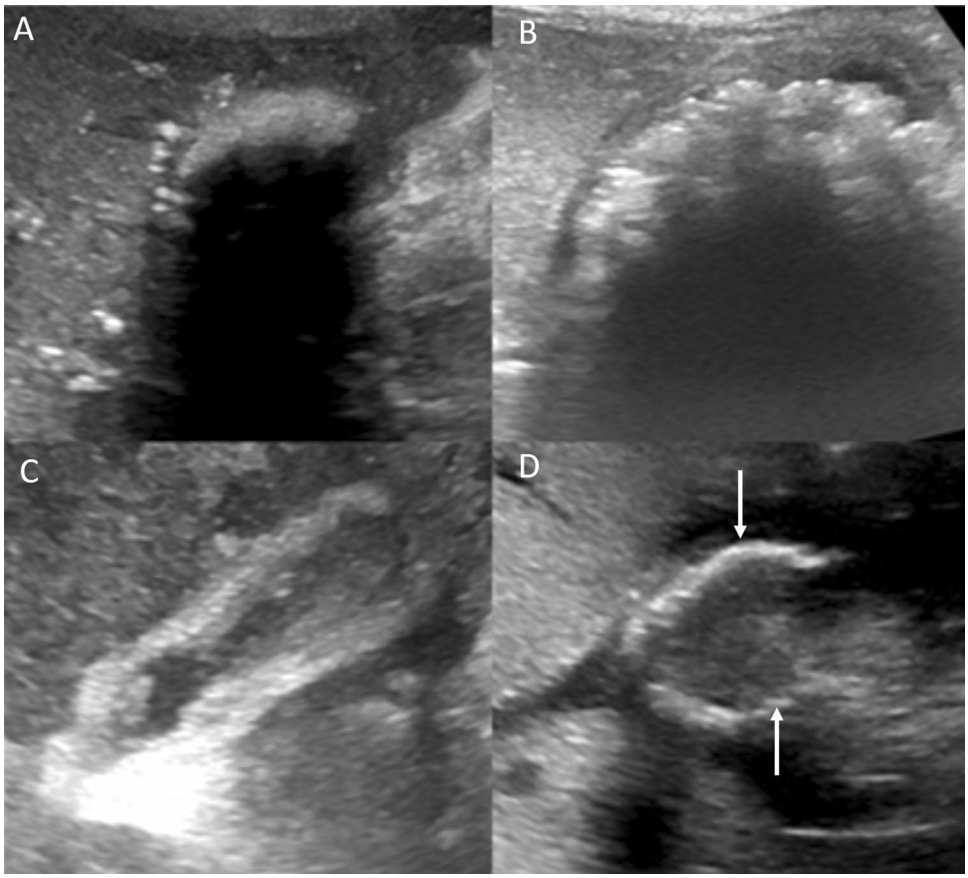


Fig. 3 GB-RADS 0 (inadequate evaluation). **a**, **b** Wall-echo-shadow complex. Almost entire wall of the gallbladder is obscured by posterior acoustic shadowing. **c** Contracted gallbladder. **d** Porcelain gallbladder. There is mural calcification (arrows) affecting the optimal assessment of the other characteristics of the wall

to applying GB-RADS to prevent the confounding effect of these illnesses on GB-RADS findings. If there are US features suggesting higher GB-RADS categories, these patients should be managed based on comprehensive clinical, biochemical (including tumor markers), and imaging evaluation rather than GB-RADS.

While applying GB-RADS, the false positive and false negative diagnoses must be kept in mind. Xanthogranulomatous cholecystitis may be associated with pericholecystic infiltration and erroneously classified as a lesion with high likelihood of malignancy based on GB-RADS [15, 45]. Less commonly, patients with complicated acute cholecystitis may present later in the course of their disease when the symptoms are more subtle [46]. In these patients, a higher GB-RADS category may be assigned due to the presence of pericholecystic changes. There may be lack of mural stratification in some cases of chronic cholecystitis, leading to assignment of GB-RADS 3 category. Finally, early-stage GBC (T1) may sometimes show mural stratification on US and hence may be assigned GB-RADS 2 category.

Several limitations to the current GB-RADS proposal must be recognized. The proposal is based on International Consensus. Although the guidance was provided by the systematic review of literature, the available literature was not representative of all the clinical situations and hence a consensus process was deemed mandatory, and acceptable. The experts involved in consensus strived to include the most objective findings in the GB-RADS lexicon with an operational definition for each finding. However, the interobserver agreement of these findings is not known and must be prospectively assessed as screening US will sometimes be performed by inexperienced technicians or radiologists. There is a marked geographical variation in the prevalence of gallbladder diseases [1]. Hence, the performance of GB-RADS must be validated prospectively using data from multiple centers across the world. Due to limited availability of equipment and expertise for MRI, the experts proposed either CT or MRI for risk categories requiring further assessment. The experts acknowledge the increasing utilization of contrast enhanced ultrasound (CEUS) for characterization of gallbladder wall [47]. However, due to the cost and limited availability, the incorporation of CEUS into risk stratification algorithm is not advocated [48]. Finally, the performance of GB-RADS must be validated in prospective, multicenter studies.

In conclusion, GB-RADS proposes US-based risk stratification of gallbladder wall thickening. GB-RADS will improve objective reporting of gallbladder wall thickening and timely detection of wall thickening type of GBC.

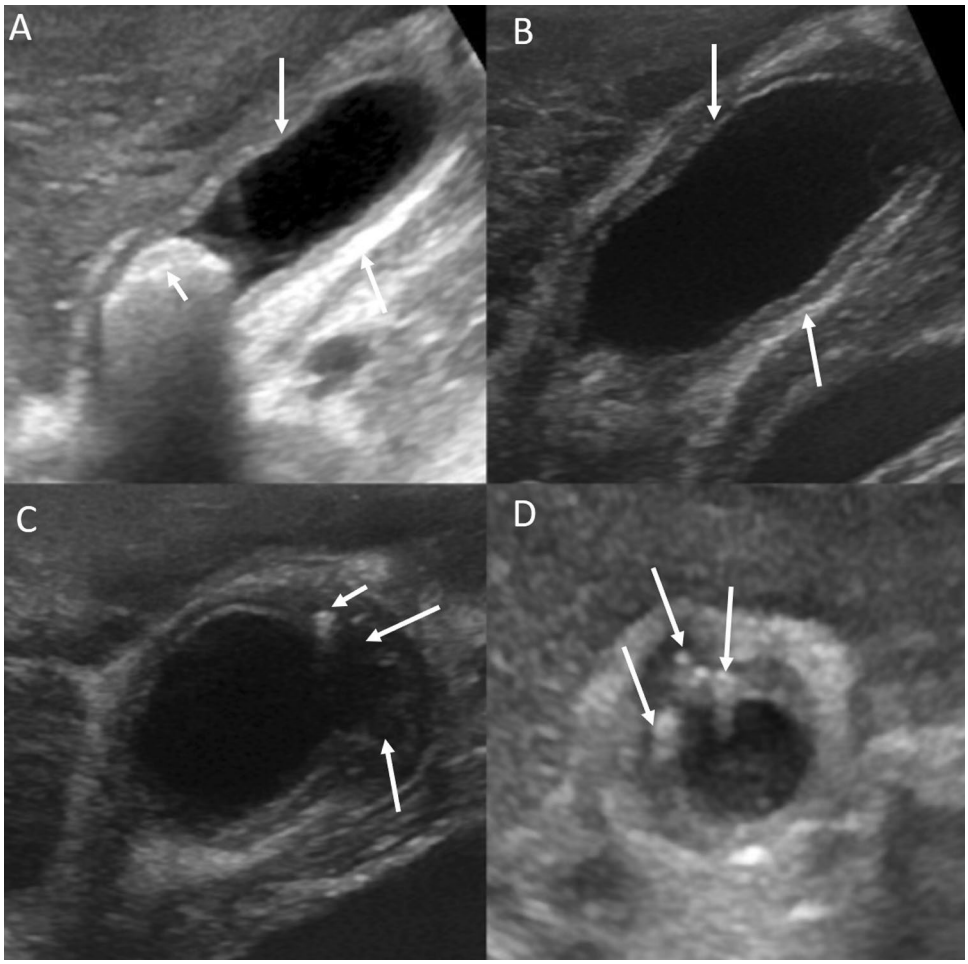


Fig. 4 GB-RADS 2 (benign). **a**, **b** Symmetric circumferential mural thickening with layered appearance. Note that the inner and outer hyperechoic layers are distinctly seen in both **a** and **b** (arrows). There is a calculus in the lumen in **a** (short arrow). **c**, **d** Focal thickening with intramural changes. There are intramural cysts (arrows) and echogenic focus (short arrow) in **c**. Note the multiple intramural echogenic foci in **d** (arrows)

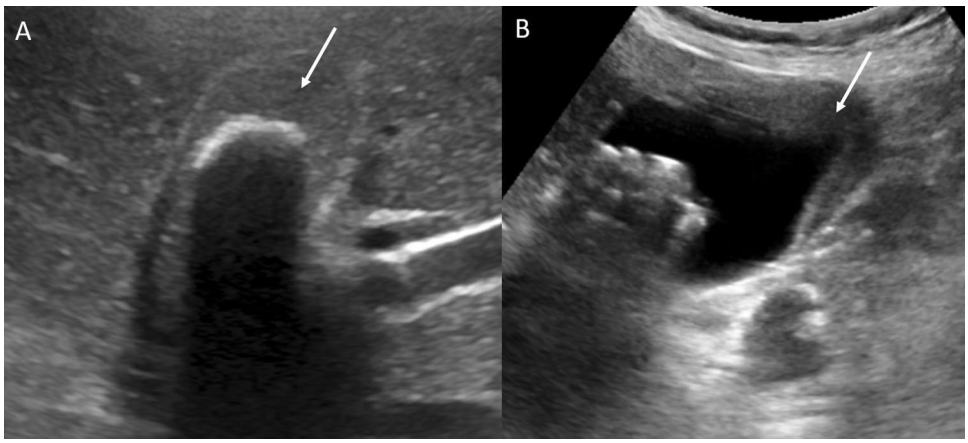


Fig. 5 GB-RADS 3 (equivocal) and GB-RADS 4 (malignancy is likely). **a** Focal thickening without intramural features along the hepatic aspect (arrow). **b** Focal thickening without intramural features along the peritoneal aspect (arrow)

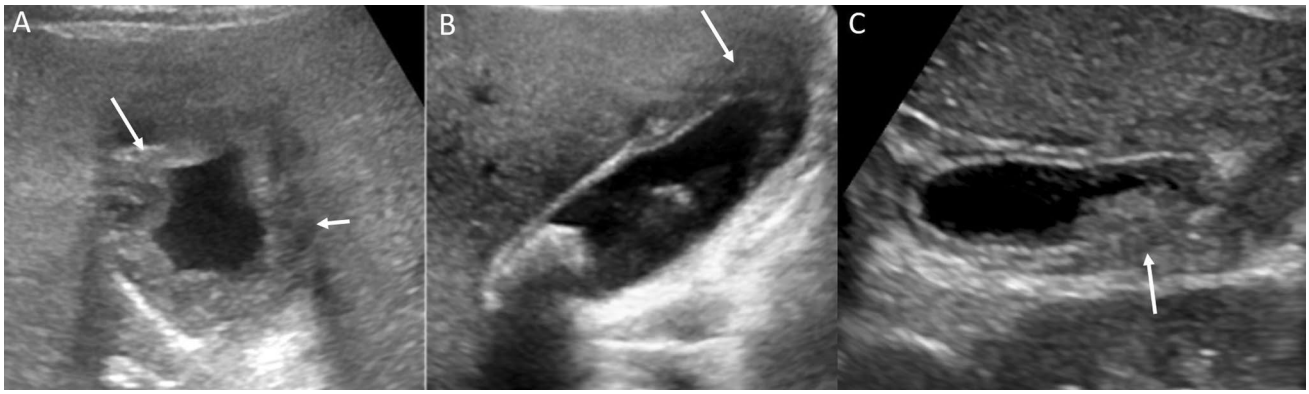


Fig. 6 GB-RADS 4 (malignancy is likely). **a** Asymmetric circumferential mural thickening (arrow) without layered appearance and with loss of interface with liver (short arrow). **b** Focal thickening in the fundus with no intramural features and loss of interface with liver (arrow). **c** Focal thickening with no intramural features along the peritoneal aspect (arrow)

Table 3 Reporting template

Clinical history
Technique: Transducer used
Findings:
Gallbladder distension: Adequate/contracted
Mural thickening: Present/absent
If present:
Thickness (in mm)
Symmetric/asymmetric
Extent of intramural changes: focal/ diffuse
Site: neck/body/fundus/hepatic aspect/peritoneal aspect
Associated intramural changes: Echogenic foci/cysts
Mural layering
Interface with liver: Distinct/indistinct
Presence of Sludge/calculus/tumor within the lumen
Number of calculi: Single/multiple
Size of the largest calculus
Presence of signs of definite extramural invasion:
Biliary or vascular involvement by the extramural extension of gallbladder wall thickening; liver mass contiguous with mural thickening
Any other significant findings
Diagnosis
Final assessment category
Recommendation

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Author contributions PG, UD: Conceived and designed the work. PG, UD, PR, RS, DK, MC: Performed the systematic review of the literature. PG, UD, MS, NK, AG, VS, VG, TDY, CKD: Developed the first draft of survey statements. PG, UD, MS, AG, NK, VS, VG, TDY, LK, SI, HS, YS, CKD, US, RN, RS, MSS, RS, NS, AE, HK, AK, RdH, VKK, SGB, AKS, AP, PG, SKP, MG, SP, AB, AKG, BS, MJ, GG, FN, VA, JCR, HSH: Participated in the 1st, 2nd, and web-based rounds of the Delphi consensus and formulated the consensus statements. PG, UD, PR, RS, DK, MC: Wrote the initial draft. PG, UD, PR, MS, AG, NK, RS, DK, MC, VS, VG, TDY, LK, SI, HS, YS, CKD, US, RN, RS, MSS, RS, NS, AE, HK, AK, RdH, VKK, SGB, AKS, AP, PG, SKP, MG, SP, AB, AKG, BS, MJ, GG, FN, VA, JCR, HSH: Critically revised the manuscript, approved the final version of the manuscript submitted to the journal, and agree to be accountable for all aspects of the work.

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Declarations

Conflict of interest All authors declare that they have no conflict of interest to disclose.

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