

Diagnostic Performance of Ultrasonography and Contrast-Enhanced Computed Tomography in Differentiating Benign from Malignant Gallbladder Wall Thickening: A Histopathological Correlation Study

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Abstract

Background: Gallbladder wall thickening is a nonspecific imaging finding that may represent benign inflammatory or hyperplastic conditions as well as gallbladder carcinoma. Differentiating these entities on imaging is challenging because of substantial overlap in their appearances.

Objective: To evaluate the diagnostic performance of ultrasonography (USG) and contrast-enhanced computed tomography (CECT) in differentiating benign from malignant gallbladder wall thickening using histopathology as the reference standard.

Methods: This prospective cross-sectional diagnostic accuracy study included 50 consecutive adults with gallbladder wall thickening who underwent USG, CECT and subsequent surgical histopathological evaluation at a tertiary-care teaching hospital. Imaging features were compared between benign and malignant lesions. Sensitivity, specificity, predictive values and diagnostic accuracy were calculated, and receiver-operating-characteristic analysis was performed for maximum wall thickness.

Results: Histopathology demonstrated 30 (60.0%) benign and 20 (40.0%) malignant lesions. Malignancy was significantly associated with greater wall thickness, focal/asymmetric thickening, loss of mural stratification, mucosal disruption, heterogeneous enhancement, loss of the gallbladder-liver interface, hepatic invasion, biliary dilatation and regional lymphadenopathy. Intramural cystic spaces and nodules favored benign disease. USG showed 80.0% sensitivity, 80.0% specificity and 80.0% accuracy, while CECT achieved 85.0%, 83.3% and 84.0%, respectively. Combined USG+CECT achieved 90.0% sensitivity, 86.7% specificity and 88.0% accuracy. A wall-thickness threshold of ≥ 6.7 mm yielded an AUC of 0.943.

Conclusion: Combined USG and CECT evaluation improves differentiation of benign and malignant gallbladder wall thickening. Morphology, mural integrity and enhancement patterns should be interpreted collectively, with histopathology remaining the definitive diagnostic standard.

Keywords: Gallbladder Diseases; Gallbladder Neoplasms; Ultrasonography; Tomography, X-Ray.

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Introduction

Gallbladder wall thickening is a common but nonspecific imaging finding that encompasses inflammatory, hyperplastic and neoplastic processes. The diagnostic problem is clinically important because early wall-thickening-type gallbladder carcinoma may closely resemble chronic cholecystitis, xanthogranulomatous cholecystitis (XGC) or adenomyomatosis, whereas advanced inflammatory disease may simulate malignant infiltration. Gallbladder cancer continues to carry a substantial global burden: GLOBOCAN-based estimates for 2022 identified more than

122,000 incident cases and approximately 89,000 deaths worldwide, with a particularly high absolute burden in South-Central and Eastern Asia.[1] The poor prognosis of gallbladder carcinoma is related in part to delayed presentation and the difficulty of recognizing early or infiltrative disease.[2,3] Gallbladder carcinoma may appear as a mass replacing the gallbladder, an intraluminal polypoidal lesion, or focal/diffuse mural thickening.[2-4] The wall thickening phenotype poses a particular diagnostic challenge because benign disorders can reproduce many malignant-

appearing findings, including marked mural thickening, heterogeneous enhancement, pericholecystic inflammatory change and apparent loss of tissue planes.[4-6] Conversely, subtle carcinoma may be overlooked when wall thickening is attributed to uncomplicated inflammatory disease. Therefore, interpretation requires integration of mural morphology, wall layering, mucosal integrity, enhancement characteristics and extramural findings rather than reliance on thickness alone.[5,6]

Ultrasonography (USG) is the usual first-line modality for gallbladder assessment and permits direct evaluation of focality, symmetry, mural stratification, intramural cystic spaces, echogenic foci and the gallbladder-liver interface. A systematic review and meta-analysis showed that intramural echogenic foci, hypoechoic nodules and lack of wall disruption favor benign disease, while focal thickening and an indistinct liver interface are useful malignant leaning features.[7] The Gallbladder Reporting and Data System (GB-RADS) has subsequently provided a structured framework for risk stratification of wall thickening on ultrasonography.[8] Contrast enhanced computed tomography (CECT) complements ultrasonography by depicting enhancement patterns, mucosal continuity, hepatic invasion, biliary obstruction, lymphadenopathy and distant disease. In a recent Korean series of 120 patients with localized gallbladder wall thickening, Min et al. identified four high-risk CT features: heterogeneously enhancing single layer or strongly enhancing thick inner layer morphology, wall thickness greater than 6.5 mm, arterial-phase hyperenhancement and absence of intramural small cystic lesions.[9]

XGC remains a major benign mimic; more recent international studies have shown that continuous mucosal enhancement and intramural hypoattenuating nodules favor XGC, whereas biliary dilatation, adjacent-organ invasion and enlarged regional nodes favor carcinoma.[10-12] Adenomyomatosis can also mimic focal carcinoma, but recognition of Rokitansky-Aschoff sinuses, intramural cystic spaces and comet-tail artifacts strongly supports a benign diagnosis.[13] Because histopathology remains the definitive reference standard for separating benign mimics from malignancy and for characterizing invasive carcinoma,[14-16] a radiology pathology correlation approach is well suited to this clinical problem. The present study evaluates ultrasonographic and CECT findings in patients with gallbladder wall thickening and correlates them with final histopathology. The primary objective is to determine the diagnostic performance of USG and CECT for differentiating benign from malignant gallbladder wall thickening

and secondary objectives are to identify individual imaging features associated with malignancy and to describe the corresponding histopathological spectrum.

Materials and Methods

This prospective cross-sectional diagnostic accuracy study was conducted jointly by the Departments of Radiodiagnosis and Pathology at a tertiary-care teaching hospital in South India, over a period of two years. Fifty consecutive adult patients with gallbladder wall thickening identified on ultrasonography, who subsequently underwent CECT and surgical histopathological evaluation, were included. The reporting structure followed the principles of the Standards for Reporting Diagnostic Accuracy Studies (STARD).[17] Gallbladder wall thickening was operationally defined as mural thickness of at least 3 mm in an adequately distended fasting gallbladder, measured perpendicular to the wall. Large mass completely replacing the gallbladder in which the wall could not be separately evaluated; isolated polypoidal lesions without mural thickening; inadequate gallbladder distension; technically suboptimal imaging; previous treatment for gallbladder malignancy; absence of surgical histopathology; or wall thickening predominantly attributable to a systemic/extra cholecystic condition were excluded.

Ultrasonographic assessment: Ultrasonography was performed after 6-8 hours of fasting using a curvilinear transducer, supplemented by a higher frequency linear transducer where appropriate. The gallbladder was assessed in multiple planes. Recorded parameters included maximum wall thickness; focal versus diffuse and symmetric versus asymmetric thickening; preservation or loss of mural stratification; mucosal regularity; intramural cystic spaces; comet-tail echogenic foci; intramural hypoechoic nodules; internal vascularity; pericholecystic inflammatory change; gallstones; and preservation or loss of the gallbladder liver interface. These parameters were selected because they correspond to established benign and malignant discriminators.[7,8]

Contrast-enhanced CT assessment: CECT images were evaluated in axial and multiplanar reformatted planes. The recorded variables were maximum wall thickness; focal/asymmetric morphology; homogeneous or heterogeneous mural enhancement; thick enhancing inner-layer or single layer morphology; continuity or disruption of the enhancing mucosal line; intramural hypoattenuating nodules; intramural cystic spaces; pericholecystic fat stranding; loss of the fat plane with the liver; direct hepatic invasion; biliary dilatation; regional lymphadenopathy; and distant metastasis. These features were chosen on the basis of contemporary CT and multimodality studies of

wall thickening type gallbladder cancer.[9,10,18-21]

Image interpretation and reference standard:

Imaging was categorized as benign or suspicious/malignant on the basis of the integrated radiological appearance. Histopathology of the resected gallbladder was treated as the reference standard. Representative sections from the fundus, body and neck, with additional sampling of areas of maximal thickening or gross abnormality, were processed and stained with hematoxylin and eosin. Lesions were categorized as benign inflammatory/hyperplastic disease or malignant neoplasia.[14-16]

Statistical Analysis: Continuous variables are presented as mean $\pm$ standard deviation (SD), and categorical variables as number and percentage. Two-sided Fisher exact tests were used for categorical comparisons. Continuous variables were compared using independent-samples t tests. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, positive likelihood ratio and negative likelihood ratio were calculated against histopathology. Exact Clopper-Pearson 95% confidence intervals were used for diagnostic proportions. Receiver-operating-characteristic (ROC) analysis was performed for maximum wall thickness; the area under the curve (AUC) and an optimal threshold based on the Youden index were reported.

Results

Among the 50 patients, 30 had benign and 20 had malignant gallbladder wall thickening on histopathology. Patients with malignancy were significantly older than those with benign disease (66.3 ± 7.4 vs 57.1 ± 7.4 years; $p < 0.001$), and age > 60 years was more frequent in the malignant group (80.0% vs 30.0%; $p = 0.001$). Jaundice (35.0% vs 6.7%; $p = 0.021$), anorexia/weight loss (50.0% vs 10.0%; $p = 0.003$), elevated bilirubin (45.0% vs 10.0%; $p = 0.007$), and elevated alkaline phosphatase (55.0% vs 20.0%; $p = 0.015$) were also significantly associated with malignancy. On ultrasonography, malignant lesions showed greater

mean wall thickness (8.2 ± 1.7 vs 5.2 ± 1.0 mm; $p < 0.001$), with higher frequencies of focal thickening (75.0% vs 26.7%), asymmetric thickening (75.0% vs 23.3%), loss of mural stratification (80.0% vs 26.7%), and loss of the gallbladder–liver interface (60.0% vs 16.7%). Conversely, intramural cystic spaces, comet-tail echogenic foci, and intramural hypoechoic nodules were more frequent in benign lesions. On CECT, malignancy was significantly associated with focal/asymmetric thickening (80.0% vs 30.0%), heterogeneous enhancement (75.0% vs 33.3%), disruption of the enhancing mucosal line (80.0% vs 23.3%), loss of the fat plane with the liver (65.0% vs 20.0%), direct hepatic invasion (40.0% vs 3.3%), biliary dilatation (40.0% vs 10.0%), and suspicious regional lymphadenopathy (50.0% vs 13.3%). Distant metastasis was observed only in the malignant group (15.0%), although this difference did not reach statistical significance ($p = 0.058$). Benign lesions accounted for 30 of 50 cases (60.0%), with chronic cholecystitis being the most frequent benign diagnosis (32.0%), followed by xanthogranulomatous cholecystitis (12.0%), acute-on-chronic cholecystitis (8.0%), and adenomyomatosis (6.0%). Malignant lesions constituted 20 cases (40.0%), predominantly adenocarcinoma (18/50, 36.0%), while adenosquamous and neuroendocrine carcinomas accounted for one case each. For detection of malignant wall thickening, ultrasonography showed a sensitivity and specificity of 80.0% each, with an overall diagnostic accuracy of 80.0%. CECT demonstrated improved performance, with sensitivity of 85.0%, specificity of 83.3%, and accuracy of 84.0%. The combined interpretation of USG and CECT yielded the highest diagnostic performance, achieving 90.0% sensitivity, 86.7% specificity, 81.8% positive predictive value, 92.9% negative predictive value, and an overall accuracy of 88.0%. Correspondingly, the positive likelihood ratio increased from 4.00 with USG alone to 6.75 with combined imaging, while the negative likelihood ratio decreased from 0.25 to 0.12, indicating improved discrimination when both modalities were interpreted together.

Table 1: Baseline demographic and clinical characteristics according to final histopathological diagnosis

	Total (n=50)	Benign (n=30)	Malignant (n=20)	P value
Age, years, mean $\pm$ SD	60.8 $\pm$ 8.6	57.1 $\pm$ 7.4	66.3 $\pm$ 7.4	<0.001
Age > 60 years	25 (50.0)	9 (30.0)	16 (80.0)	0.001
Female sex	32 (64.0)	19 (63.3)	13 (65.0)	1.000
Abdominal/right upper quadrant pain	43 (86.0)	27 (90.0)	16 (80.0)	0.416
Fever	11 (22.0)	8 (26.7)	3 (15.0)	0.489
Jaundice	9 (18.0)	2 (6.7)	7 (35.0)	0.021
Anorexia/weight loss	13 (26.0)	3 (10.0)	10 (50.0)	0.003
Gallstones	35 (70.0)	23 (76.7)	12 (60.0)	0.228
Elevated total bilirubin	12 (24.0)	3 (10.0)	9 (45.0)	0.007
Elevated alkaline phosphatase	17 (34.0)	6 (20.0)	11 (55.0)	0.015

Table 2: Ultrasonographic and contrast-enhanced CT findings in benign and malignant gallbladder wall thickening

	Benign (n=30)	Malignant (n=20)	P value
Ultrasonography			
Maximum wall thickness, mm, mean $\pm$ SD	5.2 $\pm$ 1.0	8.2 $\pm$ 1.7	<0.001
Focal wall thickening	8 (26.7)	15 (75.0)	0.001
Asymmetric wall thickening	7 (23.3)	15 (75.0)	<0.001
Loss of mural stratification	8 (26.7)	16 (80.0)	<0.001
Irregular/disrupted mucosal surface	7 (23.3)	15 (75.0)	<0.001
Intramural cystic spaces	11 (36.7)	1 (5.0)	0.016
Comet-tail echogenic foci	9 (30.0)	0 (0.0)	0.007
Intramural hypoechoic nodules	14 (46.7)	2 (10.0)	0.012
Increased internal vascularity	10 (33.3)	14 (70.0)	0.020
Pericholecystic inflammatory change	15 (50.0)	10 (50.0)	1.000
Loss of gallbladder-liver interface	5 (16.7)	12 (60.0)	0.002
Contrast-Enhanced CT			
Focal/asymmetric thickening	9 (30.0)	16 (80.0)	0.001
Heterogeneous mural enhancement	10 (33.3)	15 (75.0)	0.009
Thick enhancing inner layer/single-layer enhancement	7 (23.3)	15 (75.0)	<0.001
Disrupted enhancing mucosal line	7 (23.3)	16 (80.0)	<0.001
Intramural hypoattenuating nodules	14 (46.7)	2 (10.0)	0.012
Intramural cystic spaces	11 (36.7)	1 (5.0)	0.016
Pericholecystic fat stranding	17 (56.7)	12 (60.0)	1.000
Loss of fat plane with liver	6 (20.0)	13 (65.0)	0.003
Direct hepatic invasion	1 (3.3)	8 (40.0)	0.002
Biliary dilatation	3 (10.0)	8 (40.0)	0.017
Suspicious regional lymph nodes	4 (13.3)	10 (50.0)	0.009
Distant metastasis	0 (0.0)	3 (15.0)	0.058

Table 3: Histopathological spectrum of gallbladder wall thickening

	n	% of total	Category
Chronic cholecystitis	16	32.0	Benign
Acute-on-chronic cholecystitis	4	8.0	Benign
Xanthogranulomatous cholecystitis	6	12.0	Benign
Adenomyomatosis	3	6.0	Benign
Cholesterolosis	1	2.0	Benign
Adenocarcinoma	18	36.0	Malignant
Adenosquamous carcinoma	1	2.0	Malignant
Neuroendocrine carcinoma	1	2.0	Malignant
Total	50	100.0	

Table 4: Diagnostic performance for detection of malignant gallbladder wall thickening

Diagnostic parameter	Ultrasonography	CECT	Combined USG + CECT
True positive (n)	16	17	18
False negative (n)	4	3	2
True negative (n)	24	25	26
False positive (n)	6	5	4
Sensitivity, % (95% CI)	80.0 (56.3-94.3)	85.0 (62.1-96.8)	90.0 (68.3-98.8)
Specificity, % (95% CI)	80.0 (61.4-92.3)	83.3 (65.3-94.4)	86.7 (69.3-96.2)
Positive predictive value, % (95% CI)	72.7 (49.8-89.3)	77.3 (54.6-92.2)	81.8 (59.7-94.8)
Negative predictive value, % (95% CI)	85.7 (67.3-96.0)	89.3 (71.8-97.7)	92.9 (76.5-99.1)
Diagnostic accuracy, % (95% CI)	80.0 (66.3-90.0)	84.0 (70.9-92.8)	88.0 (75.7-95.5)
Positive likelihood ratio	4.00	5.10	6.75
Negative likelihood ratio	0.25	0.18	0.12

Discussion

In this tertiary-care cohort of 50 patients with gallbladder wall thickening, 40.0% of lesions were

malignant. The central finding was that malignant thickening was not distinguished by a single feature alone but by a cluster of abnormalities: greater wall thickness, focal/asymmetric morphology, disruption of mural stratification and mucosa, abnormal enhancement, loss of the liver interface, biliary obstruction and regional lymphadenopathy. Conversely, intramural cystic spaces, comet-tail foci and intramural hypoechoic/hypoattenuating nodules favored benign disease. The integrated USG + CECT assessment achieved 90.0% sensitivity and 86.7% specificity, supporting a multimodal pattern recognition approach rather than reliance on an isolated thickness threshold. The 40.0% malignant proportion is plausible for a surgically selected tertiary-care series, but it should not be interpreted as population prevalence. Min et al. studied 120 Korean patients with localized gallbladder wall thickening and found malignancy in 55 (45.8%), a distribution close to that observed in the present analysis.[9] In contrast, Corwin et al. examined incidentally detected focal fundal thickening in a largely surveillance-based US population and found malignancy in only 4 of 116 cases (3.4%).[22] The marked difference illustrates spectrum and referral bias: a cohort restricted to patients proceeding to surgery and histopathology is enriched for clinically suspicious lesions, whereas incidental imaging cohorts contain many stable benign abnormalities. This distinction is important when interpreting PPV and NPV, which depend on disease prevalence.

Age showed a strong association with malignancy: malignant cases were approximately nine years older than benign cases (66.3 ± 7.4 vs 57.1 ± 7.4 years), and 80.0% of malignant cases were older than 60 years. Bozer and Durgun similarly reported a median age of 72 years in gallbladder cancer compared with 60 years in XGC ($P=0.001$).[10] Gallbladder carcinoma is predominantly a disease of later adulthood,[1-3] and the age effect may reflect cumulative exposure to chronic inflammatory and lithogenic injury, acquisition of oncogenic alterations and a longer interval for progression through dysplasia to invasive carcinoma. Age, however, cannot be used as an imaging discriminator by itself because benign chronic inflammatory disease is also common in older adults. Clinical cholestatic and constitutional features were more frequent in the malignant group. Jaundice occurred in 35.0% of malignant versus 6.7% of benign cases, anorexia/weight loss in 50.0% versus 10.0%, elevated bilirubin in 45.0% versus 10.0%, and elevated alkaline phosphatase in 55.0% versus 20.0%. John et al. emphasized that gallbladder wall thickening in an older patient with elevated alkaline phosphatase should increase suspicion for carcinoma.[4] Tumors arising near the gallbladder neck or infiltrating the hepatoduodenal region can obstruct the biliary tree,

while more advanced malignancy can produce constitutional symptoms through systemic inflammatory and catabolic effects. These variables are therefore best viewed as contextual modifiers that increase or decrease the pre-test probability of malignancy rather than as stand-alone diagnostic tests.

Gallstones were common in both groups (76.7% benign and 60.0% malignant) and were not discriminatory ($P=0.228$). This does not contradict the established epidemiologic relationship between gallstones and gallbladder cancer.[2,3] Once a patient has already entered a selected cohort with wall thickening, gallstones lose specificity because they are also strongly associated with chronic cholecystitis and XGC. Thus, a factor may be relevant to long-term cancer risk while having limited value for distinguishing malignant from benign wall thickening at the point of imaging diagnosis. Wall thickness was significantly greater in malignant disease (8.2 ± 1.7 vs 5.2 ± 1.0 mm). The ROC-derived threshold of ≥ 6.7 mm yielded an AUC of 0.943, 80.0% sensitivity and 93.3% specificity. This closely parallels Min et al., who identified wall thickness >6.5 mm as one of the four most accurate CT predictors of gallbladder cancer, with an individual accuracy of 88.3%.[9] Infiltrative carcinoma produces cellular proliferation, stromal desmoplasia and tissue replacement that can result in more substantial mural expansion. Nevertheless, thickness alone is insufficient: XGC and severe chronic inflammation may also cause marked thickening, while early infiltrative carcinoma may remain relatively thin.[5,6,11,12] The principal value of a thickness threshold is therefore to contribute to a composite assessment. On ultrasonography, focal thickening was seen in 75.0% of malignant and 26.7% of benign lesions, while asymmetry was present in 75.0% versus 23.3%.

These directions agree closely with the meta-analysis by Rana et al., in which focal thickening had a pooled sensitivity of 75% and specificity of 64% for malignant wall thickening.[7] Focality and asymmetry arise because carcinoma often begins as localized mucosal and mural infiltration, whereas uncomplicated inflammatory edema is more often circumferential. The overlap in benign disease reflects focal adenomyomatosis, localized chronic cholecystitis and XGC, explaining why focality should raise suspicion but not establish malignancy. Loss of mural stratification and an irregular/disrupted mucosal surface were particularly strong malignant-leaning findings, occurring in 80.0% and 75.0% of malignant cases, respectively. GB-RADS and contemporary imaging reviews emphasize the importance of wall layering and mucosal integrity.[5,8] A continuous, orderly, layered wall reflects preservation of the epithelial

and subepithelial architecture, whereas invasive carcinoma progressively replaces normal mural layers and disrupts the mucosa. This pathological mechanism also explains why CECT mucosal line disruption was present in 80.0% of malignant versus 23.3% of benign cases in the present analysis.

Several intramural findings favored benign disease. Intramural cystic spaces were present in 36.7% of benign but only 5.0% of malignant lesions, comet-tail foci in 30.0% versus 0%, and intramural hypoechoic nodules in 46.7% versus 10.0%. Rana et al. found that echogenic foci, lack of wall disruption and hypoechoic nodules were useful benign indicators; echogenic foci had pooled sensitivity and specificity of 89% and 86%, while hypoechoic nodules had sensitivity 66% and specificity 80% for benign wall thickening.[7] In adenomyomatosis, intramural cystic spaces correspond to Rokitsky-Aschoff sinuses and cholesterol crystals within them may generate comet-tail artifacts.[13] In XGC, intramural hypoattenuating or hypoechoic nodules correspond to xanthogranulomatous inflammatory foci composed of lipid-laden macrophages, inflammatory cells and fibrosis.[10-12] These pathology-imaging correlations explain why intramural features can be more informative than absolute wall thickness. Increased internal vascularity occurred in 70.0% of malignant and 33.3% of benign lesions. Tumoral neoangiogenesis and hypervascular inflammatory stroma can both increase Doppler flow, so vascularity should be interpreted as supportive rather than definitive. Dong et al. showed that high-frequency contrast-enhanced ultrasonography improved differentiation of focal fundal wall thickening: sensitivity, specificity and accuracy were 84.3%, 90.6% and 87.5%, respectively, compared with 53.1%, 59.3% and 56.2% for conventional B-mode ultrasonography.[23]

Their observation that malignant lesions show inhomogeneous enhancement and disruption of the wall-layer structure is concordant with the present pattern, while the higher specificity of CEUS illustrates how enhancement kinetics can add information beyond conventional Doppler assessment. Pericholecystic inflammatory change was non-discriminatory: it was present in 50.0% of both groups on ultrasonography, while CT fat stranding occurred in 56.7% of benign and 60.0% of malignant lesions. This is clinically important because inflammatory extension beyond the gallbladder is a major reason XGC mimics malignancy. Giudicelli et al. described the infiltrative inflammatory behavior of XGC and emphasized that it may be difficult to separate from carcinoma preoperatively.[12] Bozer and Durgun likewise found that some extramural inflammatory

findings overlapped between XGC and cancer.[10] Therefore, pericholecystic stranding alone should not be equated with tumor invasion; the nature of the mucosal line, intramural nodules, adjacent-organ destruction and nodal disease provide more discriminating context. CECT showed several important malignant associations.

Heterogeneous mural enhancement occurred in 75.0% of malignant versus 33.3% of benign lesions, and a thick enhancing inner layer/single-layer pattern in 75.0% versus 23.3%. Min et al. found heterogeneously enhancing single-layer morphology or a strongly enhancing thick inner layer to be their most accurate individual CT feature, with 90.0% accuracy.[9] These enhancement patterns likely reflect replacement of the normal layered wall by tumor, irregular neovascularity and desmoplastic stroma. The present findings are also consistent with multimodality reviews emphasizing enhancement heterogeneity and loss of the normal layered pattern as malignant features.[3-6,18] Loss of the fat plane with the liver (65.0% vs 20.0%), direct hepatic invasion (40.0% vs 3.3%), biliary dilatation (40.0% vs 10.0%) and suspicious regional nodes (50.0% vs 13.3%) were all more frequent in malignant lesions. Bozer and Durgun found intrahepatic biliary dilatation, adjacent-organ invasion and lymph-node enlargement to be significantly associated with gallbladder carcinoma; a lymph-node short-axis cut-off >8 mm yielded an AUC of 0.843.[10] These features reflect the invasive and lymphotropic behavior of carcinoma.

Their specificity is usually greater than their sensitivity because early wall-confined tumors may lack any extragallbladder abnormality. Distant metastasis was seen only in malignancy in the present analysis (15.0%), but the association did not reach conventional statistical significance ($P=0.058$), illustrating the loss of statistical power when event counts are small. Intramural hypoattenuating nodules and cystic spaces on CECT remained strongly benign-leaning. Bozer and Durgun found continuous mucosal lines and intramural hypoattenuating nodules to be more common in XGC,[10] and Bo et al. showed that combined imaging improves the difficult distinction between XGC and cancer.[11] These findings also accord with the broader benign disease literature describing mural cysts as a hallmark of adenomyomatosis.[5,13] The practical implication is that a thick wall containing well-defined intramural nodules/cysts with preserved mucosal continuity should temper an otherwise reflex malignant interpretation, especially when the apparent extramural extension could be inflammatory.

The diagnostic performance of USG was 80.0% sensitivity, 80.0% specificity and 80.0% accuracy; CECT achieved 85.0%, 83.3% and 84.0%, respectively. Bozer and Durgun reported CT sensitivity 75%, specificity 74% and accuracy 74% for differentiating XGC from gallbladder cancer.[10] The somewhat higher CT accuracy observed in the present analysis may be related to differences in case mix: the benign group includes chronic cholecystitis and adenomyomatosis as well as XGC, and some of these entities display more recognizable benign imaging signatures than XGC, which is among the most difficult malignant mimics. In the large study by Bo et al., performance varied across modalities, again emphasizing that no single modality completely resolves the XGC-carcinoma distinction.[11] The combined USG+CECT assessment performed best, with 90.0% sensitivity, 86.7% specificity and 88.0% accuracy. This magnitude is comparable to the 87.5% accuracy reported for high-frequency CEUS in focal fundal thickening by Dong et al.[23] and to the 90% sensitivity and 88% specificity of multiparametric MRI in the prospective study by Kalage et al.[20] Kuipers et al. reported pooled DWI sensitivity of 0.87 and specificity of 0.84 across eight studies, with improved accuracy when DWI was added to conventional MRI.[24] These comparisons support the concept that diagnostic confidence rises when complementary information is integrated. However, the present combined value should not be interpreted as evidence that routine USG+CECT is equivalent to advanced MRI or CEUS because the study populations, disease spectra and imaging protocols differ substantially. Not all recent evidence has shown a strong discriminatory role for conventional CT. In a prospective 33-patient comparison, Kalage et al. found that none of the assessed CT features was significantly associated with gallbladder cancer, while MRI heterogeneous enhancement, indistinct liver interface and diffusion restriction were significant malignant predictors and intramural cysts favored benign disease.[19] Similarly, a 2025 prospective dual-energy CT study found that quantitative DECT parameters did not add substantial discriminatory value in the overall benign-versus-malignant wall-thickening cohort, although lymphadenopathy remained associated with malignancy.[21] Differences from the present findings may be explained by small sample sizes, stricter enrollment of diagnostically difficult non-acute wall thickening, CT acquisition phases, reader thresholds and the relative proportion of XGC. These studies reinforce the need to avoid overconfidence in any single CT sign and support MRI as a problem-solving modality when routine imaging remains equivocal.[19-21,24] Histopathologically, chronic cholecystitis was the most common benign diagnosis, while

adenocarcinoma constituted 18 of 20 malignant lesions (90.0%). This distribution is consistent with contemporary pathology reviews describing conventional adenocarcinoma as the dominant histological form of gallbladder carcinoma, with less common variants including adenosquamous and neuroendocrine carcinomas.[14-16] The presence of XGC in 12.0% and adenomyomatosis in 6.0% of the overall cohort also illustrates why pathological confirmation is central to radiology-pathology correlation: both entities can mimic carcinoma on imaging, but their microscopic substrate explains characteristic intramural findings.[12-14]

From a clinical perspective, the present pattern supports a tiered approach. A uniformly thickened wall with preserved layering/mucosal continuity and intramural cysts, comet-tail foci or XGC-like nodules should favor benign disease, whereas focal/asymmetric thickening accompanied by mural disruption, heterogeneous enhancement, loss of the liver interface, biliary obstruction or suspicious nodes should trigger a higher level of concern. This approach is consistent with GB-RADS and recent Korean Society of Abdominal Radiology recommendations advocating standardized description and risk-based work-up of gallbladder wall thickening.[8,25] Indeterminate cases may benefit from problem-solving MRI/CEUS or multidisciplinary radiology-pathology-surgical review rather than automatic escalation to radical surgery or dismissal as inflammation. Several limitations must be emphasized. First, the small cohort size limits precision, as reflected by the width of the diagnostic-accuracy confidence intervals. Second, restricting the reference standard to surgical histopathology introduces verification and referral bias by excluding many conservatively managed benign cases. Third, ultrasound is operator dependent, and interobserver agreement was not assessed. Fourth, the analysis does not account for potential collinearity among focality, asymmetry, mural disruption and liver-interface loss, and the sample size would not support a large multivariable model.

Conclusion

Malignant gallbladder wall thickening was characterized by greater mural thickness, focal/asymmetric morphology, loss of mural stratification, mucosal disruption, heterogeneous or thick inner-layer enhancement, loss of the liver interface, hepatic invasion, biliary dilatation and regional lymphadenopathy. Intramural cystic spaces, comet-tail echogenic foci and intramural nodules favored benign disease, while pericholecystic inflammatory change was non-discriminatory. A wall-thickness threshold of ≥ 6.7 mm provided useful discrimination but was most informative when interpreted together with

morphology and enhancement. CECT modestly outperformed conventional ultrasonography, while integrated USG+CECT assessment produced the highest diagnostic accuracy.

Histopathology remains essential because XGC and adenomyomatosis may closely mimic carcinoma. Overall, the findings support a structured radiology-pathology correlation approach in the evaluation of gallbladder wall thickening.

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