



Body Imaging

Usefulness of noncontrast MRI in differentiation between gallbladder carcinoma and benign conditions manifesting as focal mild wall thickening

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ARTICLE INFO

Keywords:

Gallbladder, carcinoma

MR-imaging

Contrast agents-intravenous noncontrast MRI

ABSTRACT

Background: Magnetic resonance imaging (MRI) is a reliable imaging tool for evaluating gallbladder carcinoma, but it is costly and time-consuming.

Purpose: To compare noncontrast MRI with multidetector row CT (MDCT) and gadoteric acid-enhanced whole MRI in distinguishing gallbladder carcinoma from benign disease.

Materials and methods: 101 patients (36 with gallbladder carcinoma and 65 with benign disease) with mild focal gallbladder wall thickening were included. Two radiologists reviewed the MDCT and MRI to determine the differential features between malignancy and benignity. Then, the diagnostic performance of MDCT and MRI (T1-, T2- and diffusion-weighted images) with and without gadoteric acid enhancement in the diagnosis of gallbladder carcinoma was evaluated.

Results: The benign group more often showed T2 necklace sign or T2 hyperintensity within the thickened wall ($P < 0.0001$) and T1 hyperintensity within the wall or gallbladder lumen ($P = 0.0002$). Meanwhile, malignancy more frequently showed T2 moderate hyperintensity of the thickened wall, papillary appearance, and diffusion restriction (all $P < 0.0001$). There were significant differences in sensitivity (79.2% vs 98.6% for observer 1; 84.7% vs 100% for observer 2) and specificity (80.7% vs 96.9%; 79.2% vs 95.4%) between the MDCT and noncontrast MRI ($P < 0.05$). We found similar diagnostic values between the noncontrast MRI and whole MRI ($P = 0.479$ – 1.000) for both observers.

Conclusion: Noncontrast MRI could be a useful alternative to gadoteric acid-enhanced MRI in the diagnosis of gallbladder carcinoma that presents as mild gallbladder wall thickening on MDCT.

1. Introduction

Thickening of the gallbladder wall can result from a broad spectrum of pathologic conditions: chronic cholecystitis, gallbladder carcinoma, and focal adenomyomatosis are all common diseases [1]. Misinterpretation of benign gallbladder wall thickening on imaging studies can lead to unnecessary cholecystectomies in patients with non-symptomatic benign gallbladder disease or without intrinsic gallbladder disease. Conversely, misdiagnosis of gallbladder carcinoma that does require cholecystectomy could result in delayed treatment with increased morbidity (with dismal prognosis), and the curative resection rate for gallbladder carcinoma is ranged only 10% to 30% [2,3].

Because multidetector row CT (MDCT) is now widely used for tumor staging in patients with malignancy in the abdomen and for surveillance for tumor recurrence after treatment, we frequently encounter

incidental, asymptomatic, mild focal gallbladder wall thickening. In that situation, in addition to the fundamental question of differentiating benign conditions from malignancy, we wonder whether contrast-enhanced whole MRI is mandatory for further evaluation. Given the high volume of MR studies performed in this very large population, as well as the recently described association between gadolinium contrast agents and nephrogenic systemic fibrosis and accumulation in the brain [4], it is worthwhile to consider noncontrast MR protocol that offers quicker examination times, lower costs, and lower patient inconvenience by preventing the need for gadolinium examination.

Diffusion-weighted imaging (DWI) has now been introduced into the routine protocol for abdominal MRI. Several studies have shown the efficacy of DWI in differentiating gallbladder carcinoma from benign diseases such as cholecystitis and adenomyomatosis using visual assessments of an apparent diffusion coefficient (ADC) map or

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<https://doi.org/10.1016/j.clinimag.2018.12.001>

Received 2 August 2018; Received in revised form 9 November 2018; Accepted 2 December 2018

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Table 1
MRI sequences and parameters.

Sequence	TR/TE (msec)	FA	Section thickness	Matrix size	Bandwidth (Hz/pixel)	Field of view (cm)	Acquisition time (sec)	No. of excitations
T1W-3D dual GRE	3.5/1.15–2.3	10°	6 mm	256 × 194	434.4	32–38 cm	14	1
BH-MS-T2WI	1623/70	90°	5 mm	324 × 235	235.2	32–38 cm	55	1
RT-SSH-HT2WI	1156/160	90°	5 mm	320 × 256	317.9	32–38 cm	120	2
T1W-3D GRE	3.1/1.5	10°	2 mm	256 × 256	995.7	32–38 cm	16.6	1
DWI	1600/70	90°	5 mm	112 × 112	79.5	32–38 cm	126	2

GRE = gradient echo, BH-MS-T2WI = breath-hold multishot T2-weighted image, RT-SSH-T2WI = respiratory-triggered single-shot heavily T2-weighted image, DWI = diffusion-weighted imaging.

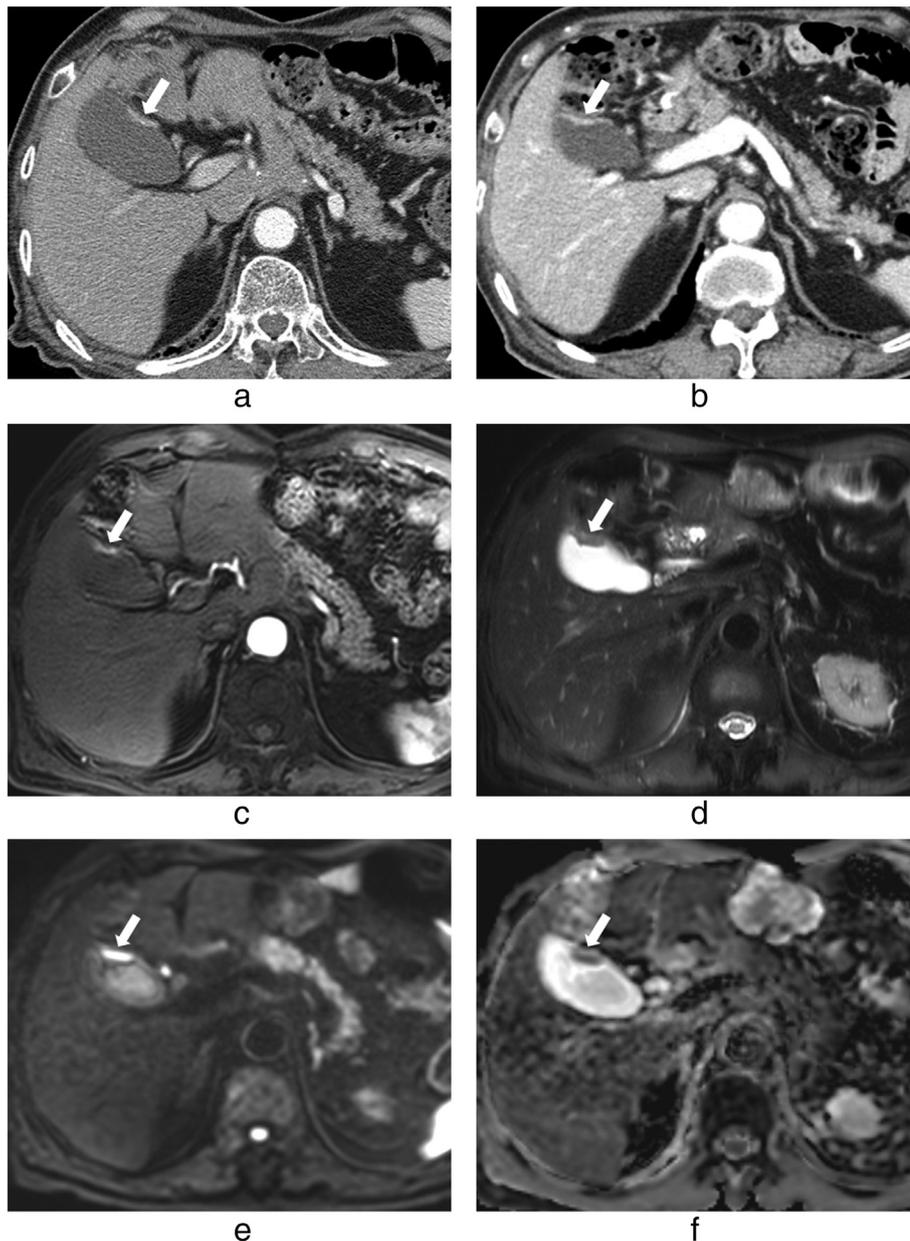


Fig. 1. Incidentally detected gallbladder adenocarcinoma (1.5 cm in diameter) after gastrectomy for gastric malignancy in a 78-year-old man. The tumor (arrows) is seen as mild focal wall thickening with mild homogeneous enhancement on the arterial phase (a) and portal venous phase (b) of MDCT. The lesion was rated as confidence grade 3, “indefinite,” by both observers. The tumor (arrows) is clearly seen as strongly enhanced focal wall thickening on the arterial phase MRI after administration of gadolinic acid (c) and as moderate hyperintensity on the T2-weighted image (d). The tumor (arrow) is seen as a hyperintense and dark area on a single-shot echo-planar diffusion weighted image at $b = 800 \text{ s/mm}^2$ (e) and the ADC map (f).

quantitative measurement of ADC values [5–9]. It is well known that T2-weighted images (T2WI) provide definitive clues, called the *necklace sign*, to diagnose adenomyomatosis via recognition of the Rokitansky-Aschoff sinus, which sometimes accompanies hyperintensity within T1-weighted images (T1WI) [10,11].

With these concepts in mind, we conducted this study to assess the usefulness of noncontrast MRI (T1WI, T2WI, and DWI) in the characterization of incidentally detected mild gallbladder wall thickening

on MDCT as benign or malignant by comparing it with MDCT and whole MRI.

2. Materials and methods

2.1. Study population

Our institutional review board approved this retrospective study,

Table 2
MR imaging characteristics of patients with GB carcinoma and benign disease.

MRI feature	GB carcinoma (N = 36)	Benign (N = 65)	Total (N = 101)	P-value*
Papillary growth pattern				< 0.0001
Absent	21 (58.3%)	62 (95.4%)	83 (82.1%)	
Present	15 (41.7%)	3 (4.6%)	18 (17.8%)	
Enhancement pattern (CT)				0.5293
Homogeneous	12 (33.3%)	26 (40.0%)	38 (37.6%)	
Layered	24 (66.7%)	39 (60.0%)	63 (62.4%)	
Enhancement pattern (MR)				0.6702
Homogeneous	12 (33.3%)	25 (38.5%)	37 (36.6%)	
Layered	24 (66.7%)	40 (61.5%)	64 (63.4%)	
Degree of enhancement (CT)				0.0341
Poor	5 (13.9%)	13 (20.0%)	18 (17.8%)	
Mild-moderate	6 (16.7%)	24 (36.9%)	30 (29.7%)	
Strong	25 (69.4%)	28 (43.1%)	53 (52.5%)	
Degree of enhancement (MR)				< 0.0001
Poor	1 (2.8%)	17 (27.2%)	50 (26.7%)	
Mild-moderate	6 (16.7%)	32 (49.2%)	35 (18.7%)	
Strong	29 (80.6%)	16 (24.6%)	102 (54.6%)	
T1 hyperintensity within thickened wall				0.0002
Absent	36 (100%)	51 (78.5%)	87 (86.1%)	
Present	0 (0.0%)	14 (21.5%)	14 (13.9%)	
Necklace sign				< 0.0001
Absent	36 (100.0%)	35 (53.8%)	71 (70.3%)	
Present	0 (0.0%)	30 (46.2%)	30 (29.7%)	
Degree of T2 hyperintensity				< 0.0001
No visibility	0 (0.0%)	50 (76.9%)	50 (49.5%)	
Moderate	36 (100.0%)	5 (7.7%)	41 (40.6%)	
High	0 (0.0%)	10 (15.4%)	10 (9.9%)	
T1 high SI in GB lumen				0.0002
Absent	26 (72.2%)	21 (32.3%)	47 (46.5%)	
Present	10 (27.8%)	44 (67.7%)	54 (53.5%)	
Diffusion restriction				< 0.0001
Absent	1 (2.8)	54 (83.1%)	55 (54.5%)	
Present	35 (97.2%)	11 (16.9%)	46 (45.5%)	
Stone				0.7082
Absent	34 (94.4%)	59 (90.8%)	93 (92.1%)	
Present	2 (5.6%)	6 (9.2%)	8 (7.9%)	

* Fisher's exact test.

and the requirement for informed consent was waived. We browsed our institution's MRI database from November 2011 to December 2016 using the search term "gallbladder." A total of 446 patients were identified. We also searched our institution's radiology report database for MRI reports created between October 2008 and May 2017 that contained terms that could describe gallbladder carcinoma, adenomyomatosis, and cholecystitis. That query yielded 333 patients. After excluding 215 patients with gallbladder disease that manifested as mass forming type gallbladder malignancy and diffuse wall thickening, including advanced gallbladder carcinoma, acute cholecystitis, xantho-granulomatous cholecystitis, and the diffuse type of adenomyomatosis, we included 118 patients.

Among those patients, we identified 101 who had undergone both MDCT and MRI within a two-week interval. Ultimately, 36 patients (21 men, 15 women; mean age [standard deviation], 53.1 [8.9] years) with gallbladder carcinoma and 65 patients (28 men, 37 women; mean age [standard deviation], 62.1 [10.4] years) with benign conditions such as chronic cholecystitis or focal adenomyomatosis met the inclusion criteria. Since our institutional policy is that gadoteric acid is chosen over extracellular agent as a MR contrast agent for patients suspected of gallbladder lesion in consideration of liver lesion, most patients had undergone gadoteric acid-enhanced MRI [12].

2.2. Reference standard

Reference standards for all malignancies were based on surgical specimens. The average time between MRI and surgery was 16 days (range, 7–30 days). Operations included cholecystectomy in 30 patients, and radical cholecystectomy in 6 patients. Forty-five cases of chronic cholecystitis were confirmed by cholecystectomy (N = 43) or radical cholecystectomy (N = 2), and 10 of those cases also had accompanying adenomyomatosis. The final diagnosis of the remaining 20 adenomyomatosis cases was based on typical imaging findings and stability for at least 12 months of follow up.

2.3. MDCT and MR examination

Multiphasic (unenhanced, arterial, and venous) CT was conducted using either a 40-MDCT scanner (Brilliance 40; Philips Healthcare) or a 64-MDCT scanner (Aquilion 64; Toshiba Medical and Light Speed VCT 64, GE Healthcare). The scanning parameters were 120 kVp, 189–200 mAs, 5-mm slice thickness with an increment (overlap) of 2.5 mm, table speed of 26.5–39.37 mm/rotation (pitch 0.828–1.07), and a single-breath-hold helical acquisition of 4–6 s, depending on liver size. Arterial phase scanning began 30–40 s after injection of 110 or 120 mL of the nonionic iodinated contrast agent iopamidol (Iopamiro 300, Bracco) at a rate of 3–4 mL/s. The contrast was administered using a bolus-triggered technique (120 kVp; 40–60 mA; monitoring frequency from 12 s after the contrast injection, 1 s; trigger threshold, 100 HU in the descending aorta; delay from trigger to initiation of scan, 18 s). Portal venous phase scanning began 70 s after injection of the contrast agent.

MRIs were acquired using a 3.0-T whole-body MRI system (InteraAchieva; Philips Healthcare, Best, The Netherlands) equipped with quadrature body coil. The baseline MRI included T1-weighted turbo-field-echo in-phase and opposed sequence, breath-hold multi-shot T2WI, and respiratory-triggered single-shot heavily T2WI.

For gadoteric acid MRI, unenhanced, arterial phase (AP; 20–35 s), portal venous phase (PVP; 60 s), transitional-phase (3 min), and 20-minute hepatobiliary phase images were obtained using a T1-weighted 3D turbo-field-echo sequence (T1 high-resolution isotropic volume examination [THRIVE; Philips Healthcare]). Contrast agent was administered intravenously using a power injector at a rate of 1 mL/s for a dose of 0.025 mmol/kg body weight, followed by 20-mL saline flush.

DWI was obtained by respiratory-triggered single-shot echo with b-values of 0, 100, and 800 s/mm² and spectral presaturation with inversion recovery for fat suppression. The ADC was calculated by a monoexponential function using b-values of 100 and 800 s/mm². The detailed parameters of the MR sequences are shown in Table 1.

2.4. Image analysis

Image analysis consisted of two sessions. In the first session, the following imaging features were assessed independently by two observers (Y.K.K, and J, H, M) who then reached consensus: (a) presence of papillary configuration on T2WI, (b) enhancement pattern (homogeneous or layered thickening), (c) enhancement degree on the AP and PVP of the MDCT and MRI (1 = poor enhancement; 2 = mild to moderate enhancement defined as enhancement degree lower than liver or spleen; 3 = strong enhancement similar to signal intensity of the spleen), (d) presence of intramural hyperintensity on T1WI, (e) presence of intramural hyperintensity (necklace sign) on T2WI, (f) signal intensity of thickened gallbladder wall on T2WI (moderate hyperintensity similar to signal intensity of the spleen or darker signal intensity or nondetectable), (g) presence of hyperintensity in the gallbladder lumen on T1WI, (h) diffusion restriction (when it was hyperintense at $b = 100$ s/mm², remained hyperintense at $b = 800$ s/mm², and showed an ADC value lower than or equal to that of the liver parenchyma), and (i) the presence of gallbladder stones.

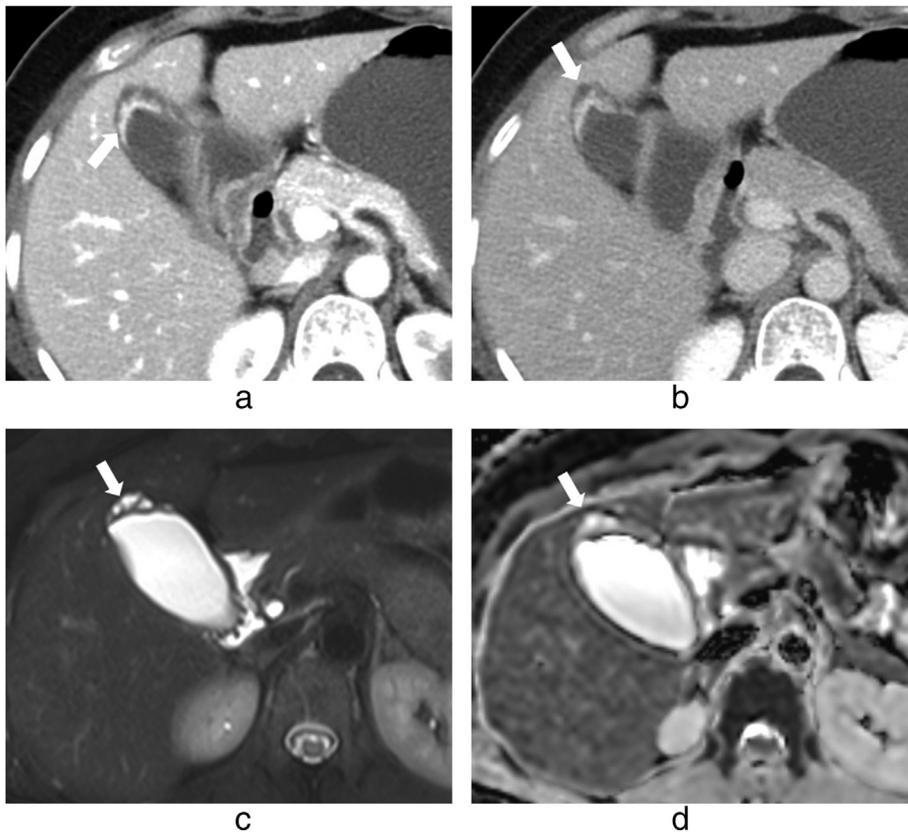


Fig. 2. Localized adenomyomatosis (2.5 cm in diameter) in a 64-year-old man. On the arterial phase (a) and portal venous phase (b) of MDCT, localized layered wall thickening (arrows) in the fundus is seen with strong enhancement of the inner layer. The lesion was rated as confidence grade 5, “malignancy,” by both observers. Multiple hyperintense cystic spaces indicating the Rokitansky-Aschoff sinus are clearly seen on the T2-weighted image (c) and ADC map (d).

In the second session, two off-site observers (D.C and J.L) independently and separately analyzed the MDCT and MRI with and without gadoteric acid MRI at four-week intervals. Prior to the image analysis, all images were anonymized, and the cases were arranged randomly. The criteria for gallbladder carcinoma on the contrast-enhanced images were homogeneously strong enhancement (or strong enhancement of the inner layer in cases of layered wall thickening) with or without the presence of a cauliflower configuration in the thickened wall. Early strong enhancement that persists to the PVP was considered to be more likely malignant than benign. On noncontrast MRI, diffusion restriction and T2 moderate hyperintensity in the thickened wall were considered to indicate gallbladder carcinoma. Intramural hyperintensity on T1WI or T2WI, including necklace sign, was considered to indicate benignity (localized adenomyomatosis).

Using those criteria, each observer was instructed to assign a score to each lesion using a 5-point scale: 1, probably benign; 2, possibly benign; 3, indeterminate; 4, possibly gallbladder carcinoma; 5, gallbladder carcinoma. At the time of this second image review, the reviewers knew that the sensitivity was calculated using the numbers of patients allocated a rating of 4 or 5, and the specificity used the number of patients with a rating of 1 or 2. The criteria above were presented to the observers as rough reference standards. However, the final decisions were made by the subjective judgment of each observer based on each lesion's features.

2.5. Statistical analysis

The frequency of MDCT or MRI features in the benign group and malignant group was calculated and compared using Fisher's exact test. For statistical analysis, lesions were divided into the following three groups: score 1–2, benign; score 3, indeterminate; score 4–5, malignant. We calculated the sensitivity, specificity, and accuracy of the diagnosis of gallbladder malignancy according to the observer and modality used. Lesions with a score of 3 (indeterminate) were arbitrarily given a

probability of 0.5 for those calculations. The differences in each parameter between the imaging modalities were compared using Bennett's test or McNemar's test.

The interobserver reliability analysis was performed using Cohen's weighted kappa statistics. The strength of agreement was scored as follows: a kappa value < 0 indicates poor agreement; 0.000–0.200, slight; 0.201–0.400, fair; 0.401–0.600, moderate; 0.601–0.800, substantial; and 0.801–1.000, almost perfect agreement.

All statistical analyses were performed using R version 3.3.2 (Vienna, Austria). *P*-values < 0.05 were considered statistically significant (two-tailed).

3. Results

The diameter of the 36 malignancies ranged from 0.9 to 2.0 cm (mean \pm SD, 1.85 \pm 0.20 cm), and the diameter of the 65 benignities ranged from 1.0 to 2.1 cm (mean \pm SD, 1.96 \pm 0.30 cm). The thickness of malignancy ranges from 0.8 cm to 1.5 cm (mean \pm SD, 1.08 \pm 0.23 cm) and the thickness of benignities ranged from 0.5 cm to 1.5 cm (mean \pm SD, 1.05 \pm 0.25 cm). Forty-two lesions were in the gallbladder fundus, 42 were in the body, and 17 were in the neck.

3.1. MDCT and MRI features

We found no significant differences in layered and homogeneous enhancement between benignities and malignancies, with both MDCT (*P* = 0.53) and gadoteric acid-enhanced MRI (*P* = 0.67). With regard to the degree of enhancement, gallbladder carcinoma showed strong enhancement, higher than that of liver parenchyma, more often than benign conditions on both MDCT (69.4% vs 43.1%) and MRI (80.6% vs 24.6%) (*P* = 0.03 and *P* < 0.0001) (Fig. 1) (Table 2).

We found significant differences between malignancies and benign conditions in the prevalence of T1 hyperintensity within the thickened wall or in the gallbladder lumen, T2 signal intensity, papillary growth

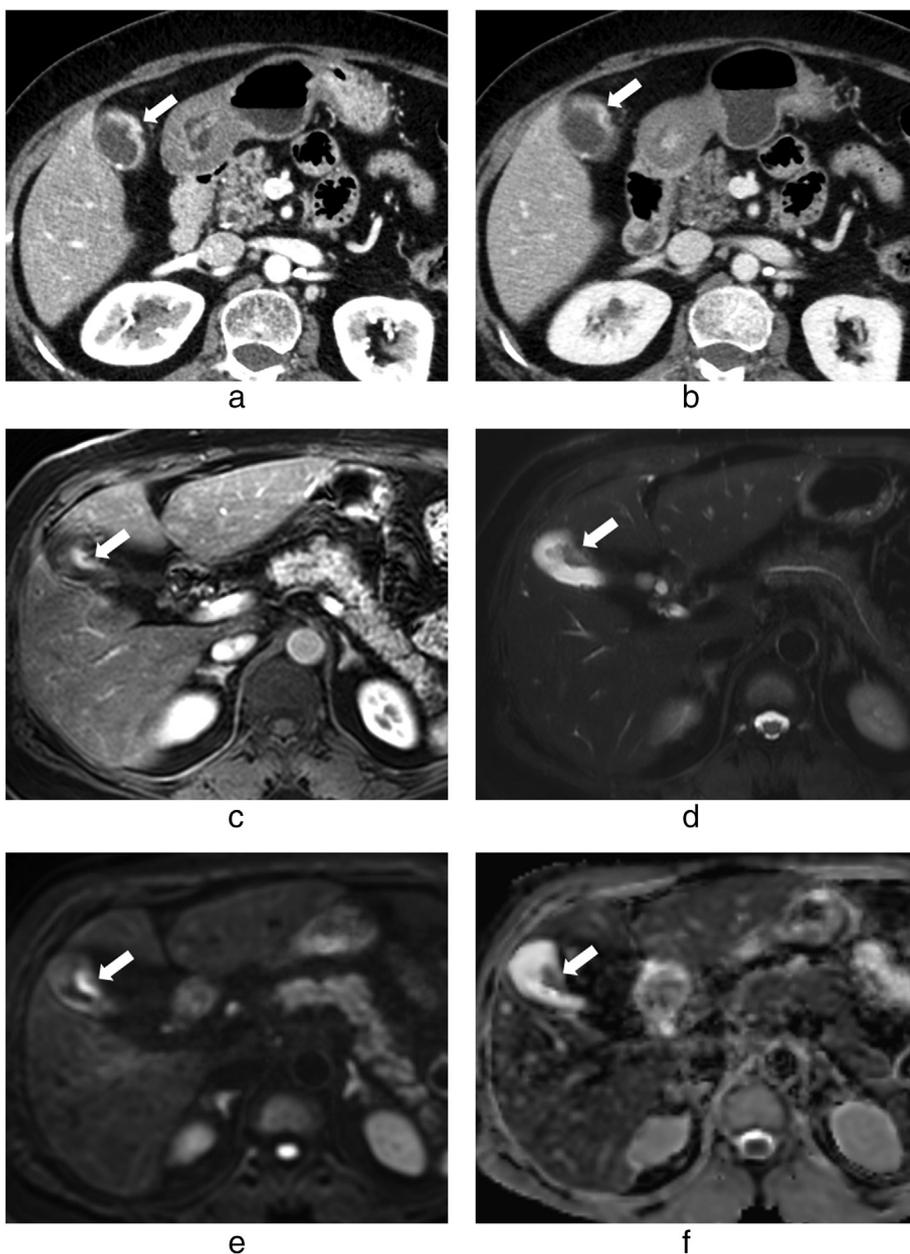


Fig. 3. Gallbladder carcinoma (2.0 cm in diameter) in a 44-year-old woman. The tumor (arrows) is seen as mild focal wall thickening with homogeneous enhancement on the arterial phase (a) and portal venous phase (b) of MDCT. The lesion was rated as confidence grade 3, “indeterminate,” by both observers. The tumor (arrows) is seen as strongly enhanced layered wall thickening on arterial phase MRI after the administration of gadolinic acid (c) and as moderate hyperintensity with a papillary configuration on the T2-weighted image (d). The tumor (arrow) is seen as a hyperintense and dark area on a single-shot echo-planar diffusion weighed image at $b = 800 \text{ s/mm}^2$ (e) and the ADC map (f).

Table 3
Scores assigned by two observers for three image sets.

		1	2	3	4	5	P-value	
Reviewer 1	Malignancy	MDCT	0 (0.0%)	2 (5.6%)	11 (30.5%)	20 (55.6%)	3 (8.3%)	< 0.0001
		Noncontrast MRI	0 (0.0%)	0 (0.0%)	1 (2.8%)	16 (44.4%)	19 (52.8%)	< 0.0001
		Whole MRI	0 (0.0%)	0 (0.0%)	1 (2.8%)	7 (19.4%)	28 (77.8%)	< 0.0001
Benign	MDCT	9 (13.8%)	36 (55.4%)	15 (23.1%)	5 (7.7%)	0 (0.0%)	< 0.0001	
	Noncontrast MRI	44 (67.7%)	18 (27.7%)	2 (3.1%)	0 (0.0%)	1 (1.5%)	< 0.0001	
	Whole MR MRI	48 (73.8%)	15 (23.1%)	0 (0.0%)	1 (1.5%)	1 (1.5%)	< 0.0001	
Reviewer 2	Malignancy	MDCT	0 (0.0%)	1 (2.8%)	9 (25.0%)	22 (61.1%)	4 (11.1%)	< 0.0001
		Noncontrast MRI	0 (0.0%)	0 (0.0%)	0 (0.0%)	18 (50.0%)	18 (50.0%)	< 0.0001
		Whole MRI	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (25.0%)	27 (75.0%)	< 0.0001
Benign	MDCT	9 (13.8%)	37 (56.9%)	11 (16.9%)	8 (12.3%)	0 (0.0%)	< 0.0001	
	Noncontrast MRI	44 (81.5%)	17 (26.2%)	2 (3.1%)	1 (1.5%)	1 (1.5%)	< 0.0001	
	Whole MRI	49 (75.4%)	14 (21.5%)	0 (0.0%)	1 (1.5%)	1 (1.5%)	< 0.0001	

Data are presented as value.
Numbers in parentheses are percentage.

Table 4
Accuracies, sensitivities, specificities, and positive (PPV) and negative predictive values (NPV) for three image sets for diagnosis of gallbladder carcinoma.

	Accuracy	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Reviewer 1					
MDCT	0.802/0.714–0.868	79.2/63.4–89.3	80.7/69.6–88.5	69.5/54.3–81.4	87.5/76.8–93.6
Noncontrast MRI	0.975/0.923–0.992	98.6/88.0–99.9	96.9/89.5–99.2	94.7/82.5–98.5	99.2/92.9–99.9
Whole MRI	0.975/0.923–0.992	98.6/88.0–99.9	96.9/89.5–99.2	94.7/82.5–98.5	99.2/92.9–99.9
Reviewer 2					
MDCT	0.812/0.725–0.876	84.7/69.7–93.0	79.2/67.9–87.3	69.3/54.6–80.9	90.4/80.0–95.7
Noncontrast MRI	0.970/0.916–0.990	100/90.4–100	95.4/87.3–98.4	92.3/79.7–97.4	100/94.2–100
Whole MRI	0.980/0.931–0.995	100/90.3–100	96.9/89.5–99.2	94.7/82.7–98.5	100/94.2–100

Data are presented as value/95% confidence interval.

Table 5
Diagnostic performance among the modalities.

	MDCT vs noncontrast MRI	MDCT vs whole MRI	Noncontrast MRI vs whole MRI
Reviewer 1			
Sensitivity	79.2% vs 98.6% (0.008)	79.2% vs 98.6% (0.008)	98.6% vs 98.6% (1.000)
Specificity	80.7% vs 96.9% (0.002)	80.7% vs 96.9% (0.001)	96.9% vs 96.9% (1.000)
Accuracy	80.2% vs 97.5% (0.001)	80.2% vs 97.5% (0.001)	97.5% vs 97.5% (1.000)
Reviewer 2			
Sensitivity	84.7% vs 100.0% (0.019)	84.7% vs 100.0% (0.019)	100.0% vs 100.0% (–)
Specificity	79.2% vs 95.4% (0.003)	79.2% vs 96.9% (0.0007)	95.4% vs 96.9% (0.479)
Accuracy	81.2% vs 97.0% (0.0004)	81.2% vs 98.0% (0.0001)	97.0% vs 98.0% (1.000)

Data are presented as percentage. Numbers in parentheses are *P* value.

patterns, and diffusion restriction ($P < 0.0001$ or $=0.0002$). T1 hyperintensity within the thickened wall was observed only in benign conditions, including adenomyomatosis ($n = 13$) with and without chronic cholecystitis and chronic cholecystitis ($n = 1$). In addition, the benign group showed the necklace sign or intramural hyperintensity on T2WI (46.2% vs 0%, $P < 0.0001$) (Fig. 2) and T1 hyperintensity within the gallbladder lumen (67.7% vs 27.8%, $P = 0.0002$) more often than malignant group. Meanwhile, the malignant group had the following features more frequently than the benign group: T2 moderate hyperintensity of the thickened wall (100% vs 7.7%, $P < 0.0001$), papillary appearance on T2WI (41.7% vs 4.6%, $P < 0.0001$), and diffusion restriction (97.2% vs 16.9%, $P < 0.0001$) (Fig. 3).

The interobserver agreement for all imaging findings except the enhancement pattern was substantial to perfect ($k = 0.81$ for T1 hyperintensity within thickened wall, $k = 0.75$ for T2 signal intensity, $k = 0.84$ for T1 hyperintensity within lumen, $k = 0.85$ for papillary appearance, and $k = 0.86$ for diffusion restriction). The interobserver agreement for the enhancement pattern on CT and MRI was fair ($k = 0.54$ and 0.61 , respectively).

3.2. Diagnostic performance of CT and non-contrast MRI

The distribution of lesions according to the scores on MDCT, non-contrast MRI, and whole MRI are presented in Table 3. The sensitivity, specificity, and accuracy for the diagnosis of gallbladder carcinoma by observer and modality are presented in Table 4. The overall diagnostic performance tended to be higher with noncontrast MRI or whole MRI than with MDCT for both observers. There were significant differences in sensitivity (79.2% vs 98.6% for observer 1, $P = 0.008$; 84.7% vs 100.0% for observer 2, $P = 0.019$), specificity (80.7% vs 96.9% for observer 1, $P = 0.002$; 79.2% vs 95.4% for observer 2, $P = 0.003$), and accuracy (80.2% vs 97.5% for observer 1, $P = 0.001$; 81.2% vs 97.0% for observer 2, $P = 0.0004$) between the noncontrast MRI and MDCT (Table 5). We found similar diagnostic values between the noncontrast MRI and whole MRI ($P = 0.479$ – 1.000) for both observers. The observers both misclassified 8 gallbladder malignancies as score 2 ($n = 7$) or 3 ($n = 1$) on MDCT, but they classified them correctly on the non-contrast MRI or whole MRI. A single malignancy was not verified by

either observer on MDCT or MRI. To the contrary, 13 benign lesions were labeled indeterminate by both observers on MDCT, but they were correctly classified on the noncontrast MRI or whole MRI. Three and four benignities were assigned as category 4 by observers 1 and 2, respectively. Two cases of chronic cholecystitis were not clearly discerned (category 3–5) by either observer in all three modalities (Fig. 4). A single case of chronic cholecystitis was misclassified as a malignancy (category 4) by both observers with the noncontrast MRI, but they correctly scored it as category 2 with MDCT or whole MRI.

3.3. Interobserver agreement

The interobserver agreement with regard to assigning benignity or malignancy based on a 5-point scale demonstrated substantial agreement for MDCT ($k = 0.727$) and excellent agreement both for non-contrast MRI ($k = 0.861$) and whole MRI ($k = 0.955$).

4. Discussion

Our study demonstrated that noncontrast MRI is superior to MDCT in differentiating gallbladder malignancy from benign conditions with regard to accuracy, sensitivity, and specificity. Another noteworthy finding of our study is that noncontrast MRI showed almost the same diagnostic performance as whole MRI using gadoxetic acid. In a clinical scenario in which MDCT was already done for another abdominal neoplasm, additionally performing whole MRI using gadolinium might be a burden because of its high cost, lengthy examination time, patient inconvenience, and the potential danger of the gadolinium-based agent. Therefore, noncontrast MRI could be a reasonable method for determining whether mild focal gallbladder wall thickening is malignant or not. Based on our results, it is also reasonable to expect that non-contrast MRI could be a good screening tool for gallbladder malignancy, with contrast-enhanced imaging reserved for tumor staging.

In MDCT, characterization of gallbladder wall thickening is based on the enhancement pattern of flat gallbladder wall thickening (i.e., layer enhancement) and the presence of an intralesional cystic area signaling adenomyomatosis [1]. However, given that all the participants in our study underwent MRI, our population might have been

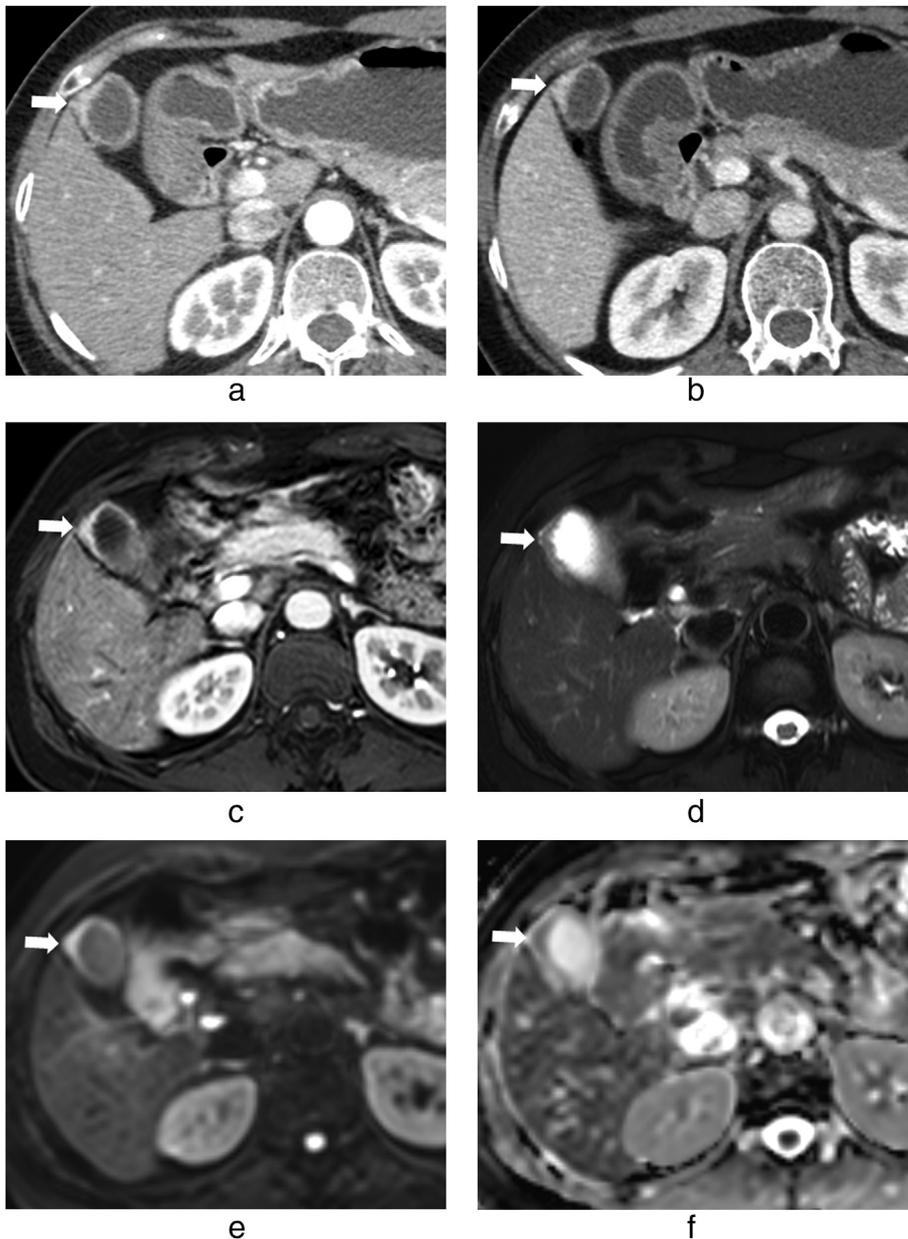


Fig. 4. Chronic cholecystitis (1.8 cm in diameter) in a 55-year-old woman. The lesion (arrows) is seen as mild focal wall thickening with homogeneous strong enhancement on the arterial phase (a) and portal venous phase (b) of MDCT. The lesion (arrows) is also seen as strongly enhancing wall thickening on the arterial phase (c) and portal venous phase (d) MRI after the administration of gadoxetic acid. On the T2-weighted image, a papillary configuration (arrow) at the thickened wall is suspicious. The lesion (arrows) is seen as a hyperintense and dark area on a single-shot echo-planar diffusion weighted image at $b = 800 \text{ s/mm}^2$ (e) and on the ADC map (f). The lesion was rated as confidence grade 4, “possibly gallbladder carcinoma,” by both observers with MDCT and MRI.

biased toward difficult cases in which the MDCT had no typical benign imaging features. According to the study by Kim et al. [13], adenomyomatosis tends to show inner layer enhancement, whereas chronic cholecystitis more often shows a one layer pattern. Gallbladder carcinoma could show both types of enhancement pattern. Thus, the degree of enhancement and papillary growth pattern were the only features for distinguishing between malignancy and benignity on MDCT and contrast-enhanced MRI. As we expected, we found no difference in the enhancement pattern between malignancy and benignity in the MDCT and gadoxetic acid-enhanced MRI. In line with the prior report [13], in which a highly enhanced thick inner wall layer seen during the AP was the most common enhancement pattern of gallbladder carcinoma, our study found that gallbladder carcinoma showed strong enhancement more often than benign conditions on both MDCT and gadoxetic acid MRI. However, our results suggest that, along with technical factors that might cause bias in contrast enhancement, judging the degree of wall enhancement with visual assessment is not robust.

We found significant differences between malignancy and benign conditions in the prevalence of T1 hyperintensity within the thickened wall or gallbladder lumen, T2 signal intensity, papillary growth

patterns, and diffusion restrictions. Intramural T1 hyperintensity was observed only in benignities, including adenomyomatosis ($n = 13$), and chronic cholecystitis ($n = 1$), and we thus consider it to be bile precipitates or inflammatory materials [11]. The necklace sign specific for adenomyomatosis was observed in seven patients, and intramural T2 hyperintensity was observed in three. Similar to a previous study [14], only 10 benign conditions showed hyperintensity within the gallbladder wall on T2WI in our study. Given that all gallbladder carcinomas showed moderate hyperintensity on T2WI as in line with previous studies [15,16], we could make a correct diagnosis in more than half of the benign conditions ($n = 40/65$, 61.5%) using bright T2 hyperintensity within the gallbladder wall or the necklace sign. Meanwhile, on MDCT, a small cystic structure indicating the Rokitansky-Aschoff sinus did not appear in any cases, including patients with adenomyomatosis. In addition, T2WI is known to be useful for delineating minute papillary projections of superficial tumors, including intraductal papillary mucinous tumors in the pancreas [17]. In this study, a papillary configuration on T2WI was more frequently observed in gallbladder carcinoma (41.7%) than in benign conditions (4.6%).

Several studies have shown the usefulness of DWI, with visual

assessment of high b-value images and quantitative measurements of ADC values, in differentiating between gallbladder carcinoma and benignities [5–9]. In this study, we did not apply a quantitative measurement of the ADC value because all cases manifested as mild focal wall thickening. All the gallbladder carcinomas but one in this study showed diffusion restriction as well as hyperintensity on high b-value images, which was significantly higher than we saw in the benign conditions (n = 11, 16.9%).

Our study had several limitations. The study is subject to selection bias because we retrospectively analyzed a cohort of patients who first underwent MDCT and then MRI for problem solving. A prospective study with predefined criteria would be warranted to investigate the performance of noncontrast MRI in the diagnosis of gallbladder malignancy. Second, gallbladder MRI in our institution was obtained using gadoxetic acid for enhanced detection of liver lesions. Thus, we are uncertain whether our results are generalizable to MRI using extracellular agents.

In conclusion, noncontrast MRI, including DWI, outperformed MDCT in the diagnosis of gallbladder carcinoma by differentiating it from chronic cholecystitis or adenomyomatosis, all of which manifest as mild focal wall thickening. The diagnostic performance of noncontrast MRI was similar to that of gadoxetic acid-enhanced MRI. Therefore, noncontrast MRI could be a useful alternative to gadoxetic acid-enhanced MRI in the diagnosis of gallbladder carcinoma, at least in patients who present with mild gallbladder wall thickening on MDCT.

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