

Discrimination of gangrenous from uncomplicated acute cholecystitis: Accuracy of CT findings

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Abstract

In acute cholecystitis, the presence of gangrene is associated with higher morbidity and mortality and necessitates open surgical intervention rather than laparoscopic cholecystectomy. As Murphy's sign may be absent, gangrene may not be detected ultrasonographically. This retrospective study evaluated indications of acute gangrenous cholecystitis on computed tomography (CT) in 25 patients, who were proven as having acute cholecystitis surgically and pathologically within 3 days of pre-operative CT. The CT images were reviewed by two board-certified radiologists blind to the initial CT report. Acute gangrenous cholecystitis was significantly correlated with the CT signs of perfusion defect (PD) of the gallbladder wall ($P = 0.02$), pericholecystic stranding (PS) ($P = 0.028$), and no-gallstone condition (No-ST) ($P = 0.026$). The presence of PD was associated with acute gangrenous cholecystitis with a relatively high accuracy (80%), a sensitivity of 70.6%, a specificity of 100%, a positive predictive value (PPV) of 100%, and a negative predictive value (NPV) of 61.5%. The combination CT signs of PD or No-ST improved the accuracy for acute gangrenous cholecystitis to 92%, with a sensitivity, specificity, PPV, and NPV of 88.2%, 100%, 100%, and 80%, respectively. Other CT signs were highly specific for acute gangrenous cholecystitis but of low sensitivity, including mucosal hemorrhage, mucosal sloughing, wall irregularity, pericholecystic abscess, gas formation, and portal venous thrombosis. CT was found to accurately diagnose acute cholecystitis, with the presence of PD, PS, or No-ST significantly correlated with that of gangrenous

change. Thus, CT is useful in the preoperative detection of acute gangrenous cholecystitis.

Key words: Acute cholecystitis—Gangrenous cholecystitis—Perfusion defect—Pericholecystic stranding—Gall stone—CT

Gangrene and necrotizing acute cholecystitis are severe advanced forms of the disease and are associated with a higher morbidity and mortality than occur in uncomplicated acute cholecystitis. Moreover, the clinical and laboratory characteristics of patients with these advanced forms are often nonspecific and indistinguishable from those of patients with acute cholecystitis without gangrene. As a result, the diagnosis is seldom made preoperatively [1].

On preoperative ultrasound, the Murphy sign may be absent due to denervation, resulting in a failure to identify acute gangrenous cholecystitis [2]. By the time the disease is suspected, patients frequently require treatment by an open surgical procedure rather than laparoscopic cholecystectomy [3, 4].

A few reports in the literature have described the computed tomography (CT) signs of gangrenous change in acute cholecystitis. The goal of this study was to identify those CT findings that would allow an accurate preoperative diagnosis of acute gangrenous cholecystitis and to compare those findings with the results reported by others.

Materials and methods

From January to May 2009, 8131 abdomen CT scans were obtained from the Picture Archiving and Communication Systems (PACS) of our institute. Of these,

cholecystitis was noted in the official radiologic report concerning 159 patients, 27 of whom underwent surgery within 3 days after CT and were subsequently diagnosed based on the pathology report as having cholecystitis. Two of these 27 patients were excluded from the study: one due to the diagnosis of chronic inflammation, detected on the pathology exam, and the other due to the presence of motion artifacts, resulting in poor image quality on the CT images. Thus, the study comprised 25 patients subsequently divided into two groups, i.e., those with gangrenous acute cholecystitis and those with uncomplicated forms of the disease. Approval for the study was granted by the institutional review board of our hospital.

Computed tomography examinations were performed on a 64-detector CT device (Light Speed QX/i Scanner, General Electric Medical Systems, Milwaukee, Wisconsin). Images were acquired from patients administered 100 mL of intravenous contrast agent. The slice thickness was 5 mm in all patients, in accordance with the departmental protocol, with the portal venous phase as the study target in all patients undergoing a multiphase study.

All CT examinations were retrospectively reviewed by two board-certified radiologists blinded to the official CT reports and to the surgical and pathologic findings. The CT images were reviewed in the context of the hospital's PACS and a consensus was reached in all cases, with disagreements resolved by drawing on the expertise of a third abdominal radiologist. The radiologists were requested to determine the presence of gallbladder wall hemorrhage (WH); irregular, intraluminal linear, and soft-tissue densities suggestive of mucosal sloughing (MS); outer wall irregularity (WI); discontinuity or decreased enhancement of the gallbladder wall, indicative of a wall perfusion defect (PD); encapsulated fluid collection adjacent to the gallbladder, suggestive of abscess (ABS); increased density of pericholecystic fat stranding (PS); abnormal gas formation in the wall or lumen or adjacent gallbladder (GAS); thrombosis or gas in the portal vein (VT); and focally increased enhancement of adjacent liver parenchyma (LC). The presence or absence of gallstone was also recorded; if no stone was perceptible (No-ST), then acalculous cholecystitis was noted in the patient's record. Correlations of CT variables with the final diagnosis of acute cholecystitis, without or with gangrenous change, were computed using the chi-square test, Fisher's exact test, or the Mann-Whitney test as appropriate; $P < 0.05$ was considered statistically significant.

Results

Gangrenous acute cholecystitis was confirmed in 17 patients and uncomplicated disease in 8 patients. The patients consisted of 14 men and 11 women; the mean age



Fig. 1. A 67-year-old man with acute gangrenous cholecystitis. Axial contrast-enhanced CT image shows acalculous acute cholecystitis with poor enhancement of the gallbladder globally (black arrow).

was 58.48 years (25–84 years). No statistical significance in age and sex existed between the two disease groups.

The percentage of each positive CT finding was as follows: WH (8.7%, $n = 2$), MS (8%, $n = 2$), WI (16%, $n = 4$), PD (48%, $n = 12$), ABS (8%, $n = 2$), PS (60%, $n = 15$), GAS (4%, $n = 1$), VT (4%, $n = 1$), LC (16%, $n = 4$), gallstone (68%, $n = 17$), No-ST (32%, $n = 8$).

Gallstones were seen in 17 patients, 9 with gangrenous disease and 8 with uncomplicated disease. In contrast, all 8 patients with No-ST status had acute gangrenous cholecystitis.

Interobserver agreement was good. Initial interobserver disagreement occurred concerning PD in three patients, No-ST in one, PS in four, and LC in one. After open discussion and the opinion of a third radiologist, consensus was achieved in all cases. A consensus regarding a global decrease in gallbladder wall enhancement (Fig. 1), seen in two patients, was obtained based on the presence of overtly decreased enhancement compared to adjacent duodenum.

Wall hemorrhage (Fig. 2) was evaluated with pre-contrast CT scanning in 23 of the patients who had undergone scanning of the upper abdomen.

A diagnosis of acute gangrenous cholecystitis was significantly correlated with PD (Fig. 2) ($P = 0.02$), PS (Fig. 3) ($P = 0.028$, odds ratio = 9.75, and 95% confidence interval: 1.38–68.78), and No-ST (Fig. 1) ($P = 0.026$). Among these variables, PD had the highest accuracy (80%) and showed a sensitivity of 70.6%, specificity of 100%, positive predictive value (PPV) of 100%, and negative predictive value (NPV) of 61.5%. The accuracy of PS and No-ST was 76% and 68%, respectively. The sensitivity, specificity, PPV, and NPV of PS were 76.5%, 75%, 86.7%, and 60%, respectively,

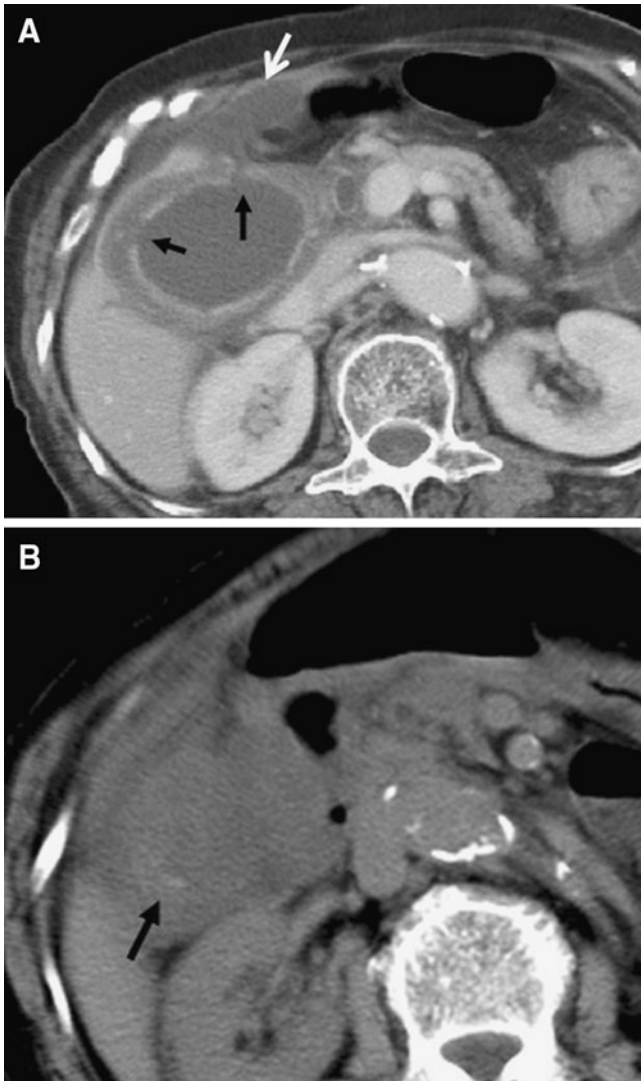


Fig. 2. An 80-year-old woman with acute gangrenous cholecystitis. **A** Axial contrast-enhanced CT image shows discontinuation of the mucosal enhancement with a gap at the gallbladder wall (*black arrow*) and an irregular wall associated with a pericholecystic fluid collection (*white arrow*), indicative of abscess formation. **B** A few centimeters below the structures seen in (**A**), a focal wall hyperdensity (*black arrow*) is suggestive of wall hemorrhage.

while the corresponding values for No-ST were 47.1%, 100%, 100%, and 47.1%, respectively. A combination of the CT signs of PD or No-ST improved the accuracy to 92% and the sensitivity, specificity, PPV, and NPV to 88.2%, 100%, 100%, and 80%, respectively.

Signs on CT of WH, MS (Fig. 4), WI (Fig. 2), ABS (Fig. 2), GAS (Fig. 5), VT (Fig. 6), or LC had high specificity but the sensitivity and accuracy of these findings were low and for acute gangrenous cholecystitis did not reach statistical significance. The data for these CT findings are provided in Tables 1 and 2.



Fig. 3. A 68-year-old man with acute gangrenous cholecystitis. Axial contrast-enhanced CT image shows wall thickening of the distended gallbladder, with increased pericholecystic stranding (*white arrow*).



Fig. 4. A 60-year-old woman with acute gangrenous cholecystitis. Axial contrast-enhanced CT image shows discontinuation of the mucosal enhancement with soft-tissue sloughing into the gallbladder lumen (*white arrow*).

Discussion

According to literature reports, the average time interval between CT and surgery is more than 2 days [1, 3]. Medical treatment is usually the initial strategy for acute cholecystitis. In our study, the interval between the CT study and surgery was limited to 3 days, since if the interval were prolonged, the CT findings would no longer accurately reflect the condition of the gallbladder at surgery.



Fig. 5. A 57-year-old woman with acute gangrenous cholecystitis. Axial contrast-enhanced CT image shows abnormal gas formation at the fundus of the gallbladder (*white arrow*).

The incidence of gangrenous cholecystitis ranges from 2% to 29.6%, according to various surgical series [2], and generally occurs in older patients. An increased incidence is seen in men and in patients with coexisting cardiovascular disease and leukocytosis $>17,000$ WBC/mL [2, 4]. The sonographic Murphy sign was found to be positive in only 33% of these patients, most likely due to denervation of the gallbladder wall [5].

Computed tomography had high sensitivity and specificity for the diagnosis of acute cholecystitis, with an overall accuracy of 94.3% [1]. The CT findings of acute gangrenous cholecystitis have been described in the literature and include gallbladder distention, wall thickening, decreased wall enhancement, irregular wall, wall striation, intraluminal membranes, pericholecystic inflammation, gallstones, pericholecystic fluid, pericholecystic liver enhancement, pericholecystic abscess, and gas in the gallbladder wall [1, 3, 6]. Gangrenous cholecystitis may also be associated with portal vein thrombosis [7] or portal vein gas [8]. Wall hemorrhage can present as a hyperdensity of the gallbladder wall on non-enhanced CT images. Patients with this sign are at high risk of acute gangrenous cholecystitis [9].

Obvious signs of acute gangrenous cholecystitis, such as pericholecystic abscess or gas-forming status, are not frequently seen on CT images, probably because they are easily detected in the primary sonography study, with CT playing a complementary role in patients with suspected acute gangrenous cholecystitis either missed or silent on ultrasound.

In our series, PD, PS, and gallstone were the most frequent findings in patients with acute gangrenous cholecystitis, in agreement with the report by Bennett et al. [1]. However, gallstones were also frequently seen in

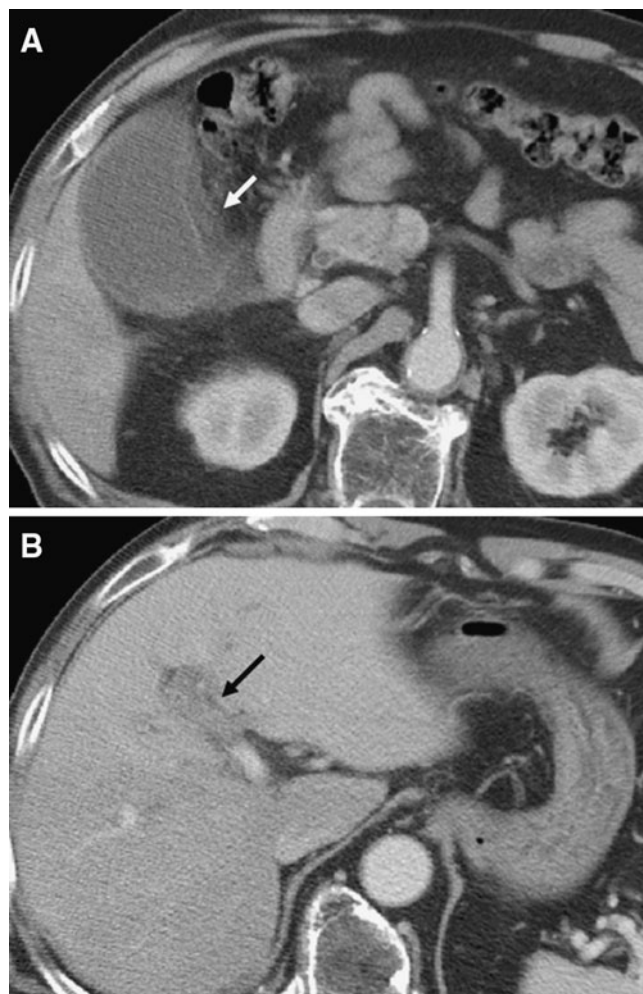


Fig. 6. A 78-year-old man with gangrenous cholecystitis but inconclusive findings on sonographic study. **A** Axial contrast-enhanced CT image shows pericholecystic stranding (*white arrow*) suggestive of acute cholecystitis. **B** A few centimeters cranial to (**A**) depicts left portal vein thrombosis (*black arrow*).

uncomplicated acute cholecystitis, whereas No-ST acute cholecystitis only occurred in patients with gangrenous disease.

The presence of PD, PS, or No-ST was statistically significant in patients with acute gangrenous cholecystitis. Among these, PD has been documented as a useful sign in the detection of the disease [1, 3]. Our data support the conclusion that if contrast-enhanced CT shows decreased wall enhancement, it is specific for acute gangrenous cholecystitis. Note that PD was often subtle and its detection required meticulous searching. The finding of PS also reflects the fact that severe gangrenous cholecystitis is more likely to induce inflammation beyond the gallbladder than in the case of uncomplicated cholecystitis. PS was seen in 76.5% ($n = 13$) of the 17 patients with acute gangrenous cholecystitis and was demonstrated intraoperatively to be the result of pericholecystic inflammation and edema.

Table 1. Correlation of individual CT signs with acute gangrenous cholecystitis

Individual factors		Gangrene (yes)	Gangrene (no)	P-value	Kappa
Wall hemorrhage (n = 23)	Yes	2	0	0.526	1
	No	13	8		
Mucosal sloughing (n = 25)	Yes	2	0	1	1
	No	15	8		
Wall irregularity (n = 25)	Yes	4	0	0.269	1
	No	13	8		
Perfusion defect (n = 25)	Yes	12	0	0.02*	0.757
	No	5	8		
Pericholecystic abscess (n = 25)	Yes	2	0	1	0.779
	No	15	8		
Pericholecystic stranding (n = 25)	Yes	13	2	0.028*	0.688
	No	4	6		
Abnormal gas (n = 25)	Yes	1	0	1	1
	No	16	8		
Portal vein thrombosis (n = 25)	Yes	1	0	1	1
	No	16	8		
Adjacent liver change (n = 25)	Yes	3	1	1	0.834
	No	14	7		
No gallstone (n = 25)	Yes	8	0	0.026*	0.911
	No	9	8		

* Fisher's exact test

Table 2. Diagnostic values of individual CT signs for acute gangrenous cholecystitis

	SS	SP	PPV	NPV	Accuracy (%)
WH	13.3	100	100	38.1	43.4
MS	11.8	100	100	34.8	40
WI	23.5	100	100	38.1	48
PD	70.6	100	100	61.5	80
ABS	11.8	100	100	34.8	40
PS	76.5	75	86.7	60	76
GAS	5.9	100	100	33.3	36
VT	5.9	100	100	33.3	36
LC	17.6	87.5	75	33.3	40
No-ST	47.1	100	100	47.1	68
PD or PS	88.2	75	88.2	75	84
PD or No-ST	88.2	100	100	80	92
PS or No-ST	82.4	75	87.5	66.7	80
PD or PS or No-ST	94.1	75	88.9	85.7	88

SS, sensitivity; SP, specificity; PPV, positive predict value; NPV, negative predict value; WH, wall hemorrhage; MS, mucosal sloughing; WI, wall irregularity; PD, perfusion defect; ABS, pericholecystic abscess; PS, pericholecystic stranding; GAS, abnormal gas; VT, portal vein thrombosis; LC, adjacent liver change; No-ST, no gallstone

Of the eight patients with acute cholecystitis but without discernible gallstones on CT, a tiny intraluminal stone was found intraoperatively in three of them. Acalculous acute cholecystitis usually occurs in critically ill patients. A previous study reported gangrene of the gallbladder in 59% of these patients [10].

In our study, we found that no single CT sign allowed an accurate diagnosis of acute gangrenous cholecystitis, as all were especially weak in terms of sensitivity and NPV. However, a combination of the CT signs of PD or No-ST increased the accuracy to 92%, sensitivity to 88.2%, specificity to 100%, PPV to 100%, and NPV to 82%, which in turn improved the accuracy, sensitivity, and NPV of CT in the diagnosis of acute gangrenous cholecystitis.

The findings with high specificity for gangrenous change in acute cholecystitis were WH (100%), WS (100%), WI (100%), ABS (100%), GAS (100%), VT (100%), LC (87.5%). Therefore, if any of these are detected, the possibility of gangrenous change in acute cholecystitis should be strongly considered.

Our study has recognized limitations, largely because of its retrospective nature and the fact that not all patients with acute cholecystitis underwent both CT and surgery. In clinical practice, patients with acute cholecystitis usually undergo a CT study when the sonographic study is inconclusive or the cause of an acute abdomen is ambiguous. An additional source of bias was that only patients with severe acute cholecystitis were operated on.

Summary

Computed tomography scanning is usually requested for patients with an acute abdomen when sonography is inconclusive, as this modality is sensitive and specific to acute cholecystitis. The correlation of PD, PS, or No-ST, as detected on CT, with gangrenous change was statistically significant. A combination of the CT signs of PD or No-ST markedly improved the accuracy, sensitivity, and NPV of CT in the diagnosis of acute gangrenous cholecystitis, while MH, WS, WI, ABS, GAS, and VT had high specificity for the disease. These findings are keys to the preoperative detection of acute gangrenous cholecystitis.

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