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Acalculous cholecystitis in hospitalized patients with hematological malignancies and the prognostic significance of sonographic gallbladder findings

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Abstract

Objectives—Patients with hematological malignancies—especially those with acute disease or those receiving intense chemotherapy—are known to develop acute acalculous cholecystitis (AAC). The aim of this study was to evaluate the diagnostic and prognostic value of the established sonographic diagnostic criteria for AAC in patients with acute hematological malignancies who were clinically suspected to have AAC.

Methods—We retrospectively studied the sonographic findings of the gallbladder in patients with hematological malignancies and correlated these findings with the duration of clinical symptoms, complications, and gallbladder-specific mortality. The major criteria were 3.5 mm or thicker wall, pericholecystic fluid, intramural gas, and sloughed mucosal membrane. The minor criteria were

echogenic bile and hydrops (gallbladder distension >4 cm). An ultrasound test was considered positive if it included 2 major criteria or 1 major and 2 minor criteria.

Results—Ninety-four (25.5%) of 368 patients with hematological malignancies had clinical signs of AAC during their acute phase of illness or during intense chemotherapy. Forty-three (45.7%) of these 94 patients had AAC-positive test results based on sonographic criteria. The mean duration of symptoms was significantly longer (7.8 days) in this group than among the patients with negative test results (3.9 days, $P<0.001$). Patients with positive test results had a higher rate of complication and/or mortality (20.9%) than did those with negative test results (0%, $P<0.001$).

Conclusions—Symptomatic patients who meet the sonographic criteria for the diagnosis of AAC have a poor prognosis. Other patients require close follow-up ultrasound examination within 1 week to detect early progression.

Keywords

acute acalculous cholecystitis; hematological malignancies; complications

Introduction

Patients with hematological malignancies are prone to develop acute acalculous cholecystitis (AAC), a necroinflammatory disease of the gallbladder in the absence of cholelithiasis, especially during advanced phases of illness, chemotherapy, and neutropenic episodes.¹⁻⁴ Although the acalculous variety is less common than calculous cholecystitis, AAC is more common in critically ill patients.⁵ Patients with hematological malignancies are often critically ill and in an advanced stage of disease and have higher rates of emergency room visits, hospitalization, and intensive care unit use.⁶⁻⁸ Clinical diagnosis of AAC in these patients is difficult because clinical features such as right upper quadrant pain and fever may be attributable to other abdominal complications such as enterocolitis, and abnormal leukocyte counts can be caused by the underlying hematological malignancy. Compared with calculous cholecystitis, AAC is associated with higher rate of complications, with gangrene found in up to 50% and gallbladder perforation in up to 10% of cases on histological examination.⁵ Therefore, early diagnosis and intervention are imperative whenever AAC is clinically suspected in patients with advanced hematological malignancies.

Imaging is used to support the clinical diagnosis of AAC. Ultrasonography is often the first modality used because it is easily accessible at the bedside, quick, relatively inexpensive, and repeatable. Sonographic criteria commonly used for the diagnosis of AAC are gallbladder wall thickening, gallbladder distension greater than 4 mm, pericholecystic fluid, sludge, sloughed mucosal membrane, and intramural gas.⁹ Different combinations of these findings have been used as criteria to diagnose AAC, with sensitivities ranging from 18% to 93%.^{10,11} Imhof et al. found that sonomorphological changes were detected within 24 hours of symptom onset, and a triad of gallbladder hydrops, wall thickening, and sludge were detected by 11 days on average.¹¹ Wang et al. used a scoring system and found a higher tendency for complications in patients with a higher score; however, this finding was not

statistically significant.¹² Cornwell et al. were able to preoperatively diagnose AAC in 13 of 14 patients using the major criteria of wall thickening, pericholecystic fluid, intramural gas, and sloughed mucosal membrane and the minor criteria of distension and sludge.¹⁰ However, a few studies of critically ill patients have shown that some of these findings may be seen in patients without AAC.^{13,14} Thus, uncertainty exists about the diagnostic value of sonographic criteria and their prognostic significance.

Although limited studies have documented AAC in patients with leukemia,^{1,4} to our knowledge no study has specifically documented the prognostic significance of AAC sonographic criteria in patients with hematological malignancies. A better understanding of what percentage of patients with similar right upper quadrant symptoms meet AAC sonographic criteria on ultrasound examination, along with the prognostic significance of these criteria, would improve clinical management and treatment plans.

Therefore, the purpose of our study was to evaluate the prognostic significance of AAC sonographic criteria in hospitalized patients with hematological malignancies. We hypothesized that the presence of positive sonographic criteria could predict a higher rate of complications and/or mortality. To test our hypothesis, we retrospectively studied AAC sonographic criteria in hospitalized patients with hematological malignancies who had clinical findings suggestive of AAC (fever, right upper quadrant pain, abnormal liver function tests, and tenderness).

Materials and Methods

This HIPAA-compliant retrospective study was approved by The University of Texas MD Anderson Cancer Center's institutional review board with a waiver for informed consent. The study subjects were identified through a search of the institutional radiology database for abdominal ultrasound studies performed for right upper quadrant symptoms in hospitalized patients with advanced hematological malignancies (leukemia, lymphoma, or myeloma) from August 2011 to August 2016. We defined advanced hematological malignancies as incurable disease at presentation or recurrent disease not eligible for potentially curative treatments per oncology notes. The search yielded 368 patients hospitalized with advanced hematological malignancies who had abdominal ultrasound examinations for right upper quadrant symptoms. Among these 368 patients, we excluded 124 patients who had gallbladder calculi, 58 patients who had calculus cholecystitis, 50 patients who had a history of cholecystectomy, 24 patients who had liver disease that could have contributed to right upper quadrant symptoms, and 14 patients who had more than 1 malignancy; another 4 patients were excluded because of limited ultrasound examination of the gallbladder inconclusive findings. In total, 94 consecutive patients who had advanced hematological malignancies and were suspected to have AAC (median age, 42.5 y; range, 6-64 y) were included in the analysis. All the patients had clinical features suspicious for AAC at the time of ultrasound examination. Specifically, all 94 patients had fever, abnormal liver function test results, right upper quadrant pain, and tenderness.

Ultrasound Protocol

All ultrasound studies were performed in a single institution on Philips IU 22 US machines (Philips Medical Systems, Bothell, WA, USA) using a curvilinear transducer (3-8 MHz). The studies were performed using standardized ultrasound examination protocols by 6 certified ultrasound technologists with experience ranging from 1 to 30 years. Static images and cine loops of the gallbladder were recorded in longitudinal and transverse planes through intercostal, subcostal, and decubitus subcostal approaches. All the images were reviewed by fellowship-trained abdominal radiologists while the patient was still in the department. The images were stored and reviewed on a standard picture archiving and communication system (PACS). Two abdominal radiologists with 5 years and 1 year of experience, who were blinded to the original ultrasound report, reviewed the gallbladder images in consensus on a PACS monitor and documented their findings. The gallbladders were evaluated for the presence of sonographic criteria⁹ as shown in Table 1. An ultrasound study was considered positive for AAC if at least 2 major criteria or 1 major and 2 minor criteria were present. Sonographic findings in a representative case are shown in Figure 1.

We also reviewed these patients' electronic medical records and collected clinical data, which included patients' age, sex, primary hematological malignancy, and absolute neutrophil count. The clinical course over 3 months following the ultrasound examination from the initial time of clinical suspicion was reviewed for the duration of symptoms, treatment, complications, follow-up imaging tests, and outcome (mortality). Our analysis included only complications related to cholecystitis that were diagnosed on subsequent imaging tests or pathology; these included gallbladder perforation, pericholecystic abscess, gallbladder hemorrhage, and septicemia due to cholecystitis.

Statistical Analysis

The patients were divided into 2 groups: patients with ultrasound-positive AAC and those with ultrasound findings negative for AAC. In the 2 groups, the duration of symptoms and the rate of complications or gallbladder-specific mortality rate were compared. The Wilcoxon rank sum test was used to compare the duration of symptoms, and the Fisher exact test was used to compare complication rates in the 2 groups. All statistical calculations were performed by using IBM SPSS statistics for Macintosh, Version 24.0 and SAS software for windows, version 9.4 (SAS Institute, Cary, NC).

Results

In this study, 368 patients with advanced hematological malignancies underwent an abdominal ultrasound examination at our institution for right upper quadrant symptoms. Of these, 94 patients (25.5%) had clinical suspicion of AAC; these included 36 patients with acute lymphocytic leukemia, 33 with acute myelogenous leukemia, 10 with chronic myelogenous leukemia, 8 with non-Hodgkin lymphoma, and 7 with multiple myeloma. Of these 94 patients, 43 (45.7%) were positive for AAC based on ultrasound criteria, and 51 (54.3%) were negative for AAC. Patient characteristics in the 2 groups are shown in Table 2.

Among the 94 patients, ultrasonography showed abnormal gallbladder wall thickening in 66 (70%), pericholecystic fluid in 45 (48%), sloughed mucosa in 15 (16%), echogenic bile/sludge in 60 (64%), and gallbladder hydrops in 38 (40%). None of the ultrasound examinations showed intramural gas. Nine patients, all of whom were in the AAC-positive group, developed complications; these included 2 patients with gallbladder perforation, 3 with pericholecystic abscess, and 4 with septicemia. None of the patients developed gallbladder hemorrhage (Table 2). We found no significant difference in the presence of any individual complication between the 2 groups (Table 3). However, a positive ultrasound diagnosis for AAC was associated with the occurrence of complications, which were seen in 9 (20.9%) of 43 patients in the positive group and none in the negative group ($P = 0.0005$, Table 3). Among ultrasonographic features, the presence of pericholecystic fluid (8 of 45 patients, $P = 0.01$), echogenic bile/sludge (9 of 51 patients, $P = 0.02$), and gallbladder distention > 4 cm (9 of 38 patients, $P = 0.0002$) were associated with the occurrence of complications (Table 4). Sloughed mucosa was seen only in the positive group (15 of 43 patients), but only 1 patient with sloughed mucosa developed a complication ($P = 0.99$). Although 2 deaths occurred in the positive group, they were unrelated to gallbladder pathology. In the negative group, 21 (41%) of the 51 patients were diagnosed with AAC on follow-up diagnostic tests: 14 (27.4%) patients were positive on repeat ultrasound exams performed within 1 week, and 7 (13.7%) were positive on follow-up hepatobiliary scans performed within 1 week. Another 14 patients (27.4%) in the negative group remained negative on subsequent follow-up tests despite persistent right upper quadrant symptoms. None of the patients diagnosed with AAC on follow-up tests developed complications. Thirty-eight patients in the positive group underwent follow-up tests; of these, 13 (34%) patients remained positive the follow-up tests. Of the 6 patients in the positive group who underwent follow-up ultrasound examinations within 1 week, 1 patient (2.6%) remained positive and 5 (13%) were negative for AAC on the subsequent examinations (Table 5).

Patients with positive AAC diagnoses based on ultrasonographic findings had a significantly longer duration of fever and right upper quadrant symptoms than those with negative diagnoses. Specifically, the mean duration of symptoms was 7.8 days in the positive group and 3.9 days in the negative group ($P < 0.0001$, Table 6). Complete resolution of fever and right upper quadrant symptoms through medical treatment occurred in 32 of the 43 patients in the positive group and in 45 of the 51 patients in the negative group. Cholecystostomy was required for 10 patients in the positive group and 4 patients in the negative group (Table 2).

Discussion

Our results indicate that patients with advanced hematological malignancies diagnosed with AAC based on sonographic criteria have a higher rate of complications and longer duration of symptoms compared with patients with negative ultrasonographic findings. In our study, the positive group had a complication rate of 20.9%. This higher rate is in concordance with complication rates in some previous studies. For example, studies have shown a higher incidence of complications such as gangrene and gallbladder perforation in AAC compared with calculous cholecystitis.¹⁵ In a series of 445 patients with postoperative AAC, Inoue et al. found a complication rate of 55% and mortality rate of 23%.¹⁶ More recent studies have

shown mortality rates ranging from 11% to 40%; the lower rates in some recent studies are likely due to the higher index of suspicion, improved imaging, and better treatment for AAC.¹⁷⁻¹⁹

Previous studies attempted to find clinical or imaging features of AAC that predict complications. Wang et al. found that high white blood cell count and older age correlated with a higher incidence of complications.¹² They used an ultrasound scoring system and found a trend toward a higher score in patients who later developed severe complications, although the trend was not statistically significant.¹² Although our study was not intended to find specific predictors of complications, a positive ultrasound study based on 2 major or 1 major and 2 minor criteria showed a significantly higher rate of complications. Interestingly, although gallbladder distension and sludge were considered minor criteria, all 9 patients in our study who developed complications had both these findings. Other studies have shown that gallbladder sludge leads to subsequent complications such as cholecystitis, cholangitis, and pancreatitis; these symptoms can be prevented by cholecystectomy.^{20,21} Overdistention of the gallbladder (which was seen in all 9 patients who experienced complications in our study) and increased intraluminal pressure are believed to cause ischemia, potentially leading to complications such as gangrene and gallbladder perforation.²²

Many risk factors have been implicated in causing AAC, including recent surgery, critical illness requiring intensive care unit admission, burns, immunosuppression, and sepsis.⁹ In patients with hematological malignancies, abdominal infections are life threatening, especially during periods of neutropenia, with reported mortality rates up to 26%.³ In patients with hematological malignancies, AAC is more common than calculous cholecystitis, and there is a high risk of sepsis.³ Leukemic infiltration of the gallbladder can also cause cholecystitis and has been reported as a rare presenting manifestation of leukemia.²³ Surgery for acute abdominal pain in patients with hematological malignancies is risky, with mortality rates up to 55%. Although early laparoscopic cholecystectomy is considered safe in patients with AAC,²⁴ individualized management based on prognosis and risk is recommended in patients with advanced malignancies and cholecystitis.²⁵

Another important feature of AAC is its rapidly progressive nature. Johnson et al. found that 40% of patients who underwent surgery 48 hours after the onset of symptoms had gallbladder perforation, whereas only 8% of those who underwent surgery earlier had perforation.²⁶ In our study, 41% of the patients in the negative group were found to be positive for AAC on follow-up ultrasound or hepatobiliary scans within 1 week. This finding reflects the rapidly progressive nature of AAC. Still, these patients had a lower rate of complications and duration of symptoms. These patients might have had early or milder presentation of AAC, resulting in initial negative ultrasound studies. Moreover, early diagnosis and treatment could explain the lower rate of complications and duration of symptoms in this group. These findings agree with the study by Jeffrey et al., who reported that 4 of 8 patients whose initial ultrasound studies were negative for AAC were found to have increased gallbladder wall thickness on follow-up ultrasound examinations performed within 24 hours.²⁷ Because of the rapidly progressive nature of AAC, several authors have emphasized the importance of daily follow-up ultrasound studies to help early detection of progression and to avoid misdiagnosis.^{11,28} Hence, follow-up ultrasonography in borderline

cases will help reduce complications and mortality by facilitating early diagnosis and prompt treatment.

Some authors have shown that ultrasound findings of AAC are nonspecific and may be found in patients without AAC. Boland et al. found no significant correlation among sonographic gallbladder abnormalities with clinical and laboratory parameters.¹³ But others have shown that when correlated with clinical features, ultrasonography is the investigation of choice for AAC in critically ill patients.⁹ Hence, diagnosis should not rely solely on ultrasound findings and should be correlated with clinical and laboratory parameters.

Our study has several limitations. Most importantly, it was a retrospective study based on search terms with inherent selection bias. Although it was possible to select a homogeneous group of hospitalized patients with a diagnosis of advanced hematological malignancy, the patients received different treatments for their primary cancer. We only included patients with right upper quadrant pain who underwent right upper quadrant ultrasound examination; it is possible that some patients who were not imaged or were imaged with other cross-sectional modalities were excluded, resulting in underestimation of complications. Also, the study was performed at a tertiary care cancer center. Thus, the generalizability of our findings in other settings is unclear. AAC was not pathologically proven in the majority of the patients (78 of 94); however, such patients in the acute phase rarely undergo cholecystectomy in routine clinical practice due to their critical condition and advanced malignancy. A significant number of ultrasound-negative patients (41%) were positive on follow-up studies; it would have been helpful to identify which ultrasound findings should prompt a follow-up imaging study, but our study did not find any statistically significant predictors. Finally, we did not assess the gallbladder for the resolution of sonographic findings following treatment because our objective was to assess their prognostic significance.

In conclusion, patients with positive sonographic criteria and clinical suspicion of AAC should be treated aggressively because they are prone to have a higher complication rate and longer duration of symptoms. In borderline cases, a repeat ultrasound study allows early detection of AAC progression and prompt treatment to significantly reduce complications.

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References

1. Buyukasik Y, Kosar A, Demiroglu H, Altinok G, Ozcebe OI, Dundar S. Acalculous acute cholecystitis in leukemia. *Journal of clinical gastroenterology*. 1998; 27(2):146–148. [PubMed: 9754777]
2. Gorschluter M, Marklein G, Hofling K, et al. Abdominal infections in patients with acute leukaemia: a prospective study applying ultrasonography and microbiology. *British journal of haematology*. 2002; 117(2):351–358. [PubMed: 11972517]
3. Gorschluter M, Mey U, Strehl J, et al. Cholecystitis in neutropenic patients: retrospective study and systematic review. *Leukemia research*. 2006; 30(5):521–528. [PubMed: 16483649]
4. Topeli A, Demiroglu H, Dundar S. Acalculous cholecystitis in patients with acute leukaemia. *The British journal of clinical practice*. 1996; 50(4):224–225. [PubMed: 8759571]

5. Howard RJ. Acute acalculous cholecystitis. *American journal of surgery*. 1981; 141(2):194–198. [PubMed: 7457736]
6. Ho TH, Barbera L, Saskin R, Lu H, Neville BA, Earle CC. Trends in the aggressiveness of end-of-life cancer care in the universal health care system of Ontario, Canada. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2011; 29(12):1587–1591. [PubMed: 21402603]
7. Hui D, Didwaniya N, Vidal M, et al. Quality of end-of-life care in patients with hematologic malignancies: a retrospective cohort study. *Cancer*. 2014; 120(10):1572–1578. [PubMed: 24549743]
8. Tang ST, Huang EW, Liu TW, Wang HM, Rau KM, Chen JS. Aggressive end-of-life care significantly influenced propensity for hospice enrollment within the last three days of life for Taiwanese cancer decedents. *Journal of pain and symptom management*. 2011; 41(1):68–78. [PubMed: 20828982]
9. Huffman JL, Schenker S. Acute acalculous cholecystitis: a review. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. 2010; 8(1):15–22. [PubMed: 19747982]
10. Cornwell EE 3rd, Rodriguez A, Mirvis SE, Shorr RM. Acute acalculous cholecystitis in critically injured patients. Preoperative diagnostic imaging. *Annals of surgery*. 1989; 210(1):52–55. [PubMed: 2662924]
11. Imhof M, Raunest J, Ohmann C, Roher HD. Acute acalculous cholecystitis complicating trauma: a prospective sonographic study. *World journal of surgery*. 1992; 16(6):1160–1165. [PubMed: 1455890]
12. Wang AJ, Wang TE, Lin CC, Lin SC, Shih SC. Clinical predictors of severe gallbladder complications in acute acalculous cholecystitis. *World journal of gastroenterology*. 2003; 9(12):2821–2823. [PubMed: 14669342]
13. Boland GW, Slater G, Lu DS, Eisenberg P, Lee MJ, Mueller PR. Prevalence and significance of gallbladder abnormalities seen on sonography in intensive care unit patients. *AJR American journal of roentgenology*. 2000; 174(4):973–977. [PubMed: 10749232]
14. Puc MM, Tran HS, Wry PW, Ross SE. Ultrasound is not a useful screening tool for acute acalculous cholecystitis in critically ill trauma patients. *The American surgeon*. 2002; 68(1):65–69. [PubMed: 12467321]
15. Gu MG, Kim TN, Song J, Nam YJ, Lee JY, Park JS. Risk factors and therapeutic outcomes of acute acalculous cholecystitis. *Digestion*. 2014; 90(2):75–80. [PubMed: 25196261]
16. Inoue T, Mishima Y. Postoperative acute cholecystitis: a collective review of 494 cases in Japan. *The Japanese journal of surgery*. 1988; 18(1):35–42. [PubMed: 3290556]
17. Blanco PA, Do Pico JJ. Ultrasound-guided percutaneous cholecystostomy in acute cholecystitis: case vignette and review of the technique. *Journal of Ultrasound*. 2015; 18(4):311–315. [PubMed: 26550068]
18. Kirkegård J, Horn T, Christensen SD, Larsen LP, Knudsen AR, Mortensen FV. Percutaneous cholecystostomy is an effective definitive treatment option for acute acalculous cholecystitis. *Scandinavian Journal of Surgery*. 2015; 104(4):238–243. [PubMed: 25567854]
19. Treinen C, Lomelin D, Krause C, Goede M, Oleynikov D. Acute acalculous cholecystitis in the critically ill: risk factors and surgical strategies. *Langenbeck's Archives of Surgery*. 2015; 400(4):421–427.
20. Hill PA, Harris RD. Clinical Importance and Natural History of Biliary Sludge in Outpatients. *Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine*. 2016; 35(3):605–610. [PubMed: 26903661]
21. Lee YS, Kang BK, Hwang IK, Kim J, Hwang JH. Long-term Outcomes of Symptomatic Gallbladder Sludge. *Journal of clinical gastroenterology*. 2015; 49(7):594–598. [PubMed: 25127114]
22. Orlando R 3rd, Gleason E, Drezner AD. Acute acalculous cholecystitis in the critically ill patient. *American journal of surgery*. 1983; 145(4):472–476. [PubMed: 6188383]
23. Bloom SH, Coad JE, Greeno EW, Ashrani AA, Hammerschmidt DE. Cholecystitis as the presenting manifestation of acute myeloid leukemia: report of a case. *American journal of hematology*. 2002; 70(3):254–256. [PubMed: 12111774]

24. Ueno D, Nakashima H, Higashida M, et al. Emergent laparoscopic cholecystectomy for acute acalculous cholecystitis revisited. *Surgery today*. 2016; 46(3):309–312. [PubMed: 25904560]
25. Jayakrishnan TT, Groeschl RT, George B, et al. Management of acute cholecystitis in cancer patients: a comparative effectiveness approach. *Surgical endoscopy*. 2014; 28(5):1505–1514. [PubMed: 24687416]
26. Johnson LB. The importance of early diagnosis of acute acalculus cholecystitis. *Surgery, gynecology & obstetrics*. 1987; 164(3):197–203.
27. Jeffrey RB Jr, Sommer FG. Follow-up sonography in suspected acalculous cholecystitis: preliminary clinical experience. *Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine*. 1993; 12(4):183–187. [PubMed: 8497021]
28. Raunest J, Imhof M, Rauen U, Ohmann C, Thon KP, Burrig KF. Acute cholecystitis: a complication in severely injured intensive care patients. *The Journal of trauma*. 1992; 32(4):433–440. [PubMed: 1569615]

Figure 1. Curcumin is a pleiotropic molecule correcting dysregulation of pathways in Alzheimer's models

Acalculous cholecystitis in a 46-year-old man with acute myelogenous leukemia.

Longitudinal (A) and transverse (B) images of the distend gallbladder in decubitus position show thickened gallbladder wall (arrowheads), sludge (asterisk), pericholecystic fluid (curved arrow), luminal diameter of gallbladder (double-headed arrow), and sloughed mucosa (straight arrow).

Table 1

A Sonographic criteria for the diagnosis of acalculous cholecystitis.

Criteria	Finding	AAC Diagnosis
Major	Wall thickness ≥ 3.5 mm	2 major or 1 major and 2 minor criteria
	Pericholecystic fluid without ascites	
	Sloughed mucosal membrane	
	Intramural gas	
Minor	Gallbladder hydrops (distension > 4 cm in transverse diameter)	
	Sludge/echogenic bile	

Abbreviation: AAC, acalculous cholecystitis.

Table 2

Summary of patient and imaging characteristics by ultrasonographic acalculous cholecystitis diagnosis status.

Characteristic	Total N	USG Diagnosis of AAC	
		Positive N (%)	Negative N (%)
Gender			
Male		18 (50.00)	18 (50.00)
Female		25 (43.10)	33 (56.90)
Cancer type			
ALL	36	16 (44.44)	20 (55.56)
AML	33	14 (42.42)	19 (57.58)
CML	10	4 (40.00)	6 (60.00)
NHL	8	5 (62.50)	3 (37.50)
Multiple Myeloma	7	4 (57.14)	3 (42.86)
Wall thickness 3.5 mm			
No	28	3 (10.71)	25 (89.29)
Yes	66	40 (60.61)	26 (39.39)
Pericholecystic fluid			
No	49	14 (28.57)	35 (71.43)
Yes	45	29 (64.44)	16 (35.56)
Sloughed mucosa			
No	79	28 (35.44)	51 (64.56)
Yes	15	15 (100.00)	0 (0)
Intramural gas			
No	94	43 (45.74)	51 (54.26)
Echogenic bile/sludge			
No	34	16 (47.06)	18 (52.94)
Yes	60	27 (45.00)	33 (55.00)
Hydrops (distension > 4 cm in transverse)			
No	56	17 (30.36)	39 (69.64)
Yes	38	26 (68.42)	12 (31.58)
Complications			
Perforation			
No	92	41 (44.6)	51 (55.4)
Yes	2	2 (100)	0 (0)
Pericholecystic abscess			
No	91	40 (44.0)	51 (56)
Yes	3	3 (100)	0 (0)
Gallbladder hemorrhage			
No	94	51 (54.3)	43 (45.7)
Yes	0	0 (0)	0 (0)
Septicemia			

Characteristic	Total N	USG Diagnosis of AAC	
		Positive N (%)	Negative N (%)
No	90	39 (43)	51 (43.3)
Yes	4	04 (100)	0 (0)
Total complications			
No	85	34 (40)	51 (60)
Yes	9	9 (100)	0 (0)
AAC treatment			
Antibiotics	77	32 (41.56)	45 (58.44)
Cholecystostomy	14	10 (71.43)	4 (28.57)
Cholecystectomy ^a	2	1 (50.00)	1 (50.00)
Watchful waiting	1	0 (0)	1 (100.00)
Total		43 (45.74)	51 (54.26)

^aThe ultrasonographic and pathological findings were congruent in the 2 patients who underwent cholecystectomy.

Abbreviations: AAC, acalculous cholecystitis; ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CML, with chronic myelogenous leukemia; NHL, non-Hodgkin lymphoma; USG, ultrasonographic.

Table 3
Summary of complications by ultrasonographic acalculous cholecystitis diagnosis status.

Type of complication	AAC Status on USG	No. Patients	Complication		<i>p</i> ^a
			Present	Absent	
			N (%)	N (%)	
Perforation	Positive	43	2 (4.7)	41 (95.3)	0.207
	Negative	51	0 (0.0)	51 (100)	
Pericholecystic abscess	Positive	43	3 (7.0)	40 (93)	0.92
	Negative	51	0 (0)	51 (100)	
Gallbladder hemorrhage	Positive	43	0 (0)	43 (100)	NA
	Negative	51	0 (0)	51 (100)	
Septicemia	Positive	43	4 (9.3)	39 (90.7)	0.05
	Negative	51	0 (0)	51 (100)	
Any complication	Positive	43	9 (20.9)	34 (79.1)	0.0005
	Negative	51	0 (0)	51 (1)	

Abbreviations: AAC, acalculous cholecystitis; USG, ultrasonography.

^a *P*-value by Fisher exact test.

Table 4

Summary of patient characteristics and ultrasonographic features by complication status.

Characteristic	Any Complication		<i>pa</i>
	No N (%)	Yes N (%)	
Gender			
Male	32 (88.89)	4 (11.11)	0.73
Female	53 (91.38)	5 (8.62)	
Cancer type			
ALL	30 (83.33)	6 (16.67)	0.52
AML	31 (93.94)	2 (6.06)	
CML	9 (90.00)	1 (10.00)	
NHL	8 (100.00)	0 (0)	
Multiple myeloma	7 (100.00)	0 (0)	
Neutropenia			
No	60 (88.24)	8 (11.76)	0.44
Yes	25 (96.15)	1 (3.85)	
Wall thickness 3.5 mm			
No	28 (100.00)	0 (0)	0.054
Yes	57 (86.36)	9 (13.64)	
Pericholecystic fluid			
No	48 (97.96)	1 (2.04)	0.01
Yes	37 (82.22)	8 (17.78)	
Sloughed mucosa			
No	71 (89.87)	8 (10.13)	> 0.99
Yes	14 (93.33)	1 (6.67)	
Intramural gas			
No	85 (90.43)	9 (9.57)	N/A
Echogenic bile/sludge			
No	34 (100.00)	0 (0)	0.02
Yes	51 (85.00)	9 (15.00)	
Hydrops (distension > 4 cm in transverse)			
No	56 (100.00)	0 (0)	0.0002
Yes	29 (76.32)	9 (23.68)	
USG AAC diagnosis			
Positive	34 (79.07)	9 (20.93)	0.0005
Negative	51 (100.00)	0 (0)	
Results of 2 imaging AAC diagnoses			
Both negative	30 (100.00)	0 (0)	0.053
Any positive	55 (85.94)	9 (14.06)	
Total	85 (90.43)	9 (9.57)	

Abbreviations: AAC, acalculous cholecystitis; ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CML, with chronic myelogenous leukemia; NHL, non-Hodgkin lymphoma; USG, ultrasonographic.

^a*P*-values by Fisher exact test.

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Table 5

Summary of initial and follow-up imaging results.

Initial USG Diagnosis	Follow-up Test within 1 Week for RUQ Clinical Symptoms	AAC Positive N (%)	AAC Negative N (%)
AAC positive	Nuclear medicine	4 (100.00)	0 (0)
	CT	5 (100.00)	0 (0)
	MRI	3 (100.00)	0 (0)
	USG	1 (16.67)	5 (83.33)
AAC negative	Nuclear medicine	7 (63.64)	4 (36.36)
	USG	14 (58.33)	10 (41.67)
Total		34 (36.17)	19 (20.21)

Abbreviations: AAC, acalculous cholecystitis; CT, computed tomography; MRI, magnetic resonance imaging; RUQ, right upper quadrant; USG, ultrasonography.

Table 6

Summary of the duration of cholecystitis symptoms by ultrasonographic acalculous cholecystitis diagnosis status.

AAC Status on USG	No. Patients	Duration of Cholecystitis Symptoms, Days			
		Mean	SD	Median	Range
Positive	43	7.79	2.50	7.00	3.00-14.00
Negative	51	3.94	1.58	4.00	1.00-7.00
Total	94	5.70	2.81	5.00	1.00-14.00

Abbreviations: AAC, acalculous cholecystitis; SD, standard deviation; USG, ultrasonography.

^a *P*-value by Wilcoxon rank sum test.