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ORIGINAL ARTICLE

Outcomes of contemporary management of gangrenous and non-gangrenous acute cholecystitis

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Abstract

Background: Gangrenous cholecystitis (GC) is considered a more severe form of acute cholecystitis. The risk factors associated with this condition and its impact on morbidity and mortality compared with those of non-gangrenous acute cholecystitis (NGAC) are poorly defined and based largely on findings from older studies.

Methods: Patients with histologically confirmed acute cholecystitis treated in specialized units in a tertiary hospital between 2005 and 2010 were identified from a prospectively maintained database. Data were reviewed retrospectively and patients with GC were compared with those with NGAC.

Results: A total of 184 patients with NGAC and 106 with GC were identified. The risk factors associated with GC included older age (69 years vs. 57 years; $P = 0.001$), diabetes (19% vs. 10%; $P = 0.049$), temperature of >38 °C (36% vs. 16%; $P < 0.001$), tachycardia (31% vs. 15%; $P = 0.002$), detection of muscle rigidity on examination (27% vs. 12%; $P = 0.01$) and greater elevations in white cell count (WCC) (13.4×10^9/l vs. 10.7×10^9/l; $P < 0.001$), C-reactive protein (CRP) (94 mg/l vs. 17 mg/l; $P = 0.001$), bilirubin (19 μmol/l vs. 17 μmol/l; $P = 0.029$), urea (5.3 mmol/l vs. 4.7 mmol/l; $P = 0.016$) and creatinine (82 μmol/l vs. 74 μmol/l; $P = 0.001$). The time from admission to operation in days was greater in the GC group (median = 1 day, range: 0–14 days vs. median = 1 day, range: 0–10 days; $P = 0.029$). There was no overall difference in complication rates between the GC and NGAC groups (22% vs. 14%; $P = 0.102$). There was a lower incidence of common bile duct stones in the GC group (5% vs. 13%; $P = 0.017$). Gangrenous cholecystitis was associated with increased mortality (4% vs. 0%; $P = 0.017$), but this was not an independent risk factor on multivariate analysis.

Conclusions: Gangrenous cholecystitis has certain clinical features and associated laboratory findings that may help to differentiate it from NGAC. It is not associated with an overall increase in complications when treated in a specialized unit.

Keywords

cholecystectomy, laparoscopy, acute cholecystitis, complications, morbidity, mortality

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Introduction

Acute cholecystitis is a common surgical problem. Gangrenous cholecystitis (GC) is generally considered a more severe form of acute cholecystitis.[1] A number of older studies have looked at risk factors that may distinguish GC from non-gangrenous acute cholecystitis (NGAC) with the aim of improving outcomes by providing more aggressive and timely treatment.[2–4] Many of these studies examined small numbers of patients in an era when early management of acute cholecystitis was not routine.

In this study, a cohort of patients with histologically proven acute cholecystitis were examined to determine factors predictive of diagnoses of GC and NGAC, respectively, and to determine factors associated with overall complications and mortality.

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Materials and methods

Acute cholecystitis was defined by a histological finding of an acute inflammatory infiltrate on examination of the gallbladder wall. When there was a concurrent chronic inflammatory infiltrate, this was defined as acute-on-chronic cholecystitis. Cases involving transmural necrosis of the gallbladder wall were defined as GC. The condition was defined as focal if one portion of the gallbladder wall was involved and as diffuse if more than one portion was involved. Emergency surgery constituted surgery performed in response to an acute presentation at hospital when acute cholecystitis was first suspected. Non-emergency cases consisted of patients who had been scheduled for surgery as outpatients and were subsequently found to have acute cholecystitis on histology and underwent surgery performed according to an elective operating list. In such cases, the time from hospital admission to surgery was considered zero days. Comparisons of blood tests used data from tests performed at the time of emergency admission or before surgery in cases of elective surgery. Length of stay (LoS) was defined as hospital stay in days from the time of surgery to discharge. A complication was considered as any adverse event that required an intervention, such as re-operation, drainage or the administration of antibiotics.

Patients

Patients treated by cholecystectomy for suspected acute cholecystitis between November 2005 and April 2010 within specialist hepatobiliary and upper gastrointestinal units in a tertiary hospital were identified from a prospectively maintained database with institutional review board approval. A retrospective analysis of preoperative, operative and postoperative data was undertaken. Only patients with histologically confirmed acute cholecystitis were included.

Preoperative assessment

Demographic data including information on age, sex, American Society of Anesthesiologists (ASA) classification, body mass index (BMI), associated medical conditions, preoperative symptoms and duration, time from admission to surgery, physical examination findings, blood test results and imaging results were noted. The need for preoperative endoscopic retrograde cholangiopancreatography (ERCP) was recorded.

Surgical procedures

Any surgical interventions performed were documented, including common bile duct (CBD) exploration and stenting procedures. Laparoscopic surgery was the preferred mode of therapy. Cystic duct ligation was achieved by clip application in the majority of cases and EndoLoop® ligatures in the remainder. Every possible effort was made to perform cholecystectomy at the next available emergency time-slot once a diagnosis of suspected acute cholecystitis had been established. Conservative management of cholecystitis followed by delayed surgery was not practised. All patients received intraoperative antibiotics and prophylactic heparin, unless these were contraindicated. Records included information on the operative technique, duration of surgery, intraoperative complications and the seniority of the surgeon (consultant or fellow/registrar trainee). Intraoperative cholangiography was performed selectively by some of the surgeons in this study and routinely by others.

Postoperative outcome

Postoperative complications and outcomes were recorded. The hospital LoS after surgery, including the intensive care unit (ICU) LoS, was noted. Patients who underwent cholecystectomy and required hospital readmissions after discharge were identified. Follow-up was based on hospital outpatient data, physician office records and readmission notes in cases of readmission.

Statistical analysis

Results are expressed as the median (range) unless otherwise stated. Comparisons between categorical variables were determined using the chi-squared or Fisher's exact test as appropriate. Non-categorical variables were assessed by Mann–Whitney *U*-test. Cox proportional analysis was undertaken to determine factors independently associated with complications and mortality using all factors for which the *P*-value was <0.01 on univariate analysis. SPSS Version 16.5 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. A *P*-value of $\leq$0.05 was considered to indicate statistical significance.

Results

Overall, 290 patients with histologically confirmed acute cholecystitis were identified. These included 106 (37%) patients with GC and 184 (63%) patients with NGAC. Of the patients with GC, 66 (62%) had diffuse transmural necrosis and the remainder had focal necrosis. In patients with NGAC, acute-on-chronic cholecystitis was noted in 95 (52%) patients and the remainder showed histological evidence of acute cholecystitis alone.

Patient characteristics

Table 1 lists the characteristics of the patients in each group. Patients in the GC group were more likely to be male, older and to have diabetes. Patients presenting with GC were more likely to be febrile, tachycardic and to exhibit muscle rigidity on examination at presentation. There was no difference between the groups in symptom duration prior to admission. The median time from admission to surgery was statistically greater in the GC group, at 1 day (range: 0–14 days) vs. 1 day (range: 0–10 days) ($P = 0.029$). When only emergency cases were compared, there was no statistical difference in median time from admission to surgery [1 day (range: 0–14 days) vs. 1 day (range: 0–10 days); $P = 0.086$].

Investigations

The laboratory and imaging findings of patients in each group are shown in Table 1. An ultrasound diagnosis of acute cholecystitis

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Table 1 Characteristics of patients with gangrenous or non-gangrenous acute cholecystitis

Characteristics	All patients (n = 290)	Non-gangrenous acute cholecystitis group (n = 184)	Gangrenous cholecystitis group (n = 106)	P-value
Male, n (%)	140 (48%)	72 (39%)	68 (64%)	<0.001
Age, years, median (range)	61 (18–94)	57 (19–92)	69 (18–94)	0.001
BMI, median (range)	29.5 (16.9–58.3)	28.7 (17.6–51.7)	30.0 (16.9–58.3)	0.836
ASA class, n (%)				0.076
I	54 (18%)	38 (21%)	16 (15%)	
II	158 (55%)	105 (57%)	53 (50%)	
III	72 (25%)	39 (21%)	33 (31%)	
IV	6 (2%)	2 (1%)	4 (4%)	
Comorbidity, n (%)				
Ischaemic heart disease	40 (14%)	21 (11%)	19 (18%)	0.121
Chronic renal failure	23 (8%)	14 (8%)	9 (9%)	0.789
Diabetes	39 (13%)	19 (10%)	20 (19%)	0.040
Chronic liver disease	10 (3%)	7 (4%)	3 (3%)	0.751
COAD	18 (6%)	11 (6%)	7 (7%)	0.832
Upper abdominal surgery	11 (4%)	7 (4%)	4 (4%)	1.000
Smoker, n (%)	61 (25%)	43 (27%)	18 (20%)	0.214
Glucosteroid use, n (%)	6 (2%)	3 (2%)	3 (3%)	0.673
Prior biliary colic, n (%)	141 (53%)	95 (56%)	46 (48%)	0.193
Emergency department referral, n (%)	260 (90%)	165 (90%)	95 (90%)	0.989
Duration, days, median (range)				
Symptoms to admission	1 (0–150)	1 (0–60)	1 (0–150)	0.115
Admission to surgery	1 (0–14)	1 (0–10)	1 (0–14)	0.029
Vital signs at presentation, n (%)				
Fever (>38 °C)	67 (23%)	29 (16%)	38 (36%)	<0.001
Tachycardia (HR > 100 bpm)	61 (21%)	28 (15%)	33 (31%)	0.001
Hypotension (BP < 100 mmHg)	19 (7%)	8 (4%)	11 (10%)	0.046
Findings at presentation, n (%)				
Muscular rigidity	51 (18%)	22 (12%)	29 (27%)	0.001
Murphy's sign positive	160 (57%)	94 (54%)	66 (62%)	0.161
Laboratory tests, median (range)				
Haemoglobin, g/l	140 (90–182)	140 (90–182)	143 (100–171)	0.313
White cell count, $\times 10^9$/l	11.7 (1.4–32.4)	10.7 (3.7–32.4)	13.4 (1.4–29.0)	<0.001
Platelets, $\times 10^9$/l	274 (73–893)	281 (73–893)	266 (69–528)	0.079
CRP, mg/l	23 (0–500)	17 (1.0–380)	94 (0–500)	0.001
Bilirubin, µmol/l	18 (5–152)	17 (5–152)	19 (8–148)	0.029
ALT, U/l	36 (6–1381)	43 (6–1381)	26 (10–705)	<0.001
ALP, U/l	83 (28–487)	85 (36–487)	79 (28–234)	0.061
GGT, U/l	41 (8–1290)	50 (8–1290)	30 (8–666)	<0.001
Albumin, g/l	39 (19–72)	39 (19–49)	39 (20–72)	0.552
Amylase, U/l	67 (15–3286)	64 (15–3286)	72 (25–615)	0.158
Lipase, U/l	24 (10–4270)	24 (10–4270)	25 (12–106)	0.443
Urea, mmol/l	4.9 (1.5–73)	4.7 (1.5–73)	5.3 (1.5–29.8)	0.016
Creatinine, µmol/l	77 (49–1070)	74 (49–394)	82 (49–1070)	0.001
Bicarbonate, mmol/l	26 (17–62)	26 (17–62)	26 (17–34)	0.597
Blood culture positive	10 (3%)	6 (3%)	4 (4%)	1.000
Radiological investigations, n (%)				
Ultrasound				
Diagnosis of acute cholecystitis	195 (71%)	113 (65%)	82 (80%)	0.012
Gallbladder wall thickening	189 (69%)	109 (64%)	80 (76%)	0.031
Pericholecystic fluid	81 (29%)	46 (26%)	35 (33%)	0.188
CBD diameter, mm, median (range)	6 (1.2–15.0)	6 (2.0–15.0)	6 (1.2–12.0)	0.557
CT diagnostic of cholecystitis, n (%)	39 (13%)	24 (13%)	15 (14%)	0.790
MRCP diagnostic of cholecystitis, n (%)	8 (3%)	4 (2%)	4 (4%)	0.471

BMI, body mass index; ASA, American Society of Anaesthesiologists; COAD, chronic obstructive airways disease; HR, heart rate; BP, blood pressure; CRP, C-reactive protein; ALT, alanine transaminase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase; CBD, common bile duct; CT, computed tomography; MRCP, magnetic resonance cholangiopancreatography. Missing values: BMI, n = 188; smoker, n = 41; glucosteroid use, n = 3; biliary colic history, n = 25; muscle rigidity, n = 1; Murphy's sign positive, n = 9; haemoglobin, n = 2; platelets, n = 3; white cell count, n = 3; CRP, n = 94; bilirubin, n = 5; ALT, n = 8; ALP, n = 5; albumin, n = 6; GGT, n = 6; amylase, n = 235; lipase n = 57; urea, n = 1; creatinine, n = 1; CBD diameter, n = 15; gallbladder thickening, n = 14; pericholecystic fluid, n = 8; MRCP status, n = 1; duration of surgery, n = 1.

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was more common in the GC group than in the NGAC group (as was the finding of gallbladder wall thickening). Patients in the GC group had greater elevations in white cell count, C-reactive protein (CRP) level, bilirubin, urea and creatinine. Patients with NGAC had greater elevations at presentation in alanine transaminase (ALT) and gamma-glutamyl transferase (GGT) levels. Seven patients (2%) were diagnosed with pancreatitis preoperatively. All were in the NGAC group.

Operative details

Operative details are noted in Table 2. Overall, 94% of patients in this series had emergency hospital admissions and surgery. This was more frequent in the GC group (98% vs. 91%; $P = 0.021$). Patients in the GC group were also more likely than those in the NGAC group to receive preoperative antibiotics at presentation (94% vs. 80%; $P = 0.001$). A total of 27 (9%) patients required ERCP prior to surgery for treatment of CBD stones. Most patients (88%) were treated by laparoscopic cholecystectomy. There were no differences between the groups in the percentage of patients undergoing laparoscopic surgery or the percentage of patients requiring conversion to open surgery. A consultant surgeon was more likely to be scrubbed in for patients in the GC group. Overall, 60% of patients underwent intraoperative cholangiography and rates did not differ between the groups. Common bile duct stones were noted in 31 (11%) cases at the time of surgery; the incidence of CBD stones did not differ between the groups. Drain tubes were more commonly utilized in the GC group.

Postoperative details

Postoperative details and complications are noted in Table 3. Overall complication rates were similar between the groups. Chest infection, cardiac complications and bile leak were the most common complications noted. However, patients in the GC group were more likely to require ICU admission postoperatively (15% vs. 7%; $P = 0.017$). Four deaths occurred in this series, all of which referred to patients in the GC group (4% vs. 0%; $P = 0.017$). The median postoperative LoS was greater in the GC than the NGAC group at 4 days (range: 0–17 days) vs. 3 days (range: 1–33 days) ($P = 0.005$). Rates of postoperative readmission and need for ERCP did not differ between groups. Four (1%) patients demonstrated retained bile duct stones; three of these underwent intraoperative cholangiography. The presence of CBD stones was noted in 60 (21%) patients and included stones detected during the pre-, intra- and postoperative periods. The incidence of CBD stones was greater in the NGAC ($n = 46$, 25%) than the GC ($n = 14$, 13%) group ($P = 0.023$).

Table 2 Comparison of operative data in patients with gangrenous and non-gangrenous acute cholecystitis

	All patients ($n = 290$)	Non-gangrenous acute cholecystitis group ($n = 184$)	Gangrenous cholecystitis group ($n = 106$)	*P*-value
Preoperative management, *n* (%)				
Preoperative ICU	9 (3%)	6 (3%)	3 (3%)	1.000
Preoperative ERCP	27 (9%)	22 (12%)	5 (5%)	0.090
Preoperative antibiotics	247 (85%)	147 (80%)	100 (94%)	0.001
Operation, *n* (%)				
Emergency surgery	272 (94%)	168 (91%)	104 (98%)	0.021
Laparoscopic surgery	254 (88%)	163 (89%)	91 (86%)	0.496
Open surgery	9 (3%)	8 (4%)	1 (1%)	0.162
Conversion to open surgery	27 (10%)	13 (7%)	14 (14%)	0.096
Drain tube *in situ*	198 (68%)	112 (61%)	86 (81%)	<0.001
IOC, *n* (%)				
IOC performed	175 (60%)	116 (63%)	59 (56%)	0.216
IOC detected stones	31 (11%)	21 (11%)	10 (9%)	0.599
Operative time, min, median (range)	100 (25–360)	100 (25–360)	105 (35–210)	0.401
Surgeon, *n* (%)				
Consultant surgeon scrubbed	150 (52%)	87 (47%)	63 (59%)	0.046
Extra procedure, *n* (%)				
Transpapillary stent	7 (2%)	3 (2%)	4 (4%)	0.429
Gallstones present at pathology examination, *n* (%)				
No gallstones identified	50 (18%)	30 (17%)	20 (19%)	0.682
Single gallstone	57 (20%)	36 (20%)	21 (20%)	0.959

ICU, intensive care unit; ERCP, endoscopic retrograde cholangiopancreatography; IOC, intraoperative cholangiogram.

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Table 3 Comparison of postoperative data in patients with gangrenous and non-gangrenous acute cholecystitis

	All patients (n = 290)	Non-gangrenous acute cholecystitis group (n = 184)	Gangrenous cholecystitis group (n = 106)	P-value
Length of stay, days, median (range)	4 (0–33)	3 (1–33)	4 (0–17)	0.005
Complication, n (%)				
Postoperative complication	49 (17%)	26 (14%)	23 (22%)	0.102
Wound infection	5 (2%)	2 (1%)	3 (3%)	
Intraoperative collection	2 (1%)	2 (1%)	0 (0%)	
Bile leak	7 (2%)	5 (3%)	2 (2%)	
Retained stone	4 (1%)	3 (2%)	1 (1%)	
Chest infection	10 (3%)	4 (2%)	6 (6%)	
Cardiac	10 (3%)	4 (2%)	6 (6%)	
Urinary retention	3 (1%)	1 (1%)	2 (2%)	
Other	13 (6%)	7 (4%)	6 (6%)	
Follow-up, n (%)				
Unplanned HDU/ICU stay	28 (10%)	12 (7%)	16 (15%)	0.017
Readmission	11 (4%)	7 (4%)	4 (4%)	1.000
Postoperative ERCP	16 (6%)	12 (7%)	4 (4%)	0.427
Death within 90 days	4 (1%)	0 (0%)	4 (4%)	0.017

HDU, high-dependency unit; ICU, intensive care unit; ERCP, endoscopic retrograde cholangiopancreatography.

Complications

Factors with significant or trending towards significant influence on complications are noted in Table 4. There was an overall non-significant trend towards increased complications in the GC group. On multivariate analysis, age >70 years [odds ratio (OR) 2.9, 95% confidence interval (CI) 1.1–7.6; P = 0.029], diabetes (OR 3.9, 95% CI 1.4–11.2; P = 0.012) and the presence of muscle rigidity on initial examination (OR 2.7, 95% CI 1.0–6.9; P = 0.042) were the only independent factors associated with increased complications.

Mortality

Factors with significant or trending towards significant influence on mortality are noted in Table 5. A diagnosis of GC, age >70 years, ischaemic heart disease, diabetes, muscle rigidity at presentation, presence of pericholecystic fluid on ultrasound, creatinine >90 μmol/l and urea >6 mmol/l were associated with increased mortality on univariate analysis. However, multivariate analysis did not identify any independent predictors of mortality.

Discussion

Gangrenous cholecystitis is considered a more severe form of acute cholecystitis. It is primarily caused by vascular compromise secondary to epithelial injury caused by sustained obstruction of the cystic duct.[5] As a result of the epithelial injury, phospholipases that degrade adjacent cell membranes are released, leading to an intense inflammatory reaction. The combination of gallbladder wall tension and the intense inflammatory reaction results in either local or global gallbladder wall ischaemia. The exact time courses of such events are unknown. It has been suggested that it may take days for such a progression to occur, although several reports indicate that the progression is far more rapid.[2,6,7]

Gangrenous cholecystitis has been reported to occur in 10–40% of all patients presenting with acute cholecystitis.[2-4] In the current series, GC occurred in 37% of all patients with acute cholecystitis. This figure is in keeping with those reported by other studies that used a histological criterion to define acute cholecystitis.[2] In this series, patients with focal transmural necrosis of the gallbladder or diffuse necrosis were considered to have GC. Whether other series with lower reported incidences of GC excluded some cases of focal necrosis is unknown. The spectrum of patients presenting with acute cholecystitis might be expected to have changed in recent years as patients with biliary type symptoms are now treated earlier, prior to the development of complications. However, in this series about half of all patients with GC or NGAC had a history of preceding biliary symptoms, a figure that has not changed from those reported in older series.[8]

A number of differences between patients with GC and NGAC have been noted in other studies. These include differences in the presence of leukocytosis, age, diabetes and delay in operation.[1–4] Disturbances in liver function tests have also been reported.[2,3] In the current study, differences were noted in patient characteristics, examination findings, laboratory tests and radiological results. Patients with GC were more likely to be male, older, to have diabetes, to be febrile, and to display an elevated pulse and muscle rigidity on examination. Ultrasonography was more likely to demonstrate thickening of the gallbladder wall and a diagnosis of

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Table 4 Factors influencing complications (of significant or trending towards significant influence)

	No postoperative complication (*n* = 241)	With postoperative complication (*n* = 49)	OR (95% CI)	*P*-value
Histopathology, *n* (%)				
Gangrenous cholecystitis	83 (35%)	23 (47%)	1.7 (0.9–3.1)	0.098
Demographic, *n* (%)				
Age > 70 years	77 (32%)	34 (69%)	4.8 (2.5–9.4)	<0.001
Comorbidity, *n* (%)				
Ischaemic heart disease	29 (12%)	11 (22%)	2.1 (1.0–4.6)	0.054
Chronic renal failure	14 (6%)	9 (18%)	3.6 (1.5–9.0)	0.003
Diabetes	23 (10%)	16 (33%)	4.6 (2.2–9.6)	<0.001
COAD	10 (4%)	8 (16%)	4.5 (1.7–12.1)	0.001
Smoker	56 (27%)	5 (10%)	0.3 (0.1–0.9)	0.026
Glucosteroid use	3 (1%)	3 (6%)	5.1 (1.0–26.1)	0.030
Fever (>38 °C)	49 (20%)	18 (37%)	2.3 (1.2–4.4)	0.016
Hypotension (BP < 100 mmHg)	13 (5%)	6 (12%)	2.5 (0.9–6.8)	0.077
Muscle rigidity	35 (15%)	16 (33%)	2.8 (1.4–5.7)	0.002
ASA class, *n* (%)			N/A	<0.001
I	50 (20.8%)	4 (8.2%)		
II	140 (58.3%)	17 (34.7%)		
III	46 (19.2%)	26 (53.1%)		
IV	4 (1.7%)	2 (4.1%)		
Haemoglobin < 130 g/l, *n* (%)	46 (19%)	17 (35%)	2.3 (1.2–4.5)	0.013
Albumin < 35 g/l, *n* (%)	47 (20%)	17 (36%)	2.3 (1.2–4.5)	0.014
Creatinine > 90 μmol/l, *n* (%)	67 (28%)	21 (43%)	1.9 (1.0–3.7)	0.033
Urea > 6 mmol/l, *n* (%)	61 (25%)	24 (49%)	2.8 (1.5–5.3)	0.001

OR, odds ratio; 95% CI, 95% confidence interval; COAD, chronic obstructive airway disease; BP, blood pressure; ASA, American Society of Anesthesiologists; N/A, not applicable.
Missing values: smoker, *n* = 41; steroid use, *n* = 3; muscle rigidity, *n* = 1; haemoglobin, *n* = 2; albumin, *n* = 6; urea, *n* = 1; creatinine, *n* = 1.

Table 5 Factors influencing mortality (of significant or trending towards significant influence)

	Alive at 90 days (*n* = 286)	Death within 90 days (*n* = 4)	OR (95% CI)	*P*-value
Histopathology, *n* (%)				
Gangrenous cholecystitis	102 (35.7%)	4 (100%)	2.8 (2.4–3.3)	0.017
Demographic, *n* (%)				
Age > 70 years	107 (37.4%)	4 (100%)	2.7 (2.3–3.1)	0.021
Comorbidity, *n* (%)				
Ischaemic heart disease	37 (12.9%)	3 (75%)	20.2 (2.1–199.0)	0.009
Diabetes	36 (12.6%)	3 (75.0%)	20.8 (2.1–205.7)	0.008
Examination findings, *n* (%)				
Muscle rigidity	48 (16.8%)	3 (75%)	14.8 (1.5–145.5)	0.018
Investigations, *n* (%)				
Pericholecystic fluid	78 (28.1%)	3 (75%)	7.7 (0.8–75.1)	0.039
White cell count > 13.5×10^9/l	91 (31.9%)	3 (75%)	6.4 (0.7–62.3)	0.103
Creatinine > 90 μmol/l	84 (29.4%)	4 (100%)	3.4 (2.8–4.1)	0.008
Urea > 6 mmol/l	81 (28.4%)	4 (100%)	3.5 (2.9–4.2)	0.007

OR, odds ratio; 95% CI, 95% confidence interval.
Missing values: muscle rigidity, *n* = 1; urea, *n* = 1; creatinine, *n* = 1.

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acute cholecystitis in the GC group, although there are no well-defined preoperative predictors on ultrasound specifically for GC.[9] Greater elevations in white cell count, CRP, bilirubin, urea and creatinine were also noted in the GC group. Despite these observed differences, it should be remembered that the clinical presentation, laboratory and imaging findings in GC can be indistinguishable from those in NGAC.

Greater delays to surgery have been noted in GC patients reported by others.[1–4] Although there was a statistically significant difference between groups in the time between hospital admission and surgery in our series, the difference did not appear to be clinically significant and the median time to surgery from admission was the same in both groups. When elective surgery cases were excluded from analysis in the current series, no statistically significant difference between the groups was noted. There was no difference in symptom duration prior to presentation in this series, suggesting that the development of GC may not simply represent a progression in the severity of acute cholecystitis. Previous studies have shown clinically significant delays in presentation and time to operation in patients with GC.[1] One reason cited by others for such delays concerns the finding that GC is more common in elderly subjects, in whom a classic clinical presentation of acute cholecystitis is less frequent.[10]

An unexpected finding in this series concerned the high rate of detection of CBD stones. The overall incidence of CBD stones was 21%. Incidences of CBD stones in the NGAC and GC groups were 25% and 13%, respectively. Approximately half the stones were detected and treated preoperatively. A similar number were detected intraoperatively, although only 60% of all patients underwent intraoperative cholangiography as a result of the selective cholangiography policy applied by some surgeons in this study. The CBD stone rate in this series is higher than that reported in uncomplicated cholelithiasis.[11] This would support routine imaging of the bile duct in such cases.

When factors contributing to complications in this series were analysed, no significant difference between the groups emerged in terms of morbidity. The overall bile leak rate was 2% without associated major bile duct injury. When the various factors associated with morbidity were assessed by multivariate analysis, age >70 years, diabetes and the presence of muscle rigidity on initial examination were found to be the only independent risk factors for increased morbidity. Others have identified age and diabetes as risk factors, but the presence of muscle rigidity has not been analysed as far as we are aware.[1–4] Previous studies have reported increased abscess formation, perforations, biliary peritonitis, increased conversion to open surgery and prolonged hospital stay with GC.[1–4,7] In our series GC was not associated with increased complications. We speculate that this may relate to a policy of early surgery when acute cholecystitis is clinically suspected and the fact that all cases are managed in specialized surgical units. The medical management of acute cholecystitis, particularly in cases of GC, is associated with a very high failure rate in older studies.[10] Early cholecystectomy as opposed to initial conservative therapy is supported by the findings of several recent studies.[12,13]

Mortality in this series occurred only in the GC group and no incidents of mortality were directly related to surgery. Several other factors were identified on univariate analysis as being associated with mortality. When these factors were analysed by multivariate analysis, none were independently associated with increased mortality. The small number of deaths in this series may be one reason why independent risk factors could not be identified.

Conclusions

Gangrenous cholecystitis accounts for approximately one third of all cases of acute cholecystitis. Patients with GC are more likely to be older, to be male, to have diabetes and to present with fever, tachycardia or abdominal rigidity on examination. Morbidity associated with the treatment of GC does not significantly differ from that related to NGAC when operative treatment within specialized units is offered soon after the clinical suspicion of acute cholecystitis is identified. Age, diabetes and identification of muscle rigidity on examination were the only independent factors affecting morbidity. Although GC was associated with increased mortality, this did not appear to be an independent risk factor.

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Conflicts of interest

None declared.

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