Antibiotic use in patients with acute cholecystitis after percutaneous cholecystostomy

Pei-Shan Wu[a,b], Chung-Kai Chou[b,c], Yun-Chen Hsieh[a,b], Chun-Ku Chen[b,d], Yi-Tsung Lin[b,e], Yi-Hsiang Huang[a,b], Ming-Chih Hou[a], Han-Chieh Lin[a], Kuei-Chuan Lee[a,b,*]

[a]Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Department of Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC; [c]Division of Gastroenterology, Department of Medicine, National Yang-Ming University Hospital, Ilan, Taiwan, ROC; [d]Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [e]Division of Infectious Diseases, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Abstract

Background: Currently, evidence regarding the strategies of antibiotic use in patients with acute cholecystitis after receiving percutaneous cholecystostomy is limited. Hence, we aimed to investigate the outcomes in patients with inoperable acute cholecystitis receiving narrow or broad-spectrum antibiotics after percutaneous cholecystostomy.

Methods: A total of 117 patients receiving percutaneous cholecystostomy were categorized into moderate and severe acute cholecystitis defined by the Tokyo guideline and then divided into group A (narrow-spectrum antibiotic use) and group B (broad-spectrum antibiotic use). The clinical outcomes and complications were analyzed.

Results: In moderate acute cholecystitis (n = 80), group A patients (n = 62) had similar early recurrent rate (11.3% vs 16.7%; p = 0.544) and a shorter length of hospital stay (13.4 ± 8.6 vs 18.6 ± 9.4 days; p = 0.009) as compared with group B patients (n = 18). No in-hospital mortality occurred in moderate acute cholecystitis. In severe acute cholecystitis (n = 37), both groups had similar length of hospital stay (16.3 ± 12.2 vs 20.9 ± 9.5 days; p = 0.051), early recurrent rate (0% vs 16.7%; p = 0.105), and in-hospital mortality rate (5.3% vs 16.7%; p = 0.340). Although group B patients with severe cholecystitis had higher serum levels of alkaline phosphatase (Alk-P) and higher proportion of underlying malignancy, American Society of Anesthesiologists (ASA) class IV and septic shock, the clinical outcomes were not inferior to patients in group A.

Conclusion: In moderate acute cholecystitis after percutaneous cholecystostomy, patients receiving narrow-spectrum antibiotics have comparable clinical outcomes as those treated with broad-spectrum antibiotics. However, in severe acute cholecystitis, broad-spectrum antibiotics might still be necessary to rescue these patients.

Keywords: Acute cholecystitis; Antibiotic strategy, Percutaneous cholecystostomy

1. INTRODUCTION

Acute cholecystitis is a disease of acute gallbladder wall inflammation, which is a common cause of hospital admission. Cholecystectomy is the only definitive treatment of acute cholecystitis, and laparoscopic cholecystectomy is the gold standard treatment for most patients. Although laparoscopic cholecystectomy has a low perioperative mortality (0.1%–0.7%),[1–3] the mortality rate remains high (up to 19%) in the elderly or critically ill patients.[4,5] Percutaneous cholecystostomy is considered as a safe alternative to laparoscopic cholecystectomy in those who are not suitable for surgery or those who fail to respond to conservative treatment.[6–9] In addition to adequate bile drainage, antibiotics play an important role in managing acute cholecystitis. The Tokyo guideline provides a recommendation for choosing antibiotics depending on the severity of acute cholecystitis.[10] Similarly, the Infectious Diseases Society of America guideline suggests treating acute cholecystitis based both on the disease severity and the underlying comorbidities.[11] To date, however, no studies investigate whether a broad-spectrum antibiotic is still necessary once successful bile drainage is obtained by percutaneous cholecystostomy in moderate to severe acute cholecystitis. Therefore, we aimed to compare the outcomes in patients with inoperable acute cholecystitis treated with narrow or broad-spectrum antibiotics after percutaneous cholecystostomy has been performed.

2. METHODS

2.1. Study design and patient selection

We retrospectively reviewed the relevant medical and microbiology records to identify consecutive patients older than 18 years of age with acute cholecystitis having received percutaneous cholecystostomy from January 2009 to August 2010. This study was approved by the Institutional Review Board of Taipei

*Address correspondence. Dr. Kuei-Chuan Lee, Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail address: kclee2@vghtpe.gov.tw (K.-C. Lee).

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2020) 83: 134-140.

Received August 5, 2019; accepted September 25, 2019.

doi: 10.1097/JCMA.0000000000000244.

Veterans General Hospital. Patients with other sources of infection, history of intra-abdominal infection or recent abdominal surgery within the previous 3 months, who were transferred to another hospital, or who were lost to follow-up after discharge were excluded. Patients who were exposed to antibiotics within 3 months before acute cholecystitis were also excluded. All patients received medical treatment and evaluation for surgical risk based on the American Society of Anesthesiologists (ASA) classification at the diagnosis of acute cholecystitis.[12] None of the patients with ASA class III or IV received early cholecystectomy because of high surgical risk. Seven patients with ASA class II refused surgery due to personal reasons. Percutaneous cholecystostomy was performed when septic shock, local gallbladder rupture, poor clinical improvement (progressive intolerant pain or persistent fever) occurred after 48-hour medical treatment.

2.2. Definitions

Acute cholecystitis was diagnosed on the basis of the clinical presentation of fever, right upper quadrant pain, laboratory findings of leukocytosis, elevated C-reactive protein, or imaging findings (computed tomography or abdominal sonography).[13] Severity grading for acute cholecystitis was categorized by the Tokyo guideline.[13] The Tokyo guideline classifies severity of acute cholecystitis into mild (grade I), moderate (grade II), and severe (grade III) acute cholecystitis based on the presence of any of the following organ dysfunction (cardiovascular, neurological, respiratory, hepatic, and hematological), white blood cell counts, palpable tender mass in the right upper abdominal quadrant, duration of complaints, and evidence of marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis).[13] Hospital-acquired acute cholecystitis was defined as those occurring after 48 hours of hospital admission, while infection obtained within 48 hours of admission was considered to be community-acquired infection.[14] Early recurrence of acute cholecystitis was defined as a recurrent episode within 2 months after the initial attack had subsided.[15] All patients were treated with broad-spectrum antibiotics before percutaneous cholecystostomy. After percutaneous cholecystostomy, the broad-spectrum antibiotics were de-escalated or kept. Patients treated with amoxicillin/clavulanic acid, ampicillin/sulbactam, first- and second-generation cephalosporin after percutaneous cholecystostomy were classified into the group with narrow-spectrum antibiotics (group A). Those treated with piperacillin/tazobactam, third- and fourth-generation cephalosporin, fluoroquinolone, or carbapenem after percutaneous cholecystostomy were defined as the treatment group with broad-spectrum antibiotics (group B). The recorded antibiotics should meet the criteria that use for >3 days and for the majority (>50%) of the treatment course.[16] If none of the antibiotic use meets the criteria, it was classified into an undefined group. An empirical antibiotic was defined as an antibiotic that was administered within 24 hours after the blood or bile samples were taken and continued for at least 48 hours. A definitive antibiotic was defined as an antibiotic that was continued or initiated on the day the susceptibility results were reported. Antibiotic use was considered "appropriate" if the bacterial isolates were susceptible in vitro to the antibiotics administered.[17]

2.3. Percutaneous cholecystostomy

Percutaneous drainage of the gall bladder was performed by radiologists under ultrasound guidance. After local anesthesia with lidocaine, an 8-Fr pigtail catheter (Bioteque Corporation, Taipei, Taiwan) was inserted into the gallbladder through the transhepatic route and was technically successful in all patients.

2.4. Data collection

The following information was collected: (1) patient demographics, including age, gender, underlying disease, ASA score, severity grading of acute cholecystitis by the Tokyo guideline; (2) clinical findings, such as vital signs on admission, septic shock; (3) laboratory results, including white blood cell counts and serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TB), alkaline phosphatase (Alk-P), creatinine (Cr), and C-reactive protein (CRP); (4) duration of antibiotic use, length of hospital stay, clinical outcomes, including early recurrence and in-hospital mortality and complication of cholecystostomy. The primary outcomes were the recurrence of acute cholecystitis after antibiotic treatment and in-hospital mortality.

2.5. Statistical analysis

The chi-squared or Fisher's exact test was used to analyze categorical data. The Mann–Whitney *U* test was applied for assessing continuous variables. For all analyses, two-tailed tests were used to determine statistical significance and a value of $p < 0.05$ was considered significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY).

3. RESULTS

3.1. Characteristics of the patients

During the study period, a total of 128 patients with acute cholecystitis having received percutaneous cholecystostomy were enrolled in this study. Among the 128 patients, antibiotic use could not be classified in 11 patients. We further categorized the remaining 117 patients by severity of acute cholecystitis and then divided them into groups treated with narrow-spectrum (group A) and broad-spectrum (group B) antibiotics (Fig. 1). Table 1 summarizes the demographic and clinical characteristics of the patients in this study. There were 90 (70.3%) male patients and 38 (29.7%) female patients with a mean age of 73.5 years. Twenty-three patients had a history of underlying malignancy. The types of malignancy for these patients are listed in Supplementary Table 1 (http://links.lww.com/JCMA/A43), in which lung cancer (n = 5) is the most common type of malignancy. Most of the patients (95.3%) with acute cholecystitis were community-acquired and most of them (93.0%) were calculous cholecystitis. None of the patients was grade I acute cholecystitis. The major severity of acute cholecystitis was grade II. The total early recurrent rate was 10.2%, and the overall in-hospital mortality rate was 4.7%. In 13 patients with early recurrence of cholecystitis, 1 patient received percutaneous cholecystostomy with antibiotic treatment, 2 patients received percutaneous cholecystostomy and delayed cholecystectomy, 6 patients received antibiotics alone, 2 patients received antibiotics and delayed cholecystectomy. Only 2 patients were treated with early cholecystectomy (<72 hours). Most of the patients (n = 11) were treated with narrow-spectrum antibiotics. Only two patients were treated with broad-spectrum antibiotics. In addition, 70 patients received cholecystectomy after remission of acute cholecystitis; 54 of them (77%) received cholecystectomy within 2 months and 25 of them (35.7%) kept percutaneous cholecystostomy tubes until cholecystectomy was performed. Some clinical characteristics of patients receiving cholecystectomy are listed in Supplementary Table 2 (http://links.lww.com/JCMA/A43).

3.2. Clinical outcomes

The clinical characteristics and outcomes in different severity of acute cholecystitis are shown in Table 2. In moderate

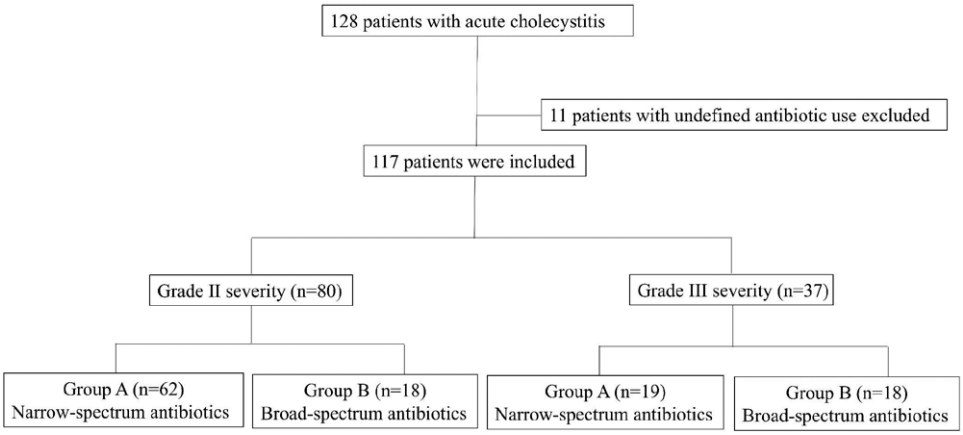

Fig. 1 Flow chart of patients receiving percutaneous cholecystostomy (n = 128) categorized by the Tokyo guideline and antibiotic use. Group A represents patients treated with narrow-spectrum antibiotic use; group B represents patients treated with broad-spectrum antibiotic use.

Table 1

Demographic characteristics of patients with acute cholecystitis treated with percutaneous cholecystostomy (n = 128)

Variables	n = 128
Age, y	73.5 ± 15.4
Gender, n (%)	
Male	90 (70.3)
Female	38 (29.7)
Comorbidity, n (%)	
Cardiovascular	73 (57.0)
Diabetes	27 (21.1)
Pulmonary	10 (7.8)
Renal	7 (5.5)
Neurologic	15 (11.7)
Malignancy	23 (18.0)
Community-acquired, n (%)	122 (95.3)
ASA classifications, n (%)	
II	7 (5.5)
III	107 (83.6)
IV	14 (10.9)
Severity grade, n (%)	
II	85 (66.4)
III	43 (33.6)
Calculous cholecystitis, n (%)	119 (93.0)
Acalculous cholecystitis, n (%)	9 (7.0)
Septic shock, n (%)	21 (16.4)
Early recurrence of cholecystitis, n (%)	13 (10.2)
In-hospital mortality, n (%)	6 (4.7)

The data are expressed as mean ± SD or number (percent). Cardiovascular comorbidities included hypertension, coronary artery disease, heart failure, valvular heart disease, or arrhythmia. Pulmonary comorbidities included chronic obstructive pulmonary disease or asthma. Renal comorbidities included chronic kidney disease or end-stage renal disease. Neurologic comorbidities included cerebral vascular accidents, Parkinsonism, or seizure.
ASA = American Society of Anesthesiologists.

acute cholecystitis, we found no significant differences between groups A and group B in terms of age, sex, laboratory data, vital signs, underlying comorbidities, duration of antibiotic use, and complications of percutaneous cholecystostomy. The early recurrent rate did not differ from each other in the two groups, but a longer hospital stay was observed in group B. In addition, there was no in-hospital mortality occurred in moderate acute cholecystitis.

In severe acute cholecystitis, patients in group B had lower mean arterial pressure, higher serum levels of Alk-P, and a higher proportion of underlying malignancy and ASA class IV. The septic shock rate was significantly higher in group B as compared with group A and group B patients were treated with a longer duration of antibiotics. Nevertheless, the length of hospital stay, clinical outcomes (early recurrence and in-hospital mortality), and complications of percutaneous cholecystostomy were similar in both groups of patients with severe cholecystitis.

3.3. Microbiological characteristics and antibiotic resistance

Nineteen (14.8%) blood culture isolates and 89 (69.5%) bile culture isolates were identified from the 128 patients with acute cholecystitis. The organisms are shown in Figure 2. *Escherichia coli* was the most common isolate in both blood and bile cultures. In addition, polymicrobial infection accounted for a great part in both cultures (26.3% vs 31.5%), in which *E. coli* and *Klebsiella* spp. were most frequently isolated mixed microorganism (Supplementary Table 3, http://links.lww.com/JCMA/A43). Table 3 lists the resistant pathogens among these patients. Antibiotic-resistant rates were 15.8% in blood cultures and 16.9% in bile cultures, respectively. Third-generation cephalosporin–resistant pathogens and extended-spectrum β-lactamase (ESBL)–producing organisms were the most frequent antibiotic-resistant isolates. Among the six patients with hospital-acquired acute cholecystitis, two were infected with resistant pathogens (Table 4). The distribution of antibiotic use was demonstrated in Figure 3. Seventy-one percent of patients received cephalosporin to treat acute cholecystitis and second-generation cephalosporin was used most commonly.

4. DISCUSSION

To avoid excessive use of antibiotic use, there has been discussion on the antibiotic strategies for acute cholecystitis after percutaneous cholecystostomy.[18–20] In our study, we found that, after percutaneous cholecystostomy was performed, narrow-spectrum antibiotics were not inferior to broad-spectrum antibiotics in treating patients with moderate acute cholecystitis. In severe acute cholecystitis, physicians tended to use broad-spectrum antibiotics to patients concomitantly with septic shock, underlying malignancy, or ASA class IV, which might lead to a similar outcome to patients with a better clinical condition. In addition, we found that a high proportion of antibiotic resistance existed

Table 2

Clinical characteristics and outcomes stratified by severity of acute cholecystitis and antibiotic groups (n = 117)

Severity Grade by Tokyo Guideline	Moderate, Grade II (n = 80)			Severe, Grade III (n = 37)		
Variables	Group A[a] (n = 62)	Group B[b] (n = 18)	*p*	Group A (n = 19)	Group B (n = 18)	*p*
Age, y	71.2 ± 16.2	77.2 ± 12.7	0.174	71.4 ± 20.4	76.7 ± 10.4	0.855
Male	37 (59.7)	11 (61.1)	0.913	17 (89.5)	15 (83.3)	0.660
BT, °C	37.3 ± 0.8	37.5 ± 0.7	0.190	37.4 ± 0.8	37.4 ± 0.9	0.915
MAP, mmHg	98.7 ± 18.1	98.0 ± 17.2	0.708	99.1 ± 19.8	84.8 ± 25.4	0.012
PR, bpm	90.5 ± 18.3	96.1 ± 15.7	0.384	91.8 ± 24.1	102.5 ± 25.8	0.236
RR, /min	19.5 ± 1.5	20.3 ± 3.0	0.466	19.8 ± 2.3	21.2 ± 3.4	0.028
Laboratory						
WBC, 1000/cumm	14.3 ± 5.6	16.0 ± 7.7	0.568	13.7 ± 7.51	16.6 ± 8.2	0.149
Cr, mg/dL	1.2 ± 1.2	1.13 ± 0.4	0.545	1.6 ± 0.8	2.0 ± 1.4	0.421
ALT, U/L	54.4 ± 61.4	108.4 ± 145.4	0.097	36.3 ± 42.7	64.3 ± 82.3	0.377
Alk-P, U/L	123.3 ± 82.3	141.5 ± 73.6	0.107	87.2 ± 38.8	192.3 ± 156.6	0.006
TB, mg/dL	1.9 ± 1.9	1.8 ± 1.9	0.985	1.5 ± 1.1	2.7 ± 2.8	0.362
CRP, mg/dL	13.7 ± 9.6	16.9 ± 2.0	0.213	13.8 ± 10.2	17.4 ± 8.8	0.316
Comorbidity						
Cardiovascular	30 (48.4)	11 (61.1)	0.342	11 (57.9)	14 (77.8)	0.197
Diabetes	8 (12.9)	5 (27.8)	0.132	4 (21.1)	7 (38.9)	0.235
Pulmonary	6 (9.7)	0 (0.0)	0.226	1 (5.3)	1 (5.6)	1.000
Renal	2 (3.2)	0 (0.0)	1.000	4 (21.1)	1 (5.6)	0.340
Neurologic	6 (9.7)	3 (16.7)	0.409	3 (15.8)	3 (16.7)	1.000
Malignancy	12 (19.4)	1 (5.6)	0.162	0 (0.0)	6 (33.3)	0.006
ASA classifications						
II	6 (9.7)	0 (0.0)	0.328	1 (5.3)	0 (0.0)	1.000
III	56 (90.3)	17 (94.4)	0.586	17 (89.5)	8 (44.4)	0.003
IV	0 (0.0)	1 (5.6)	0.225	1 (5.3)	10 (55.6)	0.001
Hospital-acquired	2 (3.2)	1 (5.6)	1.000	1 (5.3)	3 (16.7)	0.340
Acalculous cholecystitis	3 (4.8)	1 (5.6)	0.540	0 (0.0)	3 (16.7)	0.105
Septic shock	2 (3.2)	2 (11.1)	0.217	3 (15.8)	11 (61.1)	0.007
Positive blood culture	6 (9.7)	2 (11.1)	0.858	5 (26.3)	4 (22.2)	1.000
Cholangitis	5 (8.1)	2 (11.1)	0.687	1 (5.3)	3 (16.7)	0.340
Acute pancreatitis	2 (3.2)	1 (5.6)	0.540	0 (0)	1 (5.6)	0.486
Length of hospital stay, d	13.4 ± 8.6	18.6 ± 9.4	0.009	16.3 ± 12.2	20.9 ± 9.5	0.051
Duration of antibiotic use, d	12.3 ± 4.3	14.2 ± 4.2	0.064	12.3 ± 4.5	16.4 ± 7.6	0.046
Appropriate empirical antibiotics	31/40[c] (77.5)	8/11[c] (72.7)	0.741	7/12[c] (58.3)	6/14[c] (42.9)	0.431
Appropriate definitive antibiotics	31/40[c] (77.5)	10/11[c] (90.9)	0.321	9/12[c] (75.0)	13/14[c] (92.9)	0.306
Clinical outcomes						
Early recurrence	7 (11.3)	3 (16.7)	0.544	0 (0.0)	3 (16.7)	0.105
In-hospital mortality	0 (0.0)	0 (0.0)	-	1 (5.3)	3 (16.7)	0.340
Complications of cholecystostomy	7 (11.3)	3 (16.7)	0.544	3 (15.8)	3 (16.7)	1.000
Dislodge of pigtail	3 (4.8)	2 (11.1)	0.313	2 (10.5)	3 (16.7)	0.660
Bleeding	1 (1.6)	0 (0.0)	1.000	1 (5.3)	0 (0.0)	1.000
Bile leak	3 (4.8)	1 (5.6)	1.000	0 (0.0)	0 (0.0)	-

The data are expressed as mean ± SD or number (percent). *p* values were determined by the Mann–Whitney *U* test, chi-square test, or Fisher's exact test. "-" means not applicable.

[a]Group A included patients treated with amoxicillin/clavulanic acid, ampicillin/sulbactam, first- and second-generation cephalosporins.

[b]Group B included patients treated with *piperacillin/tazobactam*, third- and fourth-generation cephalosporins, fluoroquinolone, and carbapenem.

[c]Number of cultures with antimicrobial sensitivity test results.

Alk-P = alkaline phosphatase; ALT = alanine aminotransferase; ASA = American Society of Anesthesiologists; BT = body temperature; Cr = creatinine; CRP = C-reactive protein; MAP = mean arterial pressure; PR = pulse rate; RR = respiratory rate; TB = total bilirubin; WBC = white blood cell.

even in patients with community-acquired acute cholecystitis. This study provides novel information for clinical physicians in the utility of antibiotics to treat acute cholecystitis following percutaneous cholecystostomy.

In most cases, the clinical symptoms of fever, abdominal pain, and leukocytosis improve within 48 to 72 hours after percutaneous cholecystostomy in patients with acute cholecystitis.[4] One recent study showed that a short course of antibiotics (<7 days) after successful percutaneous cholecystostomy for acute cholecystitis did not predispose a worse outcome and decreased the overall use of antibiotics,[18] which might, in turn, reduce the risk of bacterial resistance.[21,22] However, no clinical studies discuss whether antibiotics can be de-escalated safely in acute cholecystitis after percutaneous cholecystostomy. One retrospective study from Nitzan et al[19] enrolled 124 patients with acute cholecystitis who underwent percutaneous cholecystostomy because of high surgical risk. This study examined the microbiology of blood and bile cultures and concordance between empirical treatment and culture susceptibility. Most patients (88%) received cefuroxime plus metronidazole to treat acute cholecystitis after percutaneous cholecystostomy and the length of hospital stay (14.3 days)

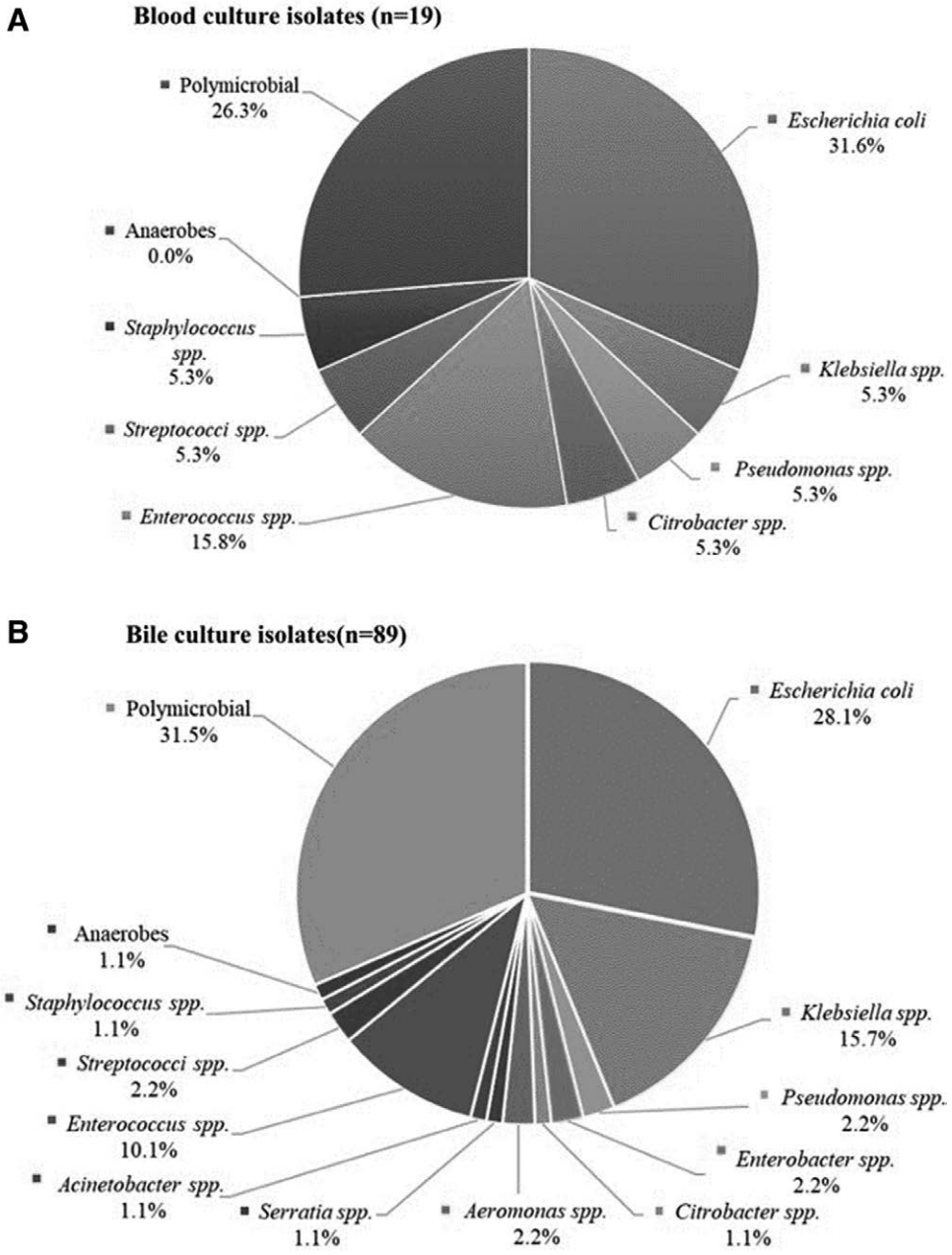

Fig. 2 Distribution of bacterial isolates from blood cultures and bile cultures. A, Blood culture isolates (n = 19). B, Bile culture isolates (n = 89).

Table 3

Antibiotic resistance from blood cultures (n = 19) and bile cultures (n = 89) from 128 patients with acute cholecystitis

Antibiotic Resistance	Blood (n = 19)	Bile (n = 89)
Third-generation cephalosporin resistance[a]	1 (5.3)	5 (5.6)
ESBL (+)[b]	1 (5.3)	5 (5.6)
Ampicillin-resistant *Enterococcus* spp.	0 (0)	4 (4.5)
Ceftazidime-resistant *Pseudomonas*	0 (0)	0 (0.0)
Methicillin-resistant *Staphylococcus* or *Streptococcus* spp.	1 (5.3)	1 (1.1)

The data are expressed as number (percent). "n" represents patient number.
ESBL = extended-spectrum β-lactamase.
[a]Third-generation cephalosporin resistance was evaluated for *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*, *Aeromonas*, *Proteus*, *Morganella*, *Serratia*, and *Acinetobacter* spp.
[b]ESBL positivity was examined for *E. coli* and *Klebsiella* spp.

and in-hospital mortality (7.3%) were not inferior to the outcomes demonstrated in other studies.[7,15,23] However, the severity of acute cholecystitis was not categorized, and the rates of septic shock were not demonstrated in Nitzan et al's[19] study. Our study clearly defined the severity of acute cholecystitis based on the Tokyo guideline and evaluated the clinical outcomes separately according to the severity. We demonstrated that the early recurrent rates and complication rates for cholecystostomy were similar in both groups and there was no in-hospital mortality developed in moderate acute cholecystitis. Narrow-spectrum antibiotics are not associated with worse outcomes in moderate acute cholecystitis after percutaneous cholecystostomy. In addition, the length of hospital stay was shorter in the group receiving narrow-spectrum antibiotics. Nevertheless, in severe acute cholecystitis, group B patients were associated with poor clinical conditions, which forced

Table 4

Bacterial isolates of samples from the six patients with hospital-acquired acute cholecystitis

	Blood Culture Pathogen	Bile Culture Pathogen
Case 1	*Pseudomonas aeruginosa*	*Pseudomonas aeruginosa* *Enterobacter cloacae* *Enterococcus* spp.[a]
Case 2	-	*Acinetobacter baumannii*[b]
Case 3	-	*Escherichia coli* *Klebsiella pneumoniae*
Case 4	-	*E. coli*
Case 5	*K. pneumoniae* *Enterococcus*	*K. pneumoniae* *Citrobacter freundii* *Enterococcus* spp.
Case 6	-	*E. coli*

"-" represents a negative culture result.

[a]Ampicillin resistant.

[b]Third-generation cephalosporin–resistant.

physicians to use stronger antibiotics for these clinically ill patients. The use of broad-spectrum antibiotics in this group may rescue these patients to have similar clinical outcomes as the patients in group A. We hence suggest that narrow-spectrum antibiotics as the treatment choice for patients with moderate acute cholecystitis once percutaneous cholecystostomy is performed. However, in severe acute cholecystitis, patients with malignancy, higher serum level of Alk-P, higher ASA class, or encounter septic shock, it remains ambiguous whether a narrow-spectrum antibiotic is enough to treat these patients even if the clinical outcome is similar.

The most commonly isolated microorganisms in this study were *E. coli*, *Klebsiella* spp., and *Enterococcus* spp., in both blood and bile cultures, as reported in the previous studies.[18–20] However, few studies have addressed the antibiotic resistance in acute cholecystitis. Coccolini et al[20] reported that the rate of resistant pathogens was 7.8% from the culture of peritoneal fluid in patients with acute cholecystitis. Risk factors for resistant pathogens were healthcare-associated infection, inadequate empirical antibiotics, and recent antibiotic use.[20] In our study, the antibiotic-resistant rate was 15.8% in blood cultures and 16.9% in bile cultures, respectively. The possible reasons for high resistant rate in this study might be attributed to the older age and worse comorbidities. Notably, these resistant pathogens were derived mostly from community-acquired acute cholecystitis. This raises concerns about the high prevalence of resistant bacteria in community-acquired acute cholecystitis. Clinical physicians must tailor the antibiotics to cover resistant pathogens once the patients with severe acute cholecystitis have poor response to initial empirical antibiotic treatment. It is challenging for a clinical physician in the balance between adequate treatment and excess antibiotic use. However, continuous use of unnecessarily broader-spectrum agents could lead to disruption of normal human gastrointestinal microbiota,[24] selective pressure for antibiotic-resistant microorganisms, increase risk of *Clostridium difficile* infection,[25] and increase overall treatment costs.[26] In the current era of antimicrobial stewardship, it is crucial to reassess the antibiotic strategies following percutaneous cholecystostomy.

The major limitation of our study is that it was a retrospective study, and there might hence exist some unmeasured variables and confounders. Second, the small case number in severe acute cholecystitis was another limitation in this study, and caution must be taken in interpreting data from a small number of cases. Third, the patients were treated in a veteran's hospital and tertiary center. Thus, the main patient group is elderly male veterans with advance comorbidities, which leads to the selection bias in this study and might not be applied to general populations. Furthermore, the microbiologic results in our study would not fit all regions because this is the data from a single center and the antibiotic resistance increases rapidly. However, several studies have shown a steady trend of ESBL-producing strains, the most commonly isolated resistant pathogen in intra-abdominal infection, in recent years.[27–29] In addition, increasing prevalence of carbapenem-resistant pathogen is reported worldwide.[30,31] The use of antibiotics should still be based on the regional and local resistant patterns. However, our study provides information regarding the antibiotic strategies for acute cholecystitis after percutaneous cholecystostomy and might inspire more studies regarding antimicrobial stewardship. In conclusion, in moderate acute cholecystitis after percutaneous cholecystostomy has been performed, narrow-spectrum antibiotics may be enough for infection control. However, in patients with severe acute cholecystitis, especially those with poor clinical conditions, such as underlying malignancy, high serum level of Alk-P and septic shock, broad-spectrum antibiotics may still be necessary after percutaneous cholecystostomy. Further prospective studies are needed to elucidate the optimal antibiotic strategies for these patients.

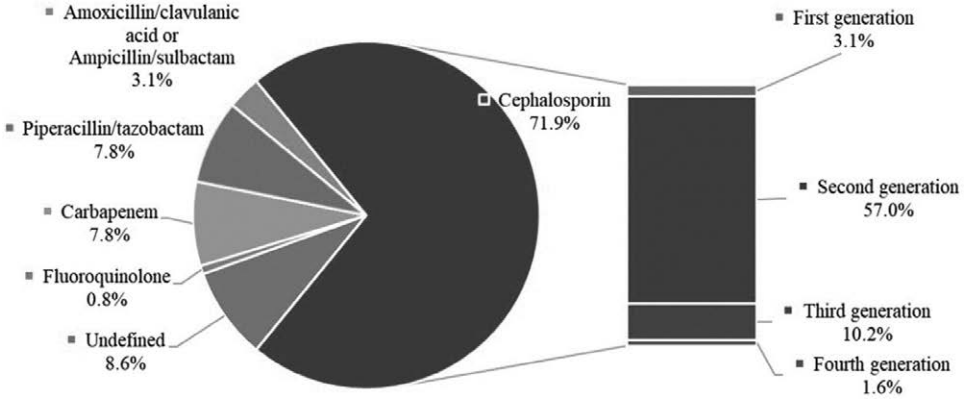

Fig. 3 Distribution of antibiotic administration for patients with acute cholecystitis after percutaneous cholecystostomy.

ACKNOWLEDGMENTS

This study was in part supported by the Taipei Veterans General Hospital (Grant No. V108C-127 and V108A-011) and Ministry of Science and Technology (Grant No. MOST108-2628-B-075-008). Supplementary data related to this article can be found at http://links.lww.com/JCMA/A43.

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