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Predictors of mortality in patients with pyogenic liver abscess

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ABSTRACT

Background: Pyogenic liver abscess (PLA) is uncommon but potentially life-threatening. The objective of this study was to identify the prognostic factors for PLA.

Methods: The medical records of 253 patients, 148 men and 105 women with a mean age of 56.4 years (SD: 15.0 years), who were hospitalised due to a PLA between January 1995 and June 2007 were reviewed. The underlying medical disorders, clinical signs and symptoms, laboratory values, imaging studies, microbiological features, treatments, morbidity and mortality were recorded. Factors related to in-hospital case fatality were analysed.

Results: The mean Acute Physiology And Chronic Health Evaluation (APACHE) II score at admission in patients with PLA was 8.7 points (SD 5.4 points). The most common co-existing disease was diabetes mellitus (41.9%), followed by biliary stone disorders (32.0%). *Klebsiella pneumoniae* was the most frequent pathogen, followed by *Escherichia coli*. The in-hospital case-fatality rate was 9.1%. Multivariate analysis revealed that gas-forming abscess (p=0.019), multi-drug resistant isolates (p=0.026), anaerobic infection (p=0.045), blood urea nitrogen level >7.86 mmol/l (p=0.004), and APACHE II score ≥15 (p= 0.004) were associated with mortality.

Conclusions: The prognosis of PLA may depend chiefly on the severity of the basic physical condition and underlying pathology. As the primary treatment for PLA is not completely effective, a more aggressive approach should be considered, especially for patients with poor prognosis.

KEYWORDS

Fatal outcome, prognosis, pyogenic liver abscess, retrospective study, risk factors

INTRODUCTION

Pyogenic liver abscess (PLA) is an uncommon but potentially life-threatening disorder with a crude annual incidence rate worldwide ranging from 2 to 45 cases per 100,000 hospital admissions.[1-4] In 1938, Ochsner *et al.* reported the first comprehensive case series of PLA, in which the case-fatality rate was 77%.[5] In the last two decades, the case-fatality rate has decreased to 6 to 26%.[2,3,6-15] Although several attempts to identify predictors of mortality in PLA patients have been made, there is no consensus regarding which factors are proven. Reported prognostic factors for PLA include older age, high Acute Physiology And Chronic Health Evaluation (APACHE) II score, elevated counts of white blood cells, blood urea nitrogen (BUN), serum creatinine, total bilirubin, low levels of serum albumin and haemoglobulin, septic shock, liver abscess of biliary origin, multiple abscesses, concomitant malignancy, and pleural effusion.[1,3,4,6-9,12-15] In some series, liver abscess is less likely to be fatal when caused by *Klebsiella pneumoniae* and is more likely to have a torpid clinical course when caused by *Escherichia coli*.[16,17] Because previous reports of patients with PLA have seldom included bacterial characteristics in the analysis of mortality, we collected microbiological data and other clinical information from PLA patients to identify the prognostic factors for this condition. We also investigated the clinical features, abscess characteristics, causative pathogens, treatments, and outcomes in these patients over a 12-year period.

PATIENTS AND METHODS

Study patients

Medical records of consecutive patients aged 18 years or older who were admitted with a first-time diagnosis of PLA to the Chung Shan Medical University Hospital, a 1250-bed medical centre in Taichung City, Taiwan, between 1 January 1995 and 30 June 2007 were reviewed by a physician. We defined a case-patient as a patient with (a) recovery of bacterial pathogens from blood or liver abscess cultures and (b) identification of one or more discrete abscess cavities in the liver by imaging studies (endoscopic retrograde cholangiopancreatography (ERCP), abdominal ultrasonography (US) and/or computerised axial tomography (CT) scans with contrast enhancement). For each case-patient identified, we reviewed records and abstracted demographic data, underlying medical conditions, clinical features, laboratory data, imaging and microbial findings, and treatment. Altogether, 262 patients were enrolled by an electronic systematic search of the patients' records for diagnostic codes. After review of these patients' records, nine patients were excluded for the following conditions: amoebic liver abscess (n=4), fungal liver abscess (n=2), tuberculous liver abscess (n=1), parasitic liver abscess (n=1), and infected biloma (n=1). The remaining 253 patients with PLA were included in this study.

Parameter definition and collection

The clinical parameters comprised demographic data, underlying medical conditions, the severity of illness at admission (the first 24-hour APACHE II score[18] after admission), the origin of liver abscess, and treatment. The origin of the abscess was based upon the available imaging studies (ERCP, abdominal US and/or CT scans with contrast enhancement) as well as clinical, pathological and/or surgical findings. Abscesses were considered cryptogenic in origin when no causative lesions could be demonstrated. Imaging parameters included location, number, and size of abscesses and the presence of gas-forming abscess, abscess rupture, and pleural effusion. Microbiological parameters included multi-drug resistant (MDR) isolates, bacteraemia, polymicrobial infection, *K. pneumoniae* infection, *E. coli* infection, and anaerobic infection. Multi-drug resistance was defined as resistance to three or more of the antimicrobial classes. Polymicrobial infection was defined as mixed bacterial recovery of blood or abscess cultures. Anaerobic infection was defined as anaerobic isolates yielded from blood or abscess cultures. The abscess specimen obtained from an invasive procedure, including image-guided (US or CT) percutaneous needle aspiration (PNA), image-guided percutaneous catheter drainage (PCD), or a direct surgical approach, had been processed for Gram stain, bacterial cultures (standard aerobic and anaerobic diagnostic methods), and tests for antimicrobial susceptibility. Antimicrobial susceptibility had been determined by the disk diffusion method (BD BBL, Sensi-Disc Antimicrobial Susceptibility Test Discs, Sparks, MD), based upon the pathogen isolated. The results were evaluated according to the recommendations of the National Committee for Clinical Laboratory Standards[19] (now known as the Clinical and Laboratory Standards Institute). Laboratory parameters included white blood cell count, prothrombin time, blood haemoglobin, serum total bilirubin, serum albumin, aspartate aminotransferase, BUN, and serum creatinine.

The initial empirical broad-spectrum antibiotics were given intravenously after the blood and/or liver abscess specimens had been drawn, and the antimicrobial agents were tailored, if necessary, based on the results of the cultures and susceptibility tests. Response to treatment was evaluated in each patient by a series of follow-up US or CT scans of the liver in the hospital and/or subsequent office visits after discharge. Case fatality was defined as death during hospitalisation.

Statistical analysis

Descriptive data were summarised as means with standard deviations (SDs) for continuous data and as percentages for categorical data. Comparisons between groups for continuous variables were made using the Student's t test. Categorical variables were compared between groups using either the χ^2 test or Fisher's exact test (if the expected value of at least one cell was <5), as appropriate. The relation between (a) demographic, clinical, imaging, microbiological, and laboratory factors and (b) mortality were analysed. The statistically significant independent factors obtained by univariate analyses were entered into a multiple stepwise logistic regression model. The prognostic factors independently related to mortality were then identified. Odds ratios (ORs) and their 95% confidence intervals (CIs) were also calculated. Statistical significance was considered to have been achieved when $p<0.05$. All p values were two-tailed.

RESULTS

Demographic data, underlying diseases, and symptoms/signs

The 253 patients with PLA, 148 men and 105 women, were a mean age of 56.4 years (SD 15.0 years) (*table 1*). Prior to admission, these patients were symptomatic for a mean of 5.5 days (SD 4.8 days). The mean APACHE II score at 24 hours after admission was 8.7 points (SD 5.4 points). The mean duration of definite diagnosis made after admission was 2.7 days (SD 6.5 days). The most common co-existing disease was diabetes mellitus, followed by biliary stone

disorders. Twenty patients had concomitant malignancies, which included hepatocellular carcinoma (n=8), colonic carcinoma (n=5), gastric cancer (n=2), cholangiocarcinoma (n=2), brain cancer (n=2), and cervical cancer with colonic metastasis (n=1). The most common symptom/sign was fever/chills (91.3%), followed by right upper quadrant tenderness (49.0%) and abdominal pain (48.6%).

Imaging, laboratory and microbiological findings

Every patient had a chest and plain abdominal x-ray on admission. All patients underwent abdominal US examination, and 88% of patients had an abdominal CT scan with contrast enhancement. The most common origin of liver abscess was biliary tract disorders (29.6%) (*table 2*). No source could be determined in 170 patients, despite thorough investigation. Twenty-four patients (9.5%) had a gas-forming abscess of the liver, and 162 patients (64.0%) had pleural effusion on admission. Among the 24 patients with gas-forming liver abscesses, 23 (95.8%) had diabetes mellitus and 22 (91.7%) had *K. pneumonia* infection. Patients with gas-forming liver abscesses had a higher frequency of diabetes mellitus (p<0.0001) and *K. pneumonia* infection (p<0.05) than those with a non-gas-forming liver abscess. Most abscesses

Table 1. *Demographic data, underlying diseases, and presenting symptoms/signs in 253 patients hospitalised with pyogenic liver abscess, 1995-2007*

Variable	No. (%) of patients
Gender, male/female	148 (58.5)/105 (41.5)
Age, mean ± SD (years)	56.4 ± 15.0
Duration of symptoms before admission, mean ± SD (days)	5.5 ± 4.8
Duration of diagnosis made after admission, mean ± SD (days)	2.7 ± 6.5
APACHE II score at admission, mean ± SD (points)	8.7 ± 5.4
Underlying diseases:[1]	
• Diabetes mellitus	106 (41.9)
• Biliary stone disorders[2]	81 (32.0)
• Alcoholism	29 (11.5)
• Liver cirrhosis	28 (11.1)
• Uraemia	24 (9.5)
• Malignancy	20 (7.9)
Symptoms:[1]	
• Fever/chills	231 (91.3)
• Abdominal pain	123 (48.6)
• Malaise	99 (39.1)
• Respiratory symptoms[3]	90 (35.6)
• Anorexia	72 (28.5)
• Nausea/emesis	68 (26.9)
• Weight loss	19 (7.5)
• Diarrhoea	18 (7.1)
Signs:[1]	
• Body temperature >38.3°C	219 (86.6)
• RUQ tenderness	124 (49.0)
• Jaundice	69 (27.3)
• Shock	40 (15.8)
• Murphy's sign[4]	39 (15.4)
• Hepatomegaly	23 (9.1)
• Disturbance of consciousness	14 (5.5)
• Ascites	10 (4.0)

APACHE = Acute Physiology and Chronic Health Evaluation; RUQ = right upper quadrant; SD = standard deviation. [1] When patients fit into more than one category, they were counted in each category. [2] Biliary stone disorders: cholelithiasis, choledocholithiasis, or hepatolithiasis. [3] Respiratory symptoms: cough, short of breath, and/or chest pain. [4] Murphy's sign: deep inspiration or cough during subcostal palpitation of the RUQ producing increased tenderness and inspiratory arrest.

Table 2. *Abscess, imaging, laboratory and microbiological characteristics in 253 patients hospitalised with pyogenic liver abscess, 1995-2007*

Variable	No. (%) of patients
Origin of abscess:	
• Biliary origin[1]	75/253 (29.6)
• Cryptogenic origin	170/253 (67.2)
• Others[2]	8/253 (3.2)
Location of abscess:	
• Right lobe	181/253 (71.5)
• Left lobe	38/253 (15.0)
• Caudate lobe	2/253 (0.8)
• Bilobar involvement	32/253 (12.6)
Abscess size, diameter:	
• <5 cm	102/253 (40.3)
• 5-10 cm	128/253 (50.6)
• >10 cm	22/253 (9.1)
Number of abscess:	
• Solitary	171/253 (67.6)
• Multiple	82/253 (32.4)
Gas-forming abscess	24/253 (9.5)
Rupture of liver abscess	3/253 (1.2)
Pleural effusion	162/253 (64.0)
Laboratory studies:	
• White blood cell count >10 x 10^9/l	191/253 (75.5)
• Haemoglobin <8.68 mmol/l in male, <7.44 mmol/l in female	196/253 (77.5)
• Aspartate aminotransferase >0.67 µkat/l	173/253 (68.9)
• Serum total bilirubin >20.52 µmol/l	88/253 (34.8)
• Blood urea nitrogen >7.86 mmol/l	58/253 (22.9)
• Serum creatinine >115 µmol/l	64/253 (25.3)
• Serum albumin <35 g/l	130/211 (61.6)
• Prothrombin time >13.1 seconds	38/141 (27.0)
Microbiological studies:	
• Bacteraemia	171/249 (68.7)
• Polymicrobial infection[3]	28/253 (11.1)
• Anaerobic infection[4]	19/253 (7.5)
• MDR isolates	22/253 (8.7)

MDR = multi-drug resistant. [1] Biliary origin of liver abscess including suppurative cholangitis and acute cholecystitis. [2] Other origin of liver abscess including subphrenic abscess (n=4), recent surgery (n=2), and receiving transcatheter arterial embolisation for hepatocellular carcinoma (n=2). [3] Polymicrobial infection: a mixture of different bacteria growing in blood or abscess cultures. [4] Anaerobic infection: anaerobic isolates growing in blood or abscess cultures.

(71.5%) were located in the right lobe of the liver. Multiple abscesses were present in 82 patients (32.4%). The liver abscess ruptured in three patients during hospitalisation. The most common laboratory abnormality was low serum haemoglobin level, which was seen in 77.5%.

The recovery frequency of blood culture was 68.7% (171/249 patients) with 184 isolates obtained in patients who had blood cultures. The recovery percentage of abscess cultures was 94.6% (227/240 patients) with 276 isolates in patients in whom abscess cultures were obtained. *K. pneumoniae* was the most commonly isolated aerobe in both blood and abscess cultures, followed by *E. coli* (*table 3*). Twenty-eight (11.1%) of the infections were polymicrobial. *Bacteroides fragilis* was the most frequently isolated anaerobic organism. Nine out of the 11 streptococci isolates obtained from abscess cultures were *Streptococcus constellatus* while the remaining two belonged to α-haemolytic viridans streptococci. Anaerobic isolates from blood and/or abscess cultures were found in 19 patients (7.5%). Among the 19 patients with anaerobic infection, 15 were infected with polymicrobial pathogens. MDR isolates were cultured in 22 patients (8.7%).

Table 3. *Microbiological spectra in patients with pyogenic liver abscess in 253 patients hospitalised with pyogenic liver abscesses, 1995-2007*

Micro-organism	Blood (249 patients)	Abscess (240 patients)
Gram-negative aerobes:		
• *Klebsiella pneumoniae*	136	175
• *Escherichia coli*	21	37
• Other *Klebsiella* spp.	2	2
• *Pseudomonas* spp.	2	6
• *Morganella* spp.		4
• *Proteus* spp.		8
• *Aeromonas* spp.		2
• *Pantoea* spp.	2	3
• *Edwardsiella* spp.		3
• *Enterobacter* spp.		2
• Unidentified Gram(–) bacilli	2	4
Gram-positive aerobes:		
• *Enterococci* spp.	5	2
• *Staphylococci* spp.	8	2
• *Streptococci* spp.		11
Anaerobes :		
• *Bacteroides fragilis*	6	6
• *Prevotella* spp.	2	2
• *Fusobacterium* spp.		3
• *Peptostreptococcus* spp.		4
• Anaerobic Gram(+) non-spore foaming bacilli	2	
Total isolates	*184*	*276*

Treatment, morbidity, and outcome

Initial empirical antibiotics included the cephalosporin group, penicillin group, aminoglycosides, and metronidazole. Most (77.1%) of the agents consisted of a first/second-generation cephalosporin and a gentamicin. All patients received appropriate antibiotic treatment on the basis of the results of the antibiotic susceptibility profiles. The use of initial treatment for PLA was based on the preference of the physician in charge or the condition of the patient. The four initial treatments were: antibiotics alone (n=21), antibiotics plus image-guided PNA (n=36), antibiotics plus image-guided PCD (n=194), and antibiotics plus surgical intervention (n=2) (*table 4*).

Patients who received only antibiotics had the following conditions: end-stage malignancies with a frail status, decision not to use any invasive treatment, or abscess location/size which was difficult to drain. Two patients, including one with concomitant peritonitis and empyema of the gallbladder and one with co-existing peritonitis and multiple abscesses with multiloculation, initially had surgery and then survived. Fourteen patients needed subsequent treatment. Two patients treated with antibiotics alone subsequently required surgery and eventually survived. Five patients who initially had image-guided PNA subsequently required PCD and recovered completely. Seven patients who received image-guided PCD as primary treatment needed a subsequent surgical intervention. Of these seven patients, four had drainage failure, and in three the abscess ruptured during hospitalisation. The four patients in whom the initial PCD was not successful, including two in whom it was decided not to perform surgery and two with co-existing hepatic cell carcinoma, died of overwhelming

Table 4. *Morbidity, treatment, and outcome in 253 patients with pyogenic liver abscess, 1995-2007*

Variable	Initial treatment				
	Antibiotics alone	PNA plus antibiotics	PCD plus antibiotics	Surgery plus antibiotics	Total
	n=21	n=36	n=194	n=2	n=253
Requirement of a subsequent treatment	2 (9.5)	5 (13.9)	7 (3.6)	0	14 (5.5)
Metastatic infection	2 (9.5)	2 (5.6)	11 (5.7)	0	15 (5.9)
Relapse	2 (9.5)	0	8 (4.1)	0	10 (4.0)
Rupture of abscess	0	0	3 (1.5)	0	3 (1.2)
Death	6 (28.6)	0	17 (8.8)	0	23 (9.1)

PCD = percutaneous catheter drainage; PNA = percutaneous needle aspiration. Values represent N (%).

sepsis. Of the three patients with a ruptured abscess, two had a good clinical response to subsequent operation, and one died of peritonitis and concomitant uncontrolled sepsis. Two patients with image-guided PCD died among these patients with relapse. Fifteen patients had metastatic infection: splenic abscess (7), subcutaneous abscess (5), endophthalmitis (2), and splenic abscess with concomitant infectious endocarditis (1). All 15 patients were infected with *K. pneumoniae*. None of these 15 patients died. Mean hospital stay in all 253 patients was 21.4 days (SD 20.3 days). The mean follow-up of patients after discharge was 5.5 months (SD 3.3 months). Mean duration of antibiotics taken was 35.4 days (SD 22.5 days). Twenty-three patients in this case series died, yielding an overall case-fatality rate of 9.1%.

Analysis of prognostic factors related to mortality

Factors associated with death on univariate analysis were diabetes mellitus, malignancy, uraemia, gas-forming abscess, multiple abscesses, MDR isolates, bacteraemia, non-*K. pneumoniae* infection, anaerobic infection, polymicrobial infection, initial antibiotics alone, serum total bilirubin level >20.52 µmol/l, BUN level >7.86 mmol/l, serum creatinine level >115 µmol/l, and APACHE II score ≥15 (*table 5*). When these 15 statistically significant variables were subjected to multivariate analysis, only five variables – gas-forming abscess, MDR isolates, anaerobic infection, BUN level >7.86 mmol/l, and APACHE II score ≥15 – fitted the stepwise logistic regression model (*table 6*).

DISCUSSION

Our findings were similar to those of previous reports in that gas-forming liver abscess, BUN, and APACHE II score are prognostic factors in predicting mortality of PLA.[7,15,20,21] In addition, our data revealed that some

Table 5. *Significant factors in relation to mortality by univariate analysis in 253 patients hospitalised with pyogenic liver abscess, 1995-2007*

Variables	Category	Mortality (%)	Odds ratio (95% CI)	P value
Diabetes mellitus	Yes	15/106 (14.2)	2.9 (1.2-7.0)	0.017
	No	8/147 (5.4)	1.0	
Uraemia	Yes	8/24 (33.3)	7.1 (2.6-19.3)	<0.0001
	No	15/229 (6.6)	1.0	
Malignancy	Yes	5/20 (25.0)	4.0 (1.3-12.2)	0.024
	No	18/233 (7.7)	1.0	
MDR isolates	Yes	10/22 (45.5)	14.0 (5.1-38.3)	<0.0001
	No	13/231 (5.6)	1.0	
Bacteraemia	Yes	19/171 (11.1)	4.8 (1.1-20.9)	0.024
	No	2/78 (2.6)	1.0	
Anaerobic infection[1]	Yes	7/19 (42.9)	7.9 (2.8-23.0)	<0.0001
	No	16/234 (6.8)	1.0	
Polymicrobial infection[2]	Yes	7/28 (25.0)	4.4 (1.6-11.8)	0.007
	No	16/225 (7.1)	1.0	
Non-*K. pneumoniae* infection[3]	Yes	11/63 (17.5)	3.1 (1.3-7.5)	0.008
	No	12/190 (6.3)	1.0	
Multiple abscesses	Yes	12/82 (14.6)	2.5 (1.1-5.9)	0.034
	No	11/171 (6.4)	1.0	
Gas-forming liver abscess	Yes	6/24 (25.0)	4.2 (1.5-11.9)	0.013
	No	17/229 (7.4)	1.0	
APACHE II score at admission	≥15	17/37 (45.9)	29.8 (10.5-84.0)	<0.0001
	<15	6/216 (2.8)	1.0	
Serum total bilirubin, µmol/l	>20.52	18/88 (20.5)	8.2 (2.9-23.0)	<0.0001
	≤20.52	5/165 (3.0)	1.0	
Blood urea nitrogen, mmol/l	>7.86	16/58 (27.6)	10.2 (4.0-26.4)	<0.0001
	≤7.86	7/195 (3.6)	1.0	
Serum creatinine, µmol/l	>115	16/64 (25.0)	8.7 (3.4-22.2)	<0.0001
	≤115	7/189 (3.7)	1.0	
Antibiotics alone	Yes	6/21 (28.6)	5.1 (1.7-14.7)	0.002
	No	17/232 (7.3)	1.0	

APACHE = Acute Physiology And Chronic Health Evaluation, CI = confidence interval, *K. pneumoniae* = *Klebsiella pneumoniae*, MDR = multi-drug resistant. [1]Anaerobic infection: anaerobic isolates growing in blood or abscess cultures. [2]Polymicrobial infection: a mixture of different bacteria growing in blood or abscess cultures. [3]Non-*K. pneumoniae* infection: other isolates rather than *K. pneumoniae* growing in blood or abscess cultures.

Table 6. *Prognostic factors in relation to mortality by multivariate analysis in 253 patients hospitalised with pyogenic liver abscess, 1995-2007*

Variable	Odds ratio (95% CI)	P value
Gas-forming liver abscess	8.3 (1.4-48.8)	0.019
MDR isolates	16.6 (1.4-197.0)	0.026
Anaerobic infection[1]	10.4 (1.1-103.3)	0.045
Blood urea nitrogen >7.86 mmol/l	30.2 (3.0-305.6)	0.004
APACHE score ≥15	8.5 (2.0-35.9)	0.004

APACHE = Acute Physiology And Chronic Health Evaluation, CI = confidence interval; MDR = multi-drug resistant. [1]Anaerobic infection: anaerobic isolates growing in blood or abscess cultures.

bacterial characteristics – anaerobic infection and MDR isolates – may play an important role in the prognosis of PLA. As far as we are aware, this finding has not been reported before. We acknowledge that our study results are limited by their retrospective nature. Our data were limited to what had been recorded in the medical records. However, there was no significant difference in missing measurements at admission between the case-fatality and the non-case-fatality groups. The possible influence of this non-random effect of missing data on the study results was minimised. On the other hand, the majority of the previous reports of prognostic factors for PLA were based upon either small sample sizes or univariate analysis.[1,3,4,6-9,12-15] We applied multivariate analysis in the present study which is one of the largest published case series on PLA.

The case-fatality rate of PLA was 9.1% in our study, which is in accordance with the level reported in the past two decades.[2,3,6-15] The predominance of *K. pneumonae* and cryptogenic causes in our study is consistent with previous Asian reports;[6,7,9,13-17] in contrast, reports from Western countries do not all reach the same conclusion.[1-3,8,11,12] PLA with *K. pneumonae* may lead to septic extrahepatic metastases, especially in diabetic patients.[16,17,22-24] Several investigators have reported that capsular serotype K1 or K2, and *magA* gene may be associated with virulence and phagocytosis resistance in *K. pneumoniae* liver abscess and these virulent factors, capsular serotype K1 especially, may play a potential determinant role in developing metastatic complications and causing PLA.[25-27] The serotype K1 isolate was uncommon among *K. pneumoniae* isolated from Western countries,[27-31] which may account for aetiological differences among regions. Some recent reports from the United States have noted an increase in the proportion of PLA patients with *K. pneumoniae*.[32,33] This phenomenon seems to indicate that *K. pneumoniae* liver abscess is an emerging infectious disease and may become a potential global concern.

The recovery frequency of anaerobic isolates in PLA patients varies in published reports, ranging from 7 to 46%.[1-3,6-9,12-14,34] The anaerobic recovery in our study, 7.5%, is located at the lower end of the range. This may be influenced by inadequate methods for transportation and cultivation of specimens. The effect of anaerobes on infection has been gradually recognised in the past 30 years. Patients experience shock, injury, or surgery, and those with blood vessel disease or malignancy are at high risk of anaerobic bacterial infection. The virulence of anaerobes – toxin production, capsule formation, and superoxide dismutase activity – may contribute to tissue damage, protect the pathogen from host defences, or induce abscesses.[35-37] Furthermore, anaerobes may not only protect facultative pathogens by suppressing phagocytic activity and/or blocking opsonic pathways but also create an environment where control and eradication of co-infecting pathogens are particularly difficult, thereby enhancing the virulence of mixed infections.[37,38] The findings of the above studies may explain why polymicrobial infection is associated with mortality in some reports and in our univariate analysis and why anaerobic, but not polymicrobial infection, is a prognostic factor for PLA mortality in multivariate analysis.

MDR isolates are known to contribute to high morbidity and mortality in several infectious diseases, such as tuberculosis, malaria, acute respiratory diseases and gastroenteritis, because they may cause infections that are more difficult to treat.[39-41] However, the influence of MDR isolates on PLA is less well understood. The emergence of MDR is a complicated problem and may be driven by numerous interconnected factors, including the use of antimicrobials in animals, plants and human beings.[42,43] Previous studies show that inappropriate antibiotic use is the most important factor responsible for increased antimicrobial resistance, especially in developing countries.[30,31] The majority of PLA patients in our study reported an average of >5 days' prodrome of fever, chills, or respiratory/gastrointestinal symptoms, and they may have received antibiotics to treat their illnesses prior to hospital admission. However, information regarding antibiotic use before admission had not been recorded in the medical records in this series, so a definite conclusion cannot be made.

Few reports have studied BUN as an indicator of mortality in PLA patients.[7] In our work, a raised BUN level was a significant prognostic factor for PLA, a finding that is consistent with previous reports.[7] Designed to measure the severity of disease for patients admitted to intensive care units, the APACHE II score system has also been used extensively to predict treatment outcome in a variety of ill patients.[18] Mischinger *et al.*[8] found a high APACHE II score to be an independently significant risk factor of mortality in PLA patients; in contrast, Alvarez Perez *et al.*[12] found a high APACHE II score (≥10) to be statistically associated with mortality in univariate analysis but not

in multivariate analysis. Recently, Hsieh *et al*. identified an APACHE II cut-off score of ≥15 as a good positive predictive indicator of mortality from PLA.[15] Similarly, we found the APACHE II score of ≥15 to be a significant predictor of adverse outcome in PLA patients, with an 8.5-fold increased risk of death compared with the risk of death in patients with a score of <15. Some parameters of the APACHE II score system that have been identified as predicting mortality in PLA patients include age, blood pressure, white blood cell count, haematocrit and serum creatinine levels, and underlying medical conditions (malignancy, liver cirrhosis, and uraemia).[1,3,4,6-9,12-15] The APACHE II score seems to be more representative and convenient than the above parameters for predicting mortality of patients with PLA. Additionally, this finding indicates that a poor underlying physical condition may be related to mortality of PLA.

Since it was first described by Smith in 1944,[46] gas-forming liver abscess has been increasingly found with the evolution of diagnostic imaging techniques. The proportion of gas-forming liver abscesses in PLA patients ranges from 11 to 29%,[20,47] and the case-fatality rate is as high as 37%.[48] In accord with previous reports,[33,36] we found gas-forming liver abscess to be an independent predictor of mortality in PLA patients. As described in previous studies, gas-forming liver abscess is associated with *K. pneumoniae* infection and diabetes mellitus.[20,21,47,48] However, this finding is less often seen in Western reports.[4] This may be attributed to variant study populations and geographical differences. A possible pathophysiological mechanism includes gas-forming pathogens that may damage local tissue through rapid catabolism and impaired transport of the end products at inflammatory sites. Diabetic microangiopathy would compound this infection by slowing the transport of catabolic end products away from these foci, resulting in gas accumulation.[21,47,49] Considering our study results and these biological mechanisms, we hypothesise that gas-forming liver abscess is associated with more severe tissue destruction and a poorer outcome than other liver abscess.

With the advances in image techniques (US or CT scans), PCD under image guidance has now become the treatment of choice for PLA in most institutions due to its less invasive approach and greater feasibility,[1-3,6-15,21] although some clinicians still prefer surgical intervention.[50] Several groups have documented that image-guided PCD is appropriate as primary treatment for PLA: it has good results with a low case-fatality rate ranging from 0 to 15%.[2,3,10,12,14,51] Evidence from our case-patient series – a success rate of 87.2% and a case-fatality rate of 8.7% in patients who had image-guided PCD – supports this recommendation.

Recently, some studies have shown that image-guided PNA produces satisfactory results, with case-fatality rates of 0 to 6%.[2,51] Similarly, in our patients with PNA no deaths and no recurrences were seen. Image-guided PNA has advantages over image-guided PCD: less invasive, less expensive, less nursing care required, more patient acceptability, and less procedure-related complications. We did not deduce which therapeutic modality is better because the patients who had different treatments were not exactly comparable, but the results seem to suggest that PNA could be an effective, and perhaps superior, alternative for treating PLA. The effectiveness of antibiotics alone for treating PLA is still disputed.[2,3,52] Patients treated with only antibiotics in our study had a high case-fatality rate – 28.6 *vs* 7.3% in all other patients – although the rate ratio did not reach statistical significance in multivariate analysis.

Several authors today believe that antibiotics alone and surgical approach are not a routine primary treatment modality for PLA; antibiotics alone may be an alternative in patients too ill to undergo invasive approaches and in patients with small multiple abscesses not amenable to drainage intervention; and surgical approach may be reserved only for patients unsuitable for further percutaneous drainage and patients with primary intra-abdominal pathology.[1-3,10,34] However, some PLA patients had a severe infection at arrival and may rapidly progress to an adverse outcome. In this situation, the patients would probably die before clinicians could change treatment strategy from percutaneous drainage to surgery. Our results suggest that physicians should use an aggressive approach as soon as possible for PLA patients with initial high fatality risk and poor response to primary treatment, especially for those patients with APACHE II score ≥15 at admission. There is still a lack of useful and definite criteria to follow when determining whether to use a surgical procedure in PLA patients; further prospective experimental studies should be conducted.

In conclusion, five main prognostic factors are related to mortality of PLA: presence of gas-forming abscesses, MDR isolates, anaerobic infection, high level of BUN, and high APACHE II score at admission. The severity of the patient's basic physical condition and underlying pathology may play an important role in the prognosis of PLA. As the primary treatment for PLA is not fully effective, a more aggressive therapeutic approach should be considered, especially for those patients with poor prognostic factors.

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