



ORIGINAL ARTICLE

Clinical characteristics and outcome of patients with community-onset *Klebsiella pneumoniae* bacteremia requiring intensive care

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KEYWORDS

Bacteremia;
Intensive care;
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Background: *Klebsiella pneumoniae* (*K. pneumoniae*) is the major pathogen of community-acquired pyogenic infections in Taiwan and can lead to poor prognosis in critically ill patients complicated with bacteremia. This study investigated the characteristics and outcome of patients with community-onset *K. pneumoniae* bacteremia who required intensive care.

Method: Adult patients with community-onset *K. pneumoniae* bacteremia requiring intensive care were retrospectively analyzed, compared with those treated in ordinary wards, and determined for risk factors for infection-related mortality and long-term mortality at a medical center in Taiwan over a 3-year period.

Results: Among the 309 patients with community-onset *K. pneumoniae* bacteremia, 58 patients (18.8%) required intensive care. Respiratory tract infection [Odds ratio (OR) = 3.67, 95% confidence interval (CI) = 1.79–7.50, $p < 0.001$] was the independent risk factor for ICU admission. Infection-related mortality was 34.5%. Higher APACHE II score (OR = 1.43; 95% CI = 1.02–2.01; $p = 0.041$) and underlying malignant neoplasm (OR = 35.48; 95% CI = 2.54–495.57; $p = 0.008$) were independent predictors of infection-related mortality on multivariate logistic regression. One-year overall mortality was 58.6% and malignant neoplasm was the predisposing factor for poor long-term outcome.

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Conclusion: Nearly one fifth of patients with community-onset *K. pneumoniae* bacteremia required intensive care and this was associated with high mortality and poor long-term prognosis. Physicians should recognize the distinct characteristics and risk factors for mortality among these patients.

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Introduction

Klebsiella pneumoniae (*K. pneumoniae*) is the second most common cause (behind *Escherichia coli*) of community- and hospital-acquired Gram-negative bloodstream infection (BSI).¹ Although nosocomial *K. pneumoniae* infections occur worldwide, in the past two decades, geographical differences have been recognized in the spectrum of community-acquired infection caused by *K. pneumoniae*, including a preponderance of severe invasive disease in Taiwan.² In Taiwan, *K. pneumoniae* is the major cause of community-onset bacteremia and pyogenic infection.^{3,4} Furthermore, *K. pneumoniae* infection can lead to a poor prognosis in critically ill patients with bacteremic community-acquired pneumonia.⁵

BSI has been associated with increased rates of hospitalization, and increased length of stay and hospital costs.^{6,7} Community-acquired bacteremia is a common cause of hospital and intensive care admission, with an associated ICU crude mortality around 40%.^{8,9} Despite advances in the development of adjunctive therapies and sophisticated life-support facilities, BSI is associated with a dismal prognosis in critically ill patients.¹⁰ Moreover, bacteremia can lead to increased risk of mortality persisting after 28 days to >1 year in critically ill patients.¹¹ The different characteristics of community-acquired and nosocomial *K. pneumoniae* bacteremia have been reported in the literature.^{12,13} However, the characteristics of community-onset *K. pneumoniae* bacteremia requiring treatment in the ICU have rarely been reported. In the literature, only one study found that 11 alcoholic patients with bacteremic *K. pneumoniae* pneumonia who needed ICU management and ventilatory support had rapidly fatal outcomes.¹⁴ Therefore, the aim of our study was to investigate the clinical manifestations, predictive factors for mortality, and long-term prognoses of patients with community-onset *K. pneumoniae* bacteremia who required intensive care.

Materials and methods

Study design, patient population, and data collection

This study was a retrospective cohort analysis of consecutive patients with community-onset bacteremia caused by *K. pneumoniae* at Taipei Veterans General Hospital, a tertiary medical center with a 2900-bed capacity. Patients with community-onset bacteremia caused by *K. pneumoniae* were identified by reviewing culture records from the Department of Microbiology from January 2007

through December 2009. We excluded patients aged <18 years. A database was created and the demographic data and clinical characteristics of the study population were collected. Potential factors associated with outcome were identified and statistically analyzed. Data enrolled in this study included those during the first 30 days after onset of *K. pneumoniae*-induced bacteremia or until death. All data were reviewed by two infectious disease specialists. This study was approved by Institutional Review Board of Taipei Veterans General Hospital.

Definitions

An episode of bacteremia was defined as the presence of >1 blood cultures positive for *K. pneumoniae* that contributed to clinical sepsis. When a patient had >1 episode of bacteremia, only the first episode was used in the analysis. We excluded hospital-acquired bacteremia if the episode occurred >48 hours after admission¹⁵ and enrolled all other episodes, which were considered as community-onset bacteremia. Community-onset bacteremia was classified as healthcare-associated or community-acquired infection according to the criteria used by Friedman et al¹⁶ In brief, episodes were classified as healthcare-associated infection when any of the following was present: intravenous therapy or specialized nursing care at home; hemodialysis within 30 days before the BSI; hospitalization for >2 days in an acute care hospital within 90 days before BSI; or resident in a nursing home or long-term care facility. Bacteremia was defined as polymicrobial when >2 different organisms were isolated from blood cultures. The probable focus of infection was assessed on the basis of microbiological and clinical findings. Inadequate empiric antimicrobial treatment was defined as patients who did not receive >1 *in vitro* active antimicrobial agent after the index blood culture had been drawn and before susceptibility results were available. Infection-related mortality was defined as death within 2 weeks after onset of *K. pneumoniae* blood culture, in the absence of known noninfectious causes of death such as intracranial hemorrhage, myocardial infarction, or pulmonary embolism. Shock was defined as systolic blood pressure <90 mmHg and the need for inotropic agents to maintain blood pressure. Chronic lung disease was defined as chronic obstructive pulmonary diseases, bronchiectasis, or any structural lung diseases with the exception of bronchogenic carcinoma.

Microbiological methods

Blood culture samples were processed by the BACTEC NR-660 system (Becton Dickinson, Sparks, MD, USA). All positive

cultures were examined by Gram staining and subcultured on blood agar plates and eosin-methylene blue agar plates for further identification. VITEK 2 system (bioMérieux, Marcy l'Etoile, France) with VITEK 2 GN card was used to confirm bacterial identification. Antimicrobial susceptibility of *K. pneumoniae* was tested by standard disk diffusion method. Clinical and Laboratory Standards Institute (CLSI) criteria were used to define susceptibility or resistance to the antimicrobial agents studied. Extended-spectrum β -lactamase (ESBL) production was screened and confirmed in accordance with CLSI standards.¹⁷

Statistical analysis

Contingency data were analyzed by two-tailed Chi-square test or Fisher's exact test; continuous data were analyzed by Student *t*-test or the Mann-Whitney U test. A *p* value <0.05 was considered statistically significant; all probabilities were two-tailed. Variables with *p* value <0.05 in univariate analyses were subsequently entered in the multivariate logistic regression model to evaluate the risk factors for ICU admission and mortality. Shock, respiratory failure, and altered mental status were not included in the multivariate logistic regression model because they are criteria for ICU admission. The Kaplan-Meier method was used to estimate 1-year all-cause mortality. Patients were followed from the date of the first episode of *K. pneumoniae* bacteremia until death or last follow-up date. Variables with a *p* value <0.05 were entered in Cox proportional hazards regression to determine factors associated with 1-year all-cause mortality. All statistical analyses were performed with SPSS version 18.0.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Clinical characteristics of patients with community-onset *K. pneumoniae* bacteremia requiring intensive care

During the 3-year study period, 309 consecutive patients with community-onset *K. pneumoniae* bacteremia, including 175 community-acquired and 134 healthcare-associated infections, were identified. Among these, 58 patients (18.8%) required intensive care during the study period and 30 patients had healthcare-associated infections. Diabetes mellitus (DM) and malignant neoplasm were the most common underlying diseases, and respiratory tract infection was the most common source of bacteremia in the patients requiring intensive care. Underlying DM was more common in community-acquired than in healthcare-associated infection [15/28 (53.6%) vs. 6/30 (20%); *p* = 0.008]. On the other hand, malignant neoplasm was more frequent in patients with healthcare-associated compared with community-acquired infections [18/30 (60.0%) vs. 5/28 (17.9%); *p* = 0.001]. We compared the clinical characteristics between patients treated in the ordinary ward (*n* = 251) versus those requiring intensive care (*n* = 58), as shown in Table 1. Older patients (74.2 ± 13.8 vs. 69.8 ± 15.3, respectively; *p* = 0.044), those with chronic lung disease (31.0% vs. 8.8%, respectively; *p* = 0.01), and

those with respiratory tract infection (48.3% vs. 13.5%, respectively; *p* < 0.001) had a significantly higher rate of ICU admission. By contrast, patients with biliary tract infection (BTI) had a significantly lower rate of requiring intensive care (10.3% vs. 28.7%; *p* = 0.006). Logistic regression analysis revealed that respiratory tract infection [Odds Ratio (OR) = 3.67, 95% confidence interval (CI) = 1.79–7.50, *p* < 0.001] was the independent risk factor mandating intensive care. Infection-related mortality rate in patients requiring intensive care was significantly higher than in those treated in ordinary wards (34.5% vs. 4.0%; *p* < 0.001).

Predictive factors for infection-related mortality and 1-year prognosis among patients requiring intensive care

We compared the clinical characteristics between the survivors (*n* = 38) and nonsurvivors (*n* = 20), as shown in Table 2. There was no significant difference in sex, age, polymicrobial infection, resistance strain, and adequacy of antibiotic use. Patients with higher Acute Physiology and Chronic Health Evaluation (APACHE) II scores (30.2 ± 6.1 vs. 23.5 ± 5.4, respectively; *p* < 0.001), healthcare-associated infection (80.0% vs. 36.8%; *p* = 0.004), underlying malignant neoplasm (80.0% vs. 18.4%; *p* < 0.001), initial presentation of respiratory failure (90.0% vs. 55.3%; *p* = 0.017), altered mental status (75.0% vs. 36.8%; *p* = 0.013), and lower leukocyte count (10.2 ± 9.9 vs. 17.6 ± 13.9 × 10⁹/L, *p* = 0.038) had a significantly higher risk of mortality. All patients with liver abscesses treated in the ICU had a favorable outcome (0% vs. 21.1%; *p* = 0.041). Logistic regression analysis (Table 3) revealed that higher APACHE II score (OR = 1.43; 95% CI = 1.02–2.01; *p* = 0.041) and underlying malignant neoplasm (OR = 35.48; 95% CI = 2.54–495.57; *p* = 0.008) were independent predictors of mortality.

Overall, the 1-year mortality in these patients admitted to ICU was 58.6% (*n* = 34). After analysis of the same variables listed in Table 2, we found that 1-year mortality-related potential risks included healthcare-associated bacteremia (*p* = 0.01), higher APACHE II score (*p* < 0.001), malignant neoplasm (*p* < 0.001), respiratory failure (*p* = 0.025), altered mental status (*p* = 0.001) and inappropriate antibiotics use (*p* = 0.042), as showed in Table 4. The Kaplan–Meier survival curves demonstrated that patients with an underlying malignant neoplasm had higher mortality than those without a malignant neoplasm (*p* < 0.001, by log-rank test) (Fig. 1). Cox hazards proportional regression revealed that the risk for 1-year all-cause mortality was underlying malignant neoplasm (Hazard Ratio = 3.14, 95% CI = 1.36–7.26, *p* = 0.007).

Discussion

A previous study demonstrated that critically ill patients with nosocomial *K. pneumoniae* bacteremia tended to experience acute renal failure, hemodynamic instability, a longer length of ICU stay, and longer ventilator dependence.¹⁸ However, few studies regarding the characteristics and outcome of critically ill patients with community-onset

Table 1 Comparison of clinical features of patients with community-onset *K. pneumoniae* bacteremia treated in an ordinary ward and in the ICU^a

Clinical feature	Overall (n = 309)	Ordinary ward (n = 251)	ICU admission (n = 58)	p ^b
Age (y)	70.6 ± 15.1	69.8 ± 15.3	74.2 ± 13.8	0.044
Male	208 (67.3)	163 (64.9)	45 (77.6)	0.090
Healthcare-associated	134 (43.4)	104 (41.4)	30 (51.7)	0.201
Underlying disease				
Diabetes mellitus	121 (39.2)	100 (39.8)	21 (36.2)	0.718
Liver cirrhosis	31 (10.0)	24 (9.6)	7 (12.1)	0.741
Chronic lung disease	40 (12.9)	22 (8.8)	18 (31.0)	0.010
Alcoholism	25 (8.1)	18 (7.2)	7 (12.1)	0.281
Congestive heart failure	28 (9.1)	21 (8.4)	7 (12.1)	0.528
Chronic kidney disease (Cr > 2 mg/dL)	26 (8.4)	18 (7.2)	8 (13.8)	0.116
CNS disease	73 (23.6)	57 (22.7)	16 (27.6)	0.538
Autoimmune disease	9 (2.9)	7 (2.8)	2 (3.4)	0.678
Transplantation	5 (1.6)	5 (2.0)	0 (0)	0.588
Malignant neoplasm	108 (35.0)	85 (33.9)	23 (39.7)	0.405
Initial presentation				
Shock	83 (26.9)	39 (15.5)	44 (75.9)	<0.001
Respiratory failure	45 (14.6)	6 (2.4)	39 (67.2)	<0.001
Altered mental status	58 (18.8)	29 (11.6)	29 (50.0)	<0.001
Onset of symptoms (d)	3.3 ± 4.8	3.4 ± 5.2	2.8 ± 2.9	0.265
Infectious focus				
Meningitis	1 (0.3)	0 (0)	1 (1.7)	0.188
Respiratory tract infection	62 (20.1)	34 (13.5)	28 (48.3)	<0.001
Liver abscess	45 (14.6)	37 (14.7)	8 (13.8)	0.854
Biliary tract infection	78 (25.2)	72 (28.7)	6 (10.3)	0.006
Intraabdominal infection	13 (4.2)	11 (4.4)	2 (3.4)	>0.999
Urinary tract infection	81 (26.2)	70 (27.9)	11 (19.0)	0.220
Skin and soft tissue infection	8 (2.6)	5 (2.0)	3 (5.2)	0.174
Primary	29 (9.4)	23 (9.2)	6 (10.3)	0.977
Polymicrobial	42 (13.6)	34 (13.5)	8 (13.8)	>0.999
ESBL strain	15 (4.9)	11 (4.4)	4 (6.9)	0.494
Inappropriate antibiotic use	6 (1.9)	2 (0.8)	4 (6.9)	0.013
Infection-related mortality	30 (9.7)	10 (4.0)	20 (34.5)	<0.001

CNS = central nervous system; Cr = creatinine; ESBL = extended-spectrum beta-lactamase; ICU = intensive care unit.

^a Data are presented as mean ± standard deviation or frequency with percentage (%).

^b These analyses were conducted by comparing patients treated in an ordinary ward with those admitted to the ICU.

K. pneumoniae bacteremia have been reported. To our knowledge, this is the first retrospective study to focus on patients with community-onset *K. pneumoniae* bacteremia requiring intensive care. We found that the ICU admission rate of patients with *K. pneumoniae* bacteremia was 18.8% and mortality rate was 34.5%. The prevalence of respiratory tract infection was significantly higher in patients admitted to the ICU than those in ordinary wards. Respiratory tract infection was also the independent risk factor for patients admitted to the ICU, possibly reflecting the fulminant course of bacteremic pneumonia caused by *K. pneumoniae*, as shown in our previous study.⁵

Consistent with previous reports regarding bacteremia in the ICU, we also found that the APACHE II score was independently associated with mortality.^{9,19} In the present study, the mortality of *K. pneumoniae* bacteremia patients in the ICU was high. With much improvement of critical care in recent years, although patients with a high APACHE II score (mean = 23.45 ± 5.35) can survive, patients with

more severe disease (mean = 30.15 ± 6.11) still have difficulty surviving, suggesting that host factors are important for the prognosis of *K. pneumoniae* bacteremia.

Malignant neoplasm was another factor independently associated with mortality in the ICU in the current study. Our cohort had a higher proportion of malignant neoplasms than the previous study,¹² which might be due to the different study period. Although we did not find that malignancy predisposed to mortality in critically ill patients with community-onset bacteremia in the literature, the prevalence of malignant neoplasms in the current study might play an important role in the outcome of *K. pneumoniae* bacteremia. In the current study, most (80%) of the mortality in community-onset *K. pneumoniae* bacteremic patients requiring intensive care, was in cancer patients, which corresponded to the poor prognosis in cancer patients with nosocomial bacteremia due to *K. pneumoniae* in our previous study.²⁰ In addition, although we failed to demonstrate the prognostic significance of appropriate

Table 2 Risk factors for infection-related mortality in patients with community-onset *Klebsiella pneumoniae* bacteremia requiring intensive care^a

Clinical feature	Overall (n = 58)	Survivor (n = 38)	Mortality (n = 20)	p ^b
Age (y)	74.2 ± 13.8	73.6 ± 14.2	75.4 ± 13.4	0.648
Male	45 (77.6)	29 (76.3)	16 (80.0)	>0.999
APACHE II score	25.8 ± 6.4	23.5 ± 5.4	30.2 ± 6.1	<0.001
Healthcare-associated	30 (51.7)	14 (36.8)	16 (80) ^c	0.004
Underlying disease				
Diabetes mellitus	21 (36.2)	16 (42.1)	5 (25.0)	0.317
Liver cirrhosis	7 (12.1)	4 (10.5)	3 (15.0)	0.683
Chronic lung disease	18 (31.0)	14 (36.8)	4 (20.0)	0.308
Alcoholism ^d	7 (12.1)	6 (15.8)	1 (5.0)	0.403
Congestive heart failure	7 (12.1)	5 (13.2)	2 (10.0)	>0.999
Chronic kidney disease (Cr > 2 mg/dL)	8 (13.8)	5 (13.2)	3 (15.0)	0.345
CNS disease	16 (27.6)	12 (31.6)	4 (20.0)	0.530
Autoimmune disease	2 (3.4)	2 (5.3)	0 (0)	0.540
Malignant neoplasm	23 (39.7)	7 (18.4)	16 (80.0)	<0.001
Initial presentation				
Shock	44 (75.9)	27 (71.1)	17 (85.0)	0.338
Respiratory failure	39 (67.2)	21 (55.3)	18 (90.0)	0.017
Altered mental status	29 (50.0)	14 (36.8)	15 (75)	0.013
Onset of symptoms in days	2.8 ± 2.9	3.2 ± 3.4	2.1 ± 1.5	0.070
WBC count (10 ⁹ /L)	15.1 ± 13.0	17.6 ± 13.9	10.2 ± 9.9	0.038
Platelet count (10 ⁹ /L)	135 ± 99	139 ± 102	118 ± 85	0.649
C-reactive protein (mg/dL)	19.0 ± 9.8	19.6 ± 10.2	16.0 ± 7.1	0.187
Infectious focus				
Meningitis	1 (1.7)	1 (2.6)	0 (0)	>0.999
Respiratory tract infection	28 (48.3)	17 (44.7)	11 (55.0)	0.640
Liver abscess	8 (13.8)	8 (21.1)	0 (0)	0.041
Biliary tract infection	6 (10.3)	4 (10.5)	2 (10.0)	>0.999
Intraabdominal infection	2 (3.4)	1 (2.6)	1 (5.0)	>0.999
Urinary tract infection	11 (19.0)	10 (26.3)	1 (5.0)	0.077
Skin and soft tissue infection	3 (5.2)	1 (2.6)	2 (10.0)	0.271
Primary	6 (10.3)	3 (7.9)	3 (15.0)	0.405
Polymicrobial	8 (13.8)	6 (15.8)	2 (10.0)	0.701
ESBL strain	4 (6.9)	3 (7.9)	1 (5.0)	>0.999
Inappropriate antibiotic use	4 (6.9)	2 (5.3)	2 (10.0)	0.602

APACHE = Acute Physiology and Chronic Health Evaluation; CNS = central nervous system; ESBL = extended-spectrum beta-lactamase; WBC = white blood cell.

^a Data are presented as mean ± standard deviation or frequency with percentage (%).

^b These analyses were conducted comparing the survivor and mortality group.

^c 13 patients had an underlying malignant neoplasm (81.3%).

^d Cases with alcoholism include 1 of UTI, 1 of peritonitis, 1 of pneumonia, and 4 of liver abscess. The case of peritonitis fulfilled the definition of infection-related mortality.

Table 3 Independent risk factors associated with infection-related mortality in the ICU due to community-onset *K. pneumoniae* bacteremia

Factors	Odds ratio (95% CI)	p
APACHE II score	1.43 (1.12–2.01)	0.041
Healthcare-associated	7.79 (0.65–93.72)	0.106
Malignant neoplasm	35.48 (2.54–495.57)	0.008
Respiratory failure	11.75 (0.28–495.85)	0.197
Altered mental status	1.21 (0.06–241.76)	0.902
WBC count (10 ⁹ /L)	1.00 (1.00–1.00)	0.063

APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; WBC = white blood cell.

empiric antibiotics in ICU patients, we do not exclude the possibility that the relatively small sample size lacked statistical power to differentiate among the impact of different antibiotics on survival.

DM is a well-known risk factor for *K. pneumoniae* infection. DM accounted for 49% among the patients of community-acquired *K. pneumoniae* bacteremia in a previous study.¹² In our study, DM was the most common underlying disease (39.2%) among all community-onset bacteremia. However, diabetes did not predispose patients to requiring ICU admission or influence their mortality. Whether diabetes has been associated with a worse prognosis with Enterobacteriaceae bacteremia is controversial.^{21,22} Information about the effect of diabetes on the prognosis

Table 4 Risk factors for 1-year mortality in the ICU due to community-onset *K. pneumoniae* bacteremia

Factor	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>p</i>	Adjusted HR	95% CI	<i>p</i>
Healthcare-associated infection	2.54	1.25–5.16	0.010	1.24	0.55–2.78	0.610
APACHE II score	1.12	1.06–1.19	<0.001	1.06	0.997–1.129	0.063
Malignant neoplasm	3.52	1.76–7.05	<0.001	3.14	1.36–7.26	0.007
Respiratory failure	2.49	1.12–5.54	0.025	1.84	0.73–4.60	0.196
Altered mental status	3.40	1.64–7.05	0.001	1.74	0.71–4.29	0.230
Inappropriate antibiotic use	3.02	1.04–8.74	0.042	2.25	0.64–7.94	0.206

APACHE = Acute Physiology and Chronic Health Evaluation; CI = confidence interval; HR = hazard ratio.

of patients with bacteremia in general, and with *K. pneumoniae* bacteremia in particular, is limited. More research is needed to delineate relations between diabetes and *K. pneumoniae* bacteremia. Jong et al found that 11 alcoholic patients with bacteremic *K. pneumoniae* pneumonia, who needed ICU management, had a rapid fatal outcome.¹⁴ In our study, only one of the seven alcoholic cases died of infection. The different focus of bacteremia between the current study and the previous one might account for the different results.

K. pneumoniae is the most commonly isolated microorganism in liver abscesses in Taiwan.² It has a potential metastatic infection and can result in endophthalmitis or central nervous system infection.^{23,24} In a study by Chen et al, the overall mortality of patients with a liver abscess caused by *K. pneumoniae*, requiring intensive care, was 23%.²⁵ In the present study, bacteremic liver abscess was not associated with a higher prevalence of ICU admission and the outcome of bacteremic liver abscess in the ICU was favorable. We could not compare the APACHE II score between the two studies, which might account for the different outcome. Management of liver abscesses has

recently improved in Taiwan because of increased physician awareness; different study periods may be another reason for the discordance.²⁶

BSI-associated sepsis and septic shock are associated with an increased risk of mortality persisting after 28 days to >1 year.¹¹ While much of the mortality attributable to bloodstream infection occurs acutely within days to weeks after onset, organ dysfunction and other complications may lead to significant mortality months or years later.²⁷ Long-term follow-up better defines the burden of illness associated with these syndromes. Herein, we present the first study of *K. pneumoniae* bacteremia in critically ill adults which evaluates the long-term (1-year) outcomes associated with these conditions. Less than 50% patients survived beyond 1 year after *K. pneumoniae* bacteremia, and malignant neoplasm was the only independent predictor of long-term mortality, suggesting that long-term mortality is more a question of underlying conditions, than of bacteremia per se. Although it is important to note that the late deaths were not directly attributable to the original bloodstream infection, our data support the notion that future studies should include longer-term endpoints, so as to better understand the natural history of sepsis and the effects of interventions on morbidity.²⁷

In conclusion, approximately one-fifth of patients with community-onset *K. pneumoniae* bacteremia required intensive care in our institution throughout the study period. Respiratory tract infection was the only independent risk factor for ICU admission. Mortality among patients admitted to the ICU was high (34.5%), and a higher APACHE II score and underlying malignant neoplasm were independent risk factors for infection-related mortality. Overall, 1-year mortality in these patients admitted to the ICU was 58.6%. Physicians should recognize the distinct characteristics and risk factors for mortality among these patients.

Acknowledgments

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References

1. Meatherall BL, Gregson D, Ross T, Pitout JD, Laupland KB. Incidence, risk factors, and outcomes of *Klebsiella pneumoniae* bacteremia. *Am J Med* 2009;122:866–73.

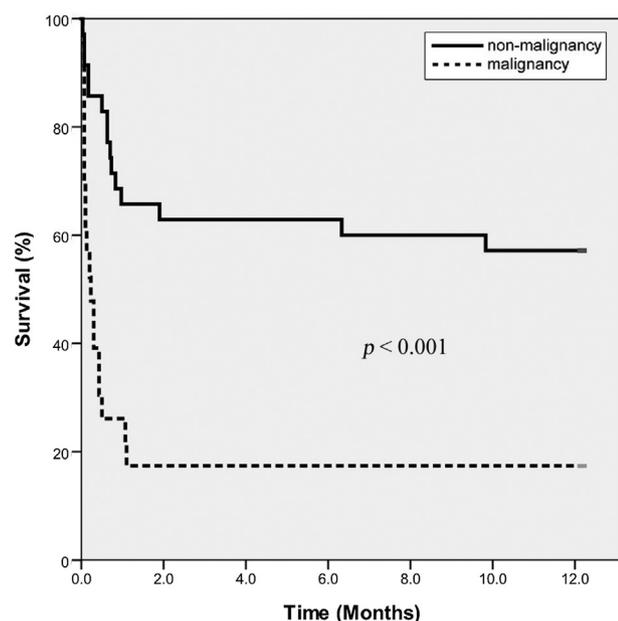


Figure 1. Comparison of Kaplan–Meier survival curves, at 1 year, between patients requiring intensive care with underlying malignancy and those without malignancy ($p < 0.001$, by log-rank test).

2. Ko WC, Paterson DL, Sagnimeni AJ, Hansen DS, Von Gottberg A, Mohapatra S, et al. Community-acquired *Klebsiella pneumoniae* bacteremia: global differences in clinical patterns. *Emerg Infect Dis* 2002;8:160–6.
3. Wu HS, Wang FD, Tseng CP, Wu TH, Lin YT, Fung CP. Characteristics of healthcare-associated and community-acquired *Klebsiella pneumoniae* bacteremia in Taiwan. *J Infect* 2012;64:162–8.
4. Lin YT, Chen TL, Siu LK, Hsu SF, Fung CP. Clinical and microbiological characteristics of community-acquired thoracic empyema or complicated parapneumonic effusion caused by *Klebsiella pneumoniae* in Taiwan. *Eur J Clin Microbiol Infect Dis* 2010;8:1003–10.
5. Lin YT, Jeng YY, Chen TL, Fung CP. Bacteremic community-acquired pneumonia due to *Klebsiella pneumoniae*: clinical and microbiological characteristics in Taiwan, 2001 ~ 2008. *BMC Infect Dis* 2010;10:307.
6. Laupland KB, Gregson DB, Flemons WW, Hawkins D, Ross T, Church DL. Burden of community-onset bloodstream infection: a population-based assessment. *Epidemiol Infect* 2007;135:1037–42.
7. Pien BC, Sundaram P, Raoof N, Costa SF, Mirrett S, Woods CW, et al. The clinical and prognostic importance of positive blood cultures in adults. *Am J Med* 2010;123:819–28.
8. Vallés J, Ferrer R. Bloodstream infection in the ICU. *Infect Dis Clin North Am* 2009;23:557–69.
9. Vallés J, Rello J, Ochagavía A, Garnacho J, Alcalá MA. Community-acquired bloodstream infection in critically ill adult patients: impact of shock and inappropriate antibiotic therapy on survival. *Chest* 2003;123:1615–24.
10. Suffredini AF, Munford RS. Novel therapies for septic shock over the past 4 decades. *JAMA* 2011;306:194–9.
11. Laupland KB, Zygun DA, Doig CJ, Bagshaw SM, Svenson LW, Fick GH. One-year mortality of bloodstream infection-associated sepsis and septic shock among patients presenting to a regional critical care system. *Intensive Care Med* 2005;2:213–9.
12. Tsay RW, Siu LK, Fung CP, Chang FY. Characteristics of bacteremia between community-acquired and nosocomial *Klebsiella pneumoniae* infection: risk factor for mortality and the impact of capsular serotypes as a herald for community-acquired infection. *Arch Intern Med* 2002;162:1021–7.
13. Kang CI, Kim SH, Bang JW, Kim HB, Kim NJ, Kim EC, et al. Community-acquired versus nosocomial *Klebsiella pneumoniae* bacteremia: clinical features, treatment outcomes, and clinical implication of antimicrobial resistance. *J Korean Med Sci* 2008;21:816–22.
14. Jong GM, Hsiue TR, Chen CR, Chang HY, Chen CW. Rapidly fatal outcome of bacteremic *Klebsiella pneumoniae* pneumonia in alcoholics. *Chest* 1995;107:214–7.
15. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definition for nosocomial infection, 1988. *Am J Infect Control* 1988;16:128–40.
16. Friedman ND, Kaye KS, Stout JE, McGarry SA, Trivette SL, Briggs JP, et al. Health care-associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. *Ann Intern Med* 2002;137:791–7.
17. Clinical and Laboratory Standard Institute. *Performance standards for antimicrobial susceptibility testing: 17th informational supplement*. CLSI document M100~S17. Wayne, PA: CLSI; 2007.
18. Blot SI, Vandewoude KH, Colardyn FA. Clinical impact of nosocomial *Klebsiella* bacteremia in critically ill patients. *Eur J Clin Microbiol Infect Dis* 2002;21:471–3.
19. Vallés J, Alvarez-Lerma F, Palomar M, Blanco A, Escoreca A, Armestar F, et al. Health-care-associated bloodstream infections at admission to the ICU. *Chest* 2011;139:810–5.
20. Lin YT, Liu CJ, Fung CP, Tzeng CH. Nosocomial *Klebsiella pneumoniae* bacteremia in adult cancer patients-characteristics of neutropenic and non-neutropenic patients. *Scand J Infect Dis* 2011;43:603–8.
21. Thomsen RW, Hundborg HH, Lervang HH, Johnsen SP, Schonheyder HC, Sorensen HT. Diabetes mellitus as a risk and prognostic factor for community-acquired bacteremia due to enterobacteria: a 10-year, population-based study among adults. *Clin Infect Dis* 2005;40:628–31.
22. Peralta G, Sanchez MB, Roiz MP, Garrido JC, Teira R, Mateo F. Diabetes does not affect outcome in patients with Enterobacteriaceae bacteremia. *BMC Infect Dis* 2009;9:94.
23. Fang CT, Lai SY, Yi WC, Hsueh PR, Liu KL, Chang SC. *Klebsiella pneumoniae* genotype K1: an emerging pathogen that causes septic ocular or central nervous system complications from pyogenic liver abscess. *Clin Infect Dis* 2007;45:284–93.
24. Chung DR, Lee SS, Lee HR, Kim HB, Choi HJ, Eom JS, et al. Emerging invasive liver abscess caused by K1 serotype *Klebsiella pneumoniae* in Korea. *J Infect* 2007;54:578–83.
25. Chen W, Chen CH, Chiu KL, Lai HC, Liao KF, Ho YJ, et al. Clinical outcome and prognostic factors of patients with pyogenic liver abscess requiring intensive care. *Crit Care Med* 2008;36:1184–8.
26. Tsai FC, Huang YT, Chang LY, Wang JT. Pyogenic liver abscess as endemic disease, Taiwan. *Emerg Infect Dis* 2008;14:1592–600.
27. Laupland KB, Svenson LW, Gregson DB, Church DL. Long-term mortality associated with community-onset bloodstream infection. *Infection* 2011;39:405–10.