#### ORIGINAL RESEARCH

# Prediction of 30-Day Mortality Using the Quick Pitt Bacteremia Score in Hospitalized Patients with *Klebsiella pneumoniae* Infection

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**Purpose:** *Klebsiella pneumoniae* is an important causative pathogen of nosocomial infections, resulting in poor prognosis owing to its hypervirulence and antibiotic resistance. A simplified quicker version of the Pitt bacteremia score (PBS) (qPitt) for acute illness severity measurement was developed recently. The goal of this study was to explore the prognostic value of qPitt in patients with *K. pneumoniae* infection.

**Patients and Methods:** Demographic information and management strategies were retrospectively collected from the records of all adult patients who visited the emergency department between January 1, 2021, and December 31, 2021, with culture-positive *K. pneumoniae*. The qPitt score was calculated based on: temperature  $<36^{\circ}$ C, systolic blood pressure  $\leq90$  mmHg or vasopressor administration, respiratory rate  $\geq25$  times/min or need of mechanical ventilation, altered mental status, and cardiac arrest event. The 30-day mortality prediction abilities of the qPitt were compared with the PBS, the sequential organ failure assessment (SOFA), and the quick sequential organ failure assessment (qSOFA) using receiver operating characteristic curves.

**Results:** Data from 867 patients (57.8% men) with a mean age of 66.9 were compiled. The 30-day mortality rate of the enrolled patients was 13.4%, and the area under the curve (AUC) of the scoring systems were as follows: SOFA, 0.91 (95% confidence interval [CI]=0.89–0.93), qPitt, 0.87 (95% CI=0.84–0.89), PBS, 0.87 (95% CI=0.85–0.89), and qSOFA, 0.73 (95% CI=0.70–0.76). The AUC of qPitt was significantly higher than that of qSOFA (p<0.01) and similar to that of PBS (p=0.65).The qPitt also demonstrated excellent mortality discrimination ability in non-bacteremic patients, AUC= 0.85 (95% CI=0.82–0.88).

**Conclusion:** The qPitt revealed excellent 30-day mortality prediction ability and also predicted mortality in non-bacteremic patients with *K. pneumoniae* infection. Clinicians can use this simplified scoring system to stratify patients earlier and initiate prompt treatment in high-risk patients.

Keywords: Klebsiella pneumoniae, organ dysfunction scores, bacteremia, prognosis

#### Introduction

*Klebsiella pneumoniae* is a gram-negative, encapsulated bacterium that usually colonizes the human gastrointestinal tract mucosal surface, but may cause extraintestinal opportunistic infections in the urinary tract, lung, brain, or bloodstream, especially in immunocompromised status.<sup>1,2</sup> *K. pneumoniae* is an important causative pathogen in approximately 10% of nosocomial infections, resulting in poor prognosis owing to its hypervirulence and antibiotic resistance.<sup>3,4</sup> It has been estimated that the mortality rate of patients with *K. pneumoniae* infection ranged from 5–30% and up to 29–54% in those with bloodstream infection.<sup>5–7</sup> The World Health Organization recently included *K. pneumoniae* in list of critical microorganisms, which pose a significant threat and major burden to global public health.<sup>2</sup>

The Pitt bacteremia score (PBS) has been a widely used scoring system for disease severity stratification in patients with bacteremia for decades and has recently been validated for its prognostic role in patients with nonbacteremic infections.<sup>8–10</sup> Recently, a simplified quicker version of the PBS (qPitt) using binary variables for acute illness severity measurement was developed, including body temperature, blood pressure, respiratory rate, cardiac arrest event, and mental status.<sup>11</sup> qPitt was investigated as an outcome prediction tool in patients with *Staphylococcus aureus* bloodstream infection,<sup>12</sup> and bloodstream infection secondary to urinary tract infection in recent studies.<sup>13</sup> Both studies revealed that qPitt has excellent mortality discrimination ability in these patients.<sup>12,13</sup> As PBS was originally derived from patients with gram-negative bloodstream infection,<sup>14</sup> and qPitt has not been validated in patients with single causative gram-negative pathogen, the goal of this study was to explore the prognostic value of qPitt in patients with nonbacteremic infection. Furthermore, we tested the mortality discrimination ability of qPitt in subgroups of patients with nonbacteremic infections.

## **Materials and Methods**

#### Study Design and Patient Enrollment

This retrospective observational cohort study was conducted at a tertiary medical center located in Kaohsiung, Taiwan. There are approximately 1100 licensed bed and 53,000 emergency department (ED) visits annually. The institutional review board waived the requirement for informed consent because of the retrospective and observational nature of the study. The study followed the principles of the Declaration of Helsinki and STROBE guidelines.

#### Inclusion Criteria

We enrolled all adult patients (aged  $\geq 18$  years) who visited the ED between January 1, 2021, and December 31, 2021, and underwent blood or other site-specific cultures which yield *K. pneumoniae* in this study. If a patient had multiple ED visits during the study period, only the first visit was included.

#### **Exclusion** Criteria

To avoid selection bias and heterogeneity, we excluded patients with bloodstream infection from site-specific infection at another body site (ie, secondary bloodstream infection).<sup>15</sup> We also excluded non-hospitalized patients and those with unrelated diagnoses (the cultured bacteria was not related to the cause of patient's infection. eg, the urine specimen yield *K. pneumoniae* but the principal diagnosis was biliary tract infection not yield *K. pneumoniae*).

## Data Collection and Study Definitions

All eligible patients and their relevant data, including demographic, clinical, microbiological information and management strategies, were collected from an anonymized electronic medical record system. The patients were divided into survivor and non-survivor groups according to their 30-day survival status for further comparison and analysis. The systemic inflammatory response syndrome (SIRS), quick sequential organ failure assessment (qSOFA), and sequential organ failure assessment (SOFA) scores were calculated based on their original definition using the initial ED physiological and laboratory parameters.<sup>16</sup> A qSOFA score  $\geq 2$  points was used as the prognostic cutoff value.<sup>17</sup> The PBS, ranging from 0 to 14, was obtained based on the following five variables: temperature, altered mental status, blood pressure, need for mechanical ventilation, and cardiac arrest event.<sup>8</sup> The qPitt score was calculated based on five scoring items: temperature <36°C, systolic blood pressure <90 mmHg or vasopressor administration, respiratory rate >25 times/ min or need of mechanical ventilation, altered mental status, and cardiac arrest event.<sup>11</sup> Each variable was assigned one point, with a maximum score of 5. The sources of K. pneumoniae infection was stratified as primary bacteremia, urinary tract infection, respiratory tract infection, intra-abdominal infection, skin/soft tissue infection, and others (minor infection sites, such as catheter-related infection).<sup>15</sup> The administered antibiotic was considered appropriate if it was active in vitro against the cultured K. pneumoniae (eg, blood, urine, sputum, or bronchoalveolar lavage) by susceptibility testing. The implementation of source control (measures to eliminate the source of infection) was determined by the treating physician's judgement and recorded according to medical records.

The primary outcome of this study was to compare the 30-day mortality prediction ability of qPitt and other commonly used sepsis severity scoring systems, including qSOFA, SOFA, and PBS, in patients with *K. pneumoniae* infection. The secondary outcome was the mortality discrimination ability of qPitt in nonbacteremic patients. Quantitative variables were expressed as mean  $\pm$  standard deviation or median (interquartile range) and were compared using a two-sample *t*-test or Mann–Whitney *U*-test, depending on whether they were normally distributed. Qualitative variables were expressed as percentages and compared using the Chi-square or Fisher's exact test. The mortality discriminative ability of qPitt and other scoring systems was tested using the area under the receiver operating characteristic (ROC) curve. The DeLong method was used to compare the area under the curve (AUC) of these variables.<sup>18</sup> The significance level for statistical testing was defined as two-tailed *p* < 0.05. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, IL, USA), version 25.0, and MedCalc Statistical Software version 18.2.1 (MedCalc Software by, Ostend, Belgium). Figures were drafted using GraphPad Prism version 8.4.3 (GraphPad Software, CA, USA).

## Results

Initially, 1569 patients with *K. pneumoniae* infection met the inclusion criteria. After excluding repetitive patients (N = 88), non-hospitalization (N = 378), secondary bacteremia (N = 90), and unrelated diagnoses (N = 146), the remaining 867 patients were included in the final analysis (Figure 1).

As shown in Table 1, the total 30-day mortality rate of the enrolled patients was 13.4% (116/867). The mean age of the patients was  $66.9\pm15.8$  years, and more than half (57.8%) were male patients. Compared with survivor group, patients in the non-survivor group had significantly higher proportion of chronic liver disease (12.9% vs 5.6%, *p*<0.01),



 $\label{eq:Figure I} \mbox{Figure I Flowchart of patient enrollment.}$ 

Variables	All (n=867)	Survivor (n=751)	Non-Survivor (n=116)	p value
Age, y, mean±SD	66.9±15.8	66.6±15.7	68.1±15.6	0.07
Male, n (%)	501 (57.8)	426 (56.7)	75 (64.7)	0.11
Comorbidities, n (%)				
Diabetes mellitus	405 (46.7)	350 (46.6)	55 (47.4)	0.88
Hypertension	498 (57.4)	432 (57.5)	66 (56.9)	0.89
Chronic liver disease	57 (6.6)	42 (5.6)	15 (12.9)	<0.01*
Chronic kidney disease	288 (33.2)	230 (30.6)	58 (50.0)	<0.01*
Malignancy	213 (24.6)	170 (22.6)	43 (37.1)	<0.01*
Cerebrovascular accident	144 (16.6)	123 (16.4)	21 (18.1)	0.69
Obstructive lung disease	61 (7.0)	48 (6.4)	3 (  .2)	0.07
Congestive heart failure	61 (7.0)	51 (6.8)	10 (8.6)	0.44
Laboratory results, median (IQR)				
Hemoglobin, g/dL	11.6 (9.7–13.5)	11.8 (9.9–13.6)	10.3 (8.7–12.9)	<0.01*
Leukocyte, ×10 <sup>9</sup> /L	10.5 (7.3–14.8)	10.5 (7.5–14.7)	10.2 (6.1–15.2)	0.21
Platelet, ×10 <sup>9</sup> /L	212 (151–286)	218 (159–289)	158 (97–244)	<0.01*
International normalized ratio	1.08 (1.02–1.19)	1.07 (1.02–1.18)	1.24 (1.13–1.46)	<0.01*
Lactate, mmol/L	1.8 (1.2–3.3)	1.7 (1.1–2.7)	3.6 (2.1–7.6)	<0.01*
Bilirubin, mg/dL	1.0 (0.5–1.9)	0.9 (0.5–1.8)	1.2 (0.6–2.0)	0.07
C-reactive protein, mg/dL	69.3 (21.4–158)	64.4 (20–150.7)	108.5 (40-203.9)	<0.01*
Creatinine, mg/dL	1.0 (0.7–1.6)	0.7 (1.0–1.4)	1.7 (1.0–2.3)	<0.01*

 Table I Baseline Characteristics of Patients with Klebsiella pneumoniae Infection

Note: \*P<0.05.

Abbreviations: SD, standard deviation; IQR, interquartile range.

chronic kidney disease (50.0% vs 30.6%, p<0.01), and malignancy (37.1% vs 22.6%, p<0.01) comorbidities. The nonsurvivor group also had significantly lower hemoglobin (10.3 [8.7–12.9] g/dL vs 11.8 [9.9–13.6] g/dL, p<0.01) and platelet (158 [97–244] ×10<sup>9</sup>/L vs 218 [159–289] ×10<sup>9</sup>/L, p<0.01) level, longer international normalized ratio (1.24 [1.13– 1.46] vs 1.07 [1.02–1.18], p<0.01), higher lactate (3.6 [2.1–7.6] mmol/L vs 1.7 [1.1–2.7] mmol/L, p<0.01), c-reactive protein (108.5 [40–203.9] mg/dL vs 64.4 [20–150.7] mg/dL, p<0.01), and creatinine levels (1.7 [1.0–2.3] mg/dL vs 0.7 [1.0–1.4] mg/dL, p<0.01) than the survivor group (Table 1).

Regarding the sepsis severity scoring systems, it was not surprising that patients in the non-survivor group had a significantly higher proportion of SIRS criteria (81.9% vs 66.0%, p<0.01), high qSOFA category (39.7% vs 13.3%, p<0.01), and higher SOFA scores (9 [7–11] vs 2 [0–4], p<0.01). Furthermore, the non-survivor group had significantly higher PBS (5 [3–8] vs 0 [0–2], p<0.01) and qPitt (3 [2–3] vs 0 [0–1], p<0.01) scores than the survivor group (Table 2).

The most common infection source in the enrolled patients was the urinary tract (32.9%), followed by the bloodstream (26.0%) and skin/soft tissue (17.3%). Approximately three-fourths (71.7%) of the patients in this study received appropriate antibiotic administration (Table 2). The patients in the non-survivor group had a significantly higher proportion of bloodstream infections (33.6% vs 24.8%, p<0.01) and a lower proportion of urinary tract infections (19.0% vs 35.0%, p<0.01) than those in the survivor group. There were comparable proportion of appropriate antibiotic administration between the survivor and non-survivor groups (p=0.85).

The 30-day mortality prediction abilities of the scoring systems were compared. As shown in Figure 2, the AUC of each scoring system was as follows: SOFA, 0.91 (95% confidence interval [CI] = 0.89-0.93), qPitt, 0.87 (95% CI = 0.84-0.89), PBS, 0.87 (95% CI = 0.85-0.89), and qSOFA, 0.73 (95% CI = 0.70-0.76). Moreover, the AUC of qPitt was significantly higher than that of qSOFA (p<0.01) and similar to that of PBS (p=0.65).

We further examined the mortality discriminative performance of the qPitt score, which ranged from 0 to 5. As shown in Figure 3, the 30-day mortality rates in the qPitt group were 0.9% (4/422), 8.4% (16/191), 27.3% (38/139), 45.1% (37/82), 60.7% (17/28), and 80.0% (4/5), respectively. The mortality risk increased significantly in a stepwise manner as qPitt increased (p<0.01). Finally, we tested the ability of qPitt to predict mortality in nonbacteremic patients. As shown in

Variables	All (n=867)	Survivor (n=751)	Non-Survivor (n=116)	p value
SIRS, n (%)	591 (68.2)	496 (66.0)	95 (81.9)	<0.01*
qSOFA score ≥ 2, n (%)	146 (16.8)	100 (13.3)	46 (39.7)	<0.01*
PBS, median (IQR)	l (0–3)	0 (0–2)	5 (3–8)	<0.01*
qPitt, median (IQR)	I (0–2)	0 (0-1)	3 (2–3)	<0.01*
SOFA score, median (IQR)	2 (0–6)	2 (0-4)	9 (7–11)	<0.01*
Infection source, n (%)				
Bloodstream infection	225 (26.0)	186 (24.8)	39 (33.6)	<0.01*
Urinary tract infection	285 (32.9)	263 (35.0)	22 (19.0)	<0.01*
Respiratory tract infection	141 (16.3)	110 (14.6)	31 (26.7)	<0.01*
Intra-abdominal infection	48 (5.5)	39 (5.2)	9 (7.8)	0.62
Skin/soft tissue infection	150 (17.3)	140 (18.6)	10 (8.6)	0.01*
Other	18 (2.1)	13 (1.7)	5 (4.3)	0.49
Appropriate antibiotics, n (%)	622 (71.7)	538 (71.6)	84 (72.4)	0.85
Source control, n (%)	3  ( 5. )	120 (16.0)	(9.5)	0.01*

 Table 2 Sepsis Severity, Source and Management of Patients with Klebsiella pneumoniae

 Infection

Note: \*P<0.05.

**Abbreviations:** SIRS, systemic inflammatory response syndrome; qSOFA, quick sepsis-related organ failure assessment; PBS, Pitt bacteremia score; IQR, interquartile range; qPitt, quick Pitt bacteremia score; SOFA, sepsis-related organ failure assessment.

Figure 4, qPitt also demonstrated excellent mortality discrimination ability in these patients (AUC= 0.85, 95% CI = 0.82-0.88, p<0.001).

#### Discussion

In this single-center, ED-based, retrospective observational study, we evaluated the predictive performance of qPitt for the 30-day mortality risk of patients with *K. pneumoniae* infection and compared it with other widely used scoring systems, including SOFA, PBS, and qSOFA. We demonstrated that qPitt had a mortality discriminative ability



Figure 2 The AUC of each scoring system.



Figure 3 30-day mortality rates in the qPitt score groups.



Figure 4 The ability of the qPitt to predict mortality in patients without bacteremia.

comparable to that of PBS and was superior to that of the qSOFA score. Furthermore, we revealed that qPitt has an excellent mortality prediction ability in nonbacteremic patients with *K. pneumoniae* infection. To the best of our knowledge, this is the first study to investigate the prognostic role of qPitt in patients with a single causative gramnegative pathogen, including both bloodstream and non-bloodstream infections.<sup>11–13,19</sup>

Susceptibility to *K. pneumoniae* infection is determined by various factors, including pathogen virulence, host defense, and extrinsic stress.<sup>1–3</sup> It was studied that individuals with advanced age or other chronic illness, such as diabetes, malignancy, liver disease, chronic obstructive lung disease, renal failure, or malnutrition, are more vulnerable to *K. pneumoniae* infections and have a poorer prognosis.<sup>1,3</sup> In patients with *K. pneumoniae* bloodstream infection, anemia, thrombocytopenia, coagulation disorders, renal failure, hypoalbuminemia, elevated c-reactive protein levels, and hyperlactatemia have been reported to be associated with mortality risk.<sup>20–22</sup> The comorbidities and laboratory results of the

non-survivors in our study were consistent with these findings, further strengthening their prognostic significance in patients with *K. pneumoniae* infections.

The proportion of infection source distribution in our patient groups was also consistent with previous studies.<sup>5</sup> Patients have bloodstream infections due to their chronic illness and are prone to undergo surgical procedures, immunosuppressant agents, and invasive devices, all of which contribute to their poor physical condition and higher mortality risk.<sup>3,5</sup> In contrast, the urinary tract is a relatively minor infection site, which may slightly influence the patient's condition, thus providing a better survival chance.<sup>5</sup> The escalating prevalence of multidrug-resistant bacteria is another global issue, and was estimated to account for one-third of all *K. pneumoniae* pathogens in a recent meta-analysis.<sup>4</sup> Fortunately, the relatively low mortality rate of bloodstream infections in our study may be attributed to the low prevalence of antibiotics resistance (ie, a high proportion of appropriate antibiotics administration).

The SOFA score was developed to quantitatively describe the degree of organ dysfunction/failure and complications of critical illness in individuals or groups of patients and is one of the most widely used scoring systems in adult intensive care settings, including sepsis.<sup>23</sup> Although the SOFA score was originally designed to evaluate the extent of organ dysfunction rather than outcome prediction, it has been well validated as a good prognostic discrimination tool in patients with infectious disease.<sup>16,24,25</sup> Therefore, it is reasonable that the SOFA score had the highest prognostic accuracy in our study. Nevertheless, the need for laboratory parameter measurements and a slightly complex calculation process sometimes makes the SOFA score not readily available for risk stratification of these patients.<sup>25</sup> Moreover, the iatrogenic confounders, inter-patient variability, and the introduction of new intervention strategies all possibly promote the need for SOFA score update.<sup>23,25</sup>

PBS has been used for three decades to stratify acute illness severity and predict mortality in various patient populations with bloodstream infections.<sup>14,26,27</sup> Similar to PBS, qPitt is a more simplified scoring system consisting of five binary variables that retain hypothermia but exclude fever from PBS.<sup>11</sup> Hypothermia is deemed a late phase of acute illness and a more severe stage of endotoxic shock in animal experimental studies; thus, it is more strongly correlated with mortality in patients with infectious diseases.<sup>28,29</sup> Another advantage of qPitt variables is the respiratory rate, which is based on the number of breaths/min rather than the oxygen concentration, and the need for mechanical ventilation may allow earlier detection of respiratory failure in these patients.<sup>12</sup> The comparable mortality prediction ability of PBS and qPitt in our study strengthens the value of outcome prediction. Larger prospective studies are required to validate these findings.

Both the qPitt and qSOFA scores were developed to identify high-risk patients based solely based on vital signs and other readily available clinical variables during an initial physical examination, and the absence of laboratory parameters allows making clinical decision more quickly.<sup>12,14</sup> Although they share some similar parameters, the slightly higher threshold in respiratory rate and systolic blood pressure parameters in qPitt may improve its specificity and positive predictive value without the expense of sensitivity or negative predictive value.<sup>11</sup> Notably, qPitt outperformed qSOFA in mortality prediction in patients with *Staphylococcus aureus* bloodstream infection in a previous study, whereas another study in patients with urinary tract infection revealed converse results.<sup>12,19</sup> The significantly superior prognostic value of qPitt in our study encourage future studies to compare both scoring systems in other cohorts, further extending the application potential of qPitt to a wide variety of infections.

Another novel finding of our study is that qPitt predicted mortality in nonbacteremic patients with *K. pneumoniae* infection, as well as in those with bacteremia. A recent multicenter prospective study investigated the prognostic role of qPitt in patients with nonbacteremic carbapenem-resistant *Enterobacteriaceae* infections and demonstrated the strong mortality prediction ability of qPitt in these patients.<sup>10</sup> These findings may allow the broader use of this simple score for risk stratification in clinical infectious diseases, even prior to the identification of the microbiological profile or site of infection.<sup>10,12</sup>

The main strength of this study was the inclusion of all patients with *K. pneumoniae* infection, regardless of the infection site, which is more practical for clinical applications. The exclusion of patients with secondary bloodstream infections also avoided misclassification of these patients. Nevertheless, this study also shares the common limitations of a retrospective observational cohort design, which is mostly subject to inherent recall bias. Although we thoroughly reviewed the electronic medical records to obtain detailed information on our enrolled patients, some unknown and

unmeasured confounders may still bias the results. Other important elements of sepsis management, including the amount of fluid or vasopressors administered to patients, were not calculated or controlled in this study. The single-center nature of this study warrants future multicenter prospective studies to validate our findings.

## Conclusion

In conclusion, in patients with *K. pneumoniae* infection, qPitt revealed excellent 30-day mortality prediction ability, similar to PBS, and outperformed the qSOFA score. The qPitt also exhibited mortality discrimination ability in nonbacteremic patients with *K. pneumoniae* infections. Clinicians can use this simplified scoring system to stratify patients earlier and initiate prompt treatment in high-risk patients.

#### Abbreviations

AUC, area under the curve; ED, emergency department; PBS, Pitt bacteremia score; qPitt, quick version of the PBS; qSOFA, quick sequential organ failure assessment; SIRS, systemic inflammatory response syndrome; SOFA, sequential organ failure assessment.

# **Ethic Approval and Informed Consent**

This study was approved by the ethics committee of the E-Da hospital (EMRP-111-081). All data were anonymized and obtained from electronic medical record systems to maintain participant's privacy. The ethics committee did not require written informed consent due to the retrospective nature of the study.

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## **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

# Disclosure

The authors report no conflicts of interest in this work.

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