Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Biomarkers augmented scoring systems to predict the mortality risk of adult patients with neutropenia bacteremia: A 10-year observational study in the emergency department

Yao-Tien Chang
Taichung Veterans General Hospital
Ming-Shun Hsieh
Taichung Veterans General Hospital
Sung-Yuan Hu
song9168@pie.com.tw

Taichung Veterans General Hospital
Chia-Hui Shen
Taichung Veterans General Hospital
Che-An Tsai
Taichung Veterans General Hospital
Shih-Che Huang
Chung Shan Medical University Hospital
Tzu-Chiang Chiang
Tunghai University

Research Article

Keywords: ANC (Absolute neutrophil count), Biomarkers, Lactate, Neutropenic bacteremia, RDW (Red blood cell distribution width), Scoring systems

Posted Date: June 18th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9638210/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background: Neutropenia (absolute neutrophil count [ANC] <1,500 cells/μL) greatly increases the risk of bacteremia. Documented mortality in neutropenic bacteremia (NB) exceeds 58%. The Mortality in Emergency Department Sepsis (MEDS) and Modified Early Warning Score (MEWS) predict outcomes in general sepsis but are not well validated in neutropenic cohorts.

Aim: This study aimed to use the MEDS and MEWS, along with added biomarkers, to predict outcomes in adult patients with NB.

Methodology: This study used a retrospective observational design. Researchers extracted serial comprehensive variables. They evaluated the original and biomarker-augmented MEDS and MEWS algorithms. The revised scores used red blood cell distribution width (RDW) (>16.5% gets 1 point, >17.5% gets 2), lactate (>45.2 mg/dL gets 1 point, >92.0 mg/dL gets 2), and ANC (<250/μL gets 1 point, <122/μL gets 2). Statistical analyses included the Chi–Square test, Fisher's exact test, the Mann–Whitney U, univariate and multivariate logistic regression. Researchers measured performance using an AUC-ROC, sensitivity, specificity, and predictive values.

Results: Among 606 enrolled patients, mortality was 58.9% (357/606). Non-survivors had higher rates of DNR orders (90.19% vs. 31.32%, $p < 0.001$), ICU admission (29.69% vs. 19.67%, $p = 0.007$), and septic shock (17.92% vs. 7.22%, $p < 0.001$). Non-survivors also showed pronounced laboratory abnormalities. These included lower hemoglobin (9.14 ± 2.47 g/dL vs. 9.80 ± 2.75, $p = 0.001$), platelets (77.73 ± 82.56 vs. 94.41 ± 75.75 ×10³/μL, $p < 0.001$), ANC (494.49 ± 457.64 vs. 656.39 ± 496.75 cells/μL, $p < 0.001$), and acidosis (pH 7.37 ± 0.11 vs. 7.41 ± 0.08, $p < 0.001$). They had higher RDW (16.73 ± 3.10% vs. 15.71 ± 3.21, $p <0.001$) and lactate (38.43 ± 30.94 vs. 26.20 ± 18.81 mg/dL, $p < 0.001$). Gram-negative pathogens were most common (75.41%). *Pseudomonas*spp. independently predicted mortality ($p= 0.045$). The original MEDS score showed the best mortality discrimination (an AUC-ROC of 0.755). The MEWS had a lower AUC-ROC of 0.588. Adding RDW, lactate, and ANC improved these scores. The MEDS-NB reached an AUC-ROC of 0.784. The MEWS-NB increased to an AUC-ROC of 0.652.

Conclusion: A 10-year analysis validated MEDS and MEWS as optimal prognostic tools for NB in the emergency department. By adding biomarkers, RDW, lactate, and ANC, significantly improved risk stratification. This provides a framework for optimizing evidence-based triage protocols for this high-mortality population with NB.

Introduction

Neutropenia is a blood disorder marked by an abnormally low absolute neutrophil count (ANC; a type of white blood cell important for fighting infections) [1, 2]. The generally accepted threshold for neutropenia is an ANC below 1,500 cells per microliter (μL) of blood [2, 3]. This deficiency makes affected individuals more prone to bacterial and fungal infections, especially bacteremia (presence of bacteria in the blood).

Neutropenia is classified by severity using ANC [2, 3]. Mild neutropenia has ANC between 1,000 and 1,500 cells/μL and carries a low infection risk. Moderate neutropenia has an ANC between 500 and 1,000 cells/μL. These patients have a moderate risk and may require outpatient care for fever, with hospitalization considered on an individual basis. Severe neutropenia is defined as an ANC below 500 cells/μL. These patients have a high risk and usually need hospitalization and antibiotics if febrile.

Neutropenia has many causes. Congenital neutropenia includes severe congenital neutropenia, a primary immunodeficiency from genetic mutations [3–5]. Acquired neutropenia includes forms caused by drugs, infections, autoimmune diseases, nutritional problems, or bone marrow disorders [4–8].

Febrile neutropenia (FN) is a serious complication, especially in chemotherapy for acute myeloid leukemia and other cancers. FN means an ANC below 1,000 cells/μL and fever (≥ 38.3°C) [9]. Patients with FN are at high risk for bacteremia and septic shock. They need urgent medical care.

Bacteremia is a major concern for neutropenic patients, especially those with central venous catheters (CVC) [10]. They are highly susceptible to both Gram-negative and Gram-positive pathogens. Common Gram-negative rods include *Escherichia coli* and *Pseudomonas aeruginosa. Common* Gram-positive organisms include *viridians* group *Streptococci* and coagulase-negative *Staphylococci* [10]. Early antibiotics such as teicoplanin and ciprofloxacin help reduce deaths and bacteremia episodes in FN [10].

Given the critical role of neutrophils (a type of white blood cell essential for immune defense) in immune defense, patients with FN (those with abnormally low neutrophil counts) who develop bacteremia are at risk of rapid clinical deterioration. Therefore, early diagnosis, timely administration of empiric antibiotic therapy, and appropriate supportive care are essential to improving clinical outcomes in patients with FN.

Several scoring systems use clinical data to help physicians quickly identify and categorize critically ill patients in the emergency department (ED) and intensive care units (ICU) [11–21]. We retrospectively analyzed clinical and laboratory data from 606 adult ED patients with neutropenic bacteremia (NB) over 10 years. Our main goal was to use the Mortality in Emergency Department Sepsis (MEDS) and Modified Early Warning Score (MEWS) to find risk factors and predict mortality in NB. We also sought to identify additional risk factors to improve the clinical utility and accuracy of these scoring systems in NB.

Methods

Data Collection and Definition

This study was approved by the Institutional Review Board of Taichung Veterans General Hospital (TCVGH) (No. CE23126B). We conducted a retrospective review of ED patients with neutropenic bacteremia confirmed by blood cultures. Data came from electronic medical records at TCVGH from January 2012 to December 2021.

This study included patients aged 18 and older. Neutropenia was defined as an ANC below 1,500 within the first 48 hours in the ED. We defined NB as a monomicrobial or polymicrobial bacteremia confirmed by blood cultures collected during this ED visit.

We gathered data on demographics, preexisting comorbid conditions, vital signs, laboratory findings, and microorganisms isolated from blood cultures. Throughout the patients' ED course, initial and serial vital signs were recorded from nursing notes. The primary outcome was defined as the overall mortality rate. Several studies have attributed higher mortality rates of NB to insufficient warnings by clinicians, potentially due to delayed or absent responses to antimicrobial therapy within the first 24 hours of admission [22–28]. To evaluate the mortality risk, we performed univariate and multivariate analyses. We also used the scoring systems to predict clinical outcomes and identified valuable laboratory predictors of mortality risk. Subsequently, we refined these scoring systems by incorporating additional scores to ameliorate their risk-predicting accuracy.

Scoring Systems

In this study, we used the following clinical scoring systems: the MEDS and MEWS scores. The MEDS comprised nine clinical parameters: age, residence in a nursing home, presence of terminal illness, respiratory distress, lower respiratory tract infection, septic shock, platelet count, band neutrophil proportion, and altered mental status. The MEWS included six parameters: body temperature (BT), heart rate (HR), systolic blood pressure (SBP), respiratory rate (RR), saturation of peripheral oxygen (SpO_2), and the level of consciousness (alert, verbal, painful, and unresponsive [AVPU]). We used both scoring systems to analyze clinical outcomes and the mortality risk. Indicators for the scoring systems are provided in Table S1 (Supplementary Materials).

Statistical Analysis

We described and compared the characteristics of survivors and non-survivors. Continuous data were presented as mean ± standard deviation (SD), while categorical variables were presented as counts and percentages. For univariate analysis, we used Chi–squared tests or Fisher’s exact test to compare categorical variables, and Mann–Whitney tests to compare continuous data on mortality risk between survivors and non-survivors. We conducted univariate and multivariate logistic regression analyses to assess potential predictors of mortality, reporting results as odds ratios (ORs) and confidence intervals (CIs). We performed Kaplan–Meier survival analysis to examine the differences between survivors and non-survivors. Additionally, we used the area under the curve (AUC) of a receiver operating characteristic (ROC) curve to compare different scoring systems in predicting the mortality of adult patients with NB. We used score cut-offs to stratify mortality risk by sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV). A p-value of < 0.05 was considered statistically significant. All analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS version 22.0; International Business Machines Corp., New York, NY, USA).

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Taichung Veterans General Hospital (IRB file code: CE23126B), with additional administrative clearance from participating hospitals. Informed consent was waived because the study involved retrospective review of routinely collected clinical records. All datasets were de-identified prior to analysis to protect patient confidentiality.

Results

Demographics and Clinical Characteristics of Adult Patients with Neutropenic Bacteremia

We reviewed cases of neutropenia (ANC below 1,500/μL) from the TCVGH ED and confirmed bacteremia through blood cultures between January 2012 and December 2021, spanning 10 years. A total of 606 cases were included in the study (Table 1), comprising 249 males (58.74%) and 250 females (41.25%). In total, 357 patients died, including 220 males (61.62%) and 137 females (38.37%). The average age of the patients was 62.85 ± 14.03 years. The majority of 281 patients fell within the 41–64 years age range, with other age distributions of 18–40 years (6.93%), 41–64 years (46.36%), 65–74 years (26.07%), and ≥ 75 years (20.62%). In total, 400 patients (66%) had a "Do Not Resuscitate" (DNR) order, and non-survivors (90.19%) had a significantly higher rate of DNR orders than survivors (31.32%), $p < 0.001$. 518 patients (85.40%) with malignancy under active treatment (chemotherapy and or radiotherapy) had the most common comorbidity. Regarding the vital signs of the overall cases, including SBP, diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, respiratory RR, BT, Glasgow coma scale (GCS), and SpO_2, the only significant differences were the HR and SpO_2 between the survivors and non-survivors. The average HR across all cases was 106.47 ± 21.4/min, in survivors (102.43 ± 20.71/min) and non-survivors (109.28 ± 21.52/min), $p < 0.001$. The average SpO2 was 96.66% ± 4.06%, in the survivors (96.44% ± 4.02%) and non-survivors (96.81% ± 4.08%), $p = 0.018$.

Table 1
Demographics and clinical characteristics of 606 adult patients with neutropenic bacteremia.

Characteristics	Total (*n* = 606)	Survivors (*n* = 249)	Non-survivors (*n* = 357)	*p*-Value
ICU admission	155(25.57%)	49(19.67%)	106(29.69%)	0.007**
DNR	400(66%)	78(31.32%)	322(90.19%)	< 0.001**
Sex				0.101
Male	356(58.74%)	136(54.61%)	220(61.62%)	
Female	250(41.25%)	113(45.38%)	137(38.37%)	
Age	62.85 ± 14.03	62.61 ± 14.76	63.02 ± 13.51	0.763
18–40	42(6.93%)	21(8.43%)	21(5.88%)	0.292
41–64	281(46.36%)	114(45.78%)	167(46.77%)	0.874
65–74	158(26.07%)	59(23.69%)	99(27.73%)	0.308
≥ 75	125(20.62%)	55(22.08%)	70(19.6%)	0.522
Vital signs				
SBP	110.56 ± 25.30	110.33 ± 23.51	110.72 ± 26.52	0.969
DBP	65.34 ± 16.31	64.45 ± 14.61	65.96 ± 17.39	0.329
MAP	80.41 ± 18.02	79.74 ± 16.22	80.88 ± 19.19	0.625
HR	106.47 ± 21.44	102.43 ± 20.71	109.28 ± 21.52	< 0.001**
RR	19.35 ± 3.26	18.95 ± 2.82	19.63 ± 3.50	0.087
BT	37.82 ± 1.13	37.92 ± 1.09	37.74 ± 1.16	0.114
GCS	14.73 ± 1.27	14.80 ± 1.11	14.68 ± 1.37	0.147
SpO2	96.66 ± 4.06	96.44 ± 4.02	96.81 ± 4.08	0.018*
BMI	23.36 ± 4.57	23.79 ± 5.05	23.04 ± 4.16	0.039*

Chi–Square test, Fisher's exact test, and Mann–Whitney U test. *$p < 0.05$, **$p < 0.01$, Statistically significant. Continuous data are expressed as mean ± SD. Categorical data are expressed as numbers and percentages. Abbreviations: BMI, Body mass index; BT, Body temperature; DBP, Diastolic blood pressure; DNR, Do not resuscitate; GCS, Glasgow coma scale; HR, Heart rate; ICU, intensive care unit; MAP, Mean arterial pressure; Oxygen saturation, SpO2; RR, Respiratory rate; and SBP, Systolic blood pressure.

Laboratory Data of Adult Patients with Neutropenic Bacteremia

We summarized the laboratory results in Table 2. The blood cell analysis of non-survivors showed statistically significantly lower values, including hemoglobin ($p = 0.001$), hematocrit ($p = 0.001$), platelet counts ($p < 0.001$), ANC ($p < 0.001$), and neutrophils ($p < 0.001$). Conversely, the lymphocyte count analysis of non-survivors revealed statistically significantly higher values ($p = 0.002$). Further analysis of neutrophil-lymphocyte count ratio (NLCR), platelet-to-lymphocyte ratio (PLR), and red blood cell distribution width (RDW) showed lower NLCR ($p < 0.001$) and PLR ($p < 0.001$) values in the non-survivors, while RDW was relatively higher in non-survivors ($p < 0.001$).

Table 2
Laboratory data of 606 adult patients with neutropenic bacteremia.

Laboratory data	Total (*n* = 606)	Survivors (*n* = 249)	Non-survivors (*n* = 357)	*p*-Value
Blood cell counts				
WBC	2368.33 ± 13506.01	1498.76 ± 3679.50	2974.85 ± 17310.96	0.169
Hct	25.64 ± 6.08	26.79 ± 6.26	24.82 ± 5.83	0.001**
Hgb	9.41 ± 2.61	9.80 ± 2.75	9.14 ± 2.47	0.001**
PLT	84.58 ± 80.19	94.41 ± 75.75	77.73 ± 82.56	< 0.001**
Band	4.37 ± 6.90	3.60 ± 4.61	4.92 ± 8.14	0.802
Neutrophil	57.47 ± 26.94	60.66 ± 25.88	54.68 ± 27.61	0.049*
Lymphocyte	38.49 ± 27.41	34.24 ± 25.57	41.45 ± 28.28	0.002**
NLCR	3.04 ± 5.22	3.73 ± 6.02	2.57 ± 4.54	< 0.001**
PLR	5.61 ± 11.47	6.80 ± 11.54	4.79 ± 11.36	< 0.001**
RDW	16.31 ± 3.18	15.71 ± 3.21	16.73 ± 3.10	< 0.001**
ANC	561.01 ± 480.36	656.39 ± 496.75	494.49 ± 457.64	< 0.001**
ANC < 500	321(52.97%)	112(44.97%)	209(58.54%)	0.001**
ANC 500–999	142(23.43%)	61(24.49%)	81(22.68%)	0.675
ANC 1000–5000	143(23.59%)	76(30.52%)	67(18.76%)	0.001**
Biochemistry				
Albumin	2.87 ± 0.62	3.01 ± 0.63	2.78 ± 0.59	< 0.001**
Total bilirubin	1.33 ± 2.25	1.09 ± 1.05	1.49 ± 2.76	0.093
Direct bilirubin	0.87 ± 1.65	0.57 ± 0.60	1.06 ± 2.02	0.002**
ALK-P	156.15 ± 160.18	125.82 ± 82.26	177.39 ± 194.58	0.015*
GPT	52.58 ± 78.02	54.57 ± 91.27	51.19 ± 67.39	0.664
LDH	388.05 ± 477.30	300.04 ± 221.15	446.84 ± 582.57	0.001**

Chi–Square test, Fisher's exact test, Mann–Whitney U test. *$p < 0.05$, **$p < 0.01$, Statistically significant. Continuous data are expressed as mean ± SD. Categorical data are expressed as numbers and percentages. Abbreviations: ALK-P, Alkaline phosphatase; ANC, Absolute neutrophil count; APTT, Activated partial prothrombin time; BUN, Blood urea nitrogen; CRP, C-reactive protein; Cr, Creatinine; GPT, Alanine Aminotransferase; Hct, hematocrit; Hgb, Hemoglobin; K, Potassium; LDH, Lactate dehydrogenase; NLCR, Neutrophil-lymphocyte count ratio; Na, Sodium; PLR, Platelet-to-lymphocyte ratio; PLT, Platelet; PT, Prothrombin time; RDW, red cell distribution width.

Laboratory data	Total (*n* = 606)	Survivors (*n* = 249)	Non-survivors (*n* = 357)	*p*-Value
BUN	33.17 ± 24.23	30.72 ± 22.49	34.90 ± 25.28	0.022*
Cr	1.79 ± 1.67	1.85 ± 1.92	1.76 ± 1.48	0.463
BUN/Cr	21.53 ± 10.32	20.31 ± 9.18	22.39 ± 10.98	0.028*
Na	133.31 ± 5.89	133.74 ± 5.61	133.01 ± 6.07	0.090
K	3.80 ± 0.74	3.71 ± 0.62	3.85 ± 0.80	0.036*
CRP	14.32 ± 11.40	12.30 ± 10.49	15.72 ± 11.81	< 0.001**
Lactate	33.75 ± 27.58	26.20 ± 18.81	38.43 ± 30.94	< 0.001**
Glucose	154.20 ± 87.98	152.41 ± 78.65	155.42 ± 93.91	0.797
Coagulation				
PT	12.87 ± 4.34	11.93 ± 1.94	13.44 ± 5.22	< 0.001**
APTT	34.22 ± 11.01	33.00 ± 12.85	34.98 ± 9.65	0.001**
Arterial blood gas				
pH	7.39 ± 0.10	7.41 ± 0.08	7.37 ± 0.11	< 0.001**
$PaCO_2$	35.93 ± 10.27	36.05 ± 8.94	35.87 ± 10.99	0.868
PaO_2	72.45 ± 60.98	68.27 ± 48.03	74.90 ± 67.40	0.749
HCO_3	21.18 ± 5.99	22.45 ± 5.43	20.43 ± 6.19	0.003**

Chi–Square test, Fisher's exact test, Mann–Whitney U test. *$p < 0.05$, **$p < 0.01$, Statistically significant. Continuous data are expressed as mean ± SD. Categorical data are expressed as numbers and percentages. Abbreviations: ALK-P, Alkaline phosphatase; ANC, Absolute neutrophil count; APTT, Activated partial prothrombin time; BUN, Blood urea nitrogen; CRP, C-reactive protein; Cr, Creatinine; GPT, Alanine Aminotransferase; Hct, hematocrit; Hgb, Hemoglobin; K, Potassium; LDH, Lactate dehydrogenase; NLCR, Neutrophil-lymphocyte count ratio; Na, Sodium; PLR, Platelet-to-lymphocyte ratio; PLT, Platelet; PT, Prothrombin time; RDW, red cell distribution width.

In the biochemistry of non-survivors, lower levels of albumin ($p < 0.001$) and bicarbonate ($HCO3^-$) ($p < 0.001$) were observed, along with more pronounced acidosis and lower pH ($p < 0.001$). There were significantly higher levels of several biomarkers in non-survivors, including direct bilirubin ($p = 0.002$), alkaline phosphatase (ALK-P) ($p = 0.015$), lactate dehydrogenase (LDH) ($p = 0.015$), blood urea nitrogen (BUN) ($p = 0.022$), potassium ($p = 0.036$), BUN/creatinine (Cr) ratio ($p = 0.028$), C-reactive protein (CRP) ($p < 0.001$), and lactate ($p < 0.001$). Additionally, prothrombin time (PT) ($p < 0.001$) and activated partial thromboplastin time (APTT) ($p < 0.001$) showed significant differences between survivors and non-survivors.

Microbiology and Comorbidities of Adult Patients with Neutropenic Bacteremia

There is no significant difference in the causative microbial pathogens between the survivors and non-survivors, including both Gram-positive and Gram-negative pathogens (Table 3). The majority of bacteremia cases were caused by a single pathogen (87.29%), while a small proportion involved multiple pathogens (12.71%). Among these, Gram-negative bacteria accounted for the majority (75.41%), while Gram-positive bacteria constituted 29.37%. The top three Gram-negative bacteria were *Escherichia* spp. (33.99%), *Klebsiella* spp. (18.31%), and *Pseudomonas* spp. (14.02%), followed by *Pseudomonas* spp. (14.02%). The most common Gram-positive bacteria were *Staphylococcus* spp. (14.52%). The clinical prognosis of neutropenia affected by comorbidity does not show significant differences between the survivors and non-survivors (Table 4).

Table 3
Microorganisms of 606 adult patients with neutropenic bacteremia.

Microbiology	**Total (*n* = 606)**	**Survivors (*n* = 249)**	**Non-survivors (*n* = 357)**	***p*-Value**
Gram positive	178(29.37%)	76(30.52%)	102(28.57%)	0.669
Staphylococcus spp.	88(14.52%)	44(17.67%)	44(12.32%)	0.085
Streptococcus spp.	49(8.08%)	16(6.42%)	33(9.24%)	0.271
Enterococcus spp.	13(2.14%)	4(1.6%)	9(2.52%)	0.632
Gram negative	457(75.41%)	182(73.09%)	275(77.03%)	0.312
Escherichia spp.	206(33.99%)	82(32.93%)	124(34.73%)	0.709
Klebsiella spp.	111(18.31%)	43(17.26%)	68(19.04%)	0.653
Pseudomonas spp.	85(14.02%)	26(10.44%)	59(16.52%)	0.045*
Salmonella spp.	13(2.14%)	8(3.21%)	5(1.4%)	0.219
Enterobacter spp.	14(2.31%)	7(2.81%)	7(1.96%)	0.681
Proteus spp.	9(1.48%)	3(1.2%)	6(1.68%)	0.892

Chi–Square test, Fisher's exact test, Mann–Whitney U test. *$p < 0.05$, Statistically significant. Continuous data are expressed as mean ± SD. Abbreviations: spp., species.

Table 4
Comorbidities of 606 adult patients with neutropenic bacteremia.

Comorbidities	Total (*n* = 606)	Survivors (*n* = 249)	Non-Survivors (*n* = 357)	*p*-Value
Cardiovascular disease	59(9.73%)	30(12.04%)	29(8.12%)	0.143
CVA	24(3.96%)	12(4.81%)	12(3.36%)	0.488
DM	130(21.45%)	53(21.28%)	77(21.56%)	1.000
Hypertension	294(48.51%)	127(51%)	167(46.77%)	0.347
Hyperlipidemia	115(18.97%)	55(22.08%)	60(16.8%)	0.127
Gout	53(8.74%)	24(9.63%)	29(8.12%)	0.615
COPD	72(11.88%)	33(13.25%)	39(10.92%)	0.457
Asthma	40(6.6%)	14(5.62%)	26(7.28%)	0.520
GI disease	231(38.11%)	92(36.94%)	139(38.93%)	0.681
CKD/Uremia	137(22.6%)	65(26.1%)	72(20.16%)	0.105
BPH	100(16.5%)	38(15.26%)	62(17.36%)	0.565
Transplant	10(1.65%)	6(2.4%)	4(1.12%)	0.331
Immune disorder	38(6.27%)	19(7.63%)	19(5.32%)	0.326
Malignancy	518(85.47%)	204(81.92%)	314(87.95%)	0.051

Chi–Square test, Fisher's exact test, Mann–Whitney U test. *$p < 0.05$, **$p < 0.01$, Statistically significant. Continuous data are expressed as mean ± SD. Abbreviations: BPH, Benign prostate hyperplasia; CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; CVA, Cerebrovascular accident; DM, Diabetes mellitus; GI: Gastrointestinal.

Clinical Course of Adult Patients with Neutropenic Bacteremia

The overall in-hospital mortality rate of patients with NB was 58.9% (357/606). The non-survivor group had a statistically significantly higher rate of ICU admission ($p = 0.007$) (Table 5). Compared to the non-survivor group, the survivor group had a longer hospital stay (days), including ICU stay ($p < 0.001$) and total stay ($p < 0.001$). Septic shock occurred in 82 (13.52%) cases of NB, and in the survivors (7.22%) and non-survivors (17.92%) ($p < 0.001$). Vasopressor was used in 266 cases (43.89%), and in the survivors (31.32%) and non-survivors (52.66%) ($p < 0.001$). CVC was implanted in 124 cases (20.46%), including survivors (13.65%) and non-survivors (25.21%) ($p < 0.001$). Respiratory failure occurred in 75 (12.37%) cases of NB, and in the survivors (8.33%) and non-survivors (14.84%) ($p = 0.037$).

Table 5
Clinical course of 606 adult patients with neutropenic bacteremia.

Clinical course	Total (*n* = 606)	Survivors (*n* = 249)	Non-survivors (*n* = 357)	*p*-Value
Total stay (days)	15.76 ± 15.88	18.36 ± 16.12	13.93 ± 15.48	< 0.001**
ICU admission	155(25.57%)	49(19.67%)	106(29.69%)	0.007**
ICU stay	10.93 ± 14.16	16.37 ± 16.80	8.42 ± 12.04	< 0.001**
Septic shock	82(13.53%)	18(7.22%)	64(17.92%)	< 0.001**
Vasopressor use	266(43.89%)	78(31.32%)	188(52.66%)	< 0.001**
CVC implant	124(20.46%)	34(13.65%)	90(25.21%)	< 0.001**
Respiratory failure	75(12.37%)	22(8.83%)	53(14.84%)	0.037*

Chi–Square test, Fisher's exact test, Mann–Whitney test. *$p < 0.05$, **$p < 0.01$, Continuous data were expressed mean ± SD, Categorical data were expressed number and percentage. CVC, Central venous catheter; ICU, Intensive care unit.

Scoring Systems of Patients with Adult Neutropenic Bacteremia

This study applied two scoring systems to compare the survivors and non-survivors (Table 6). The scores on the original MEDS were significantly higher in non-survivors (12.64 ± 3.88) than in survivors (8.41 ± 4.67), $p < 0.001$. The original MEWS scores were significantly higher in non-survivors (2.74 ± 2.17) than in survivors (2.06 ± 1.79), $p < 0.001$.

Table 6
Scoring systems of MEDS and MEWS for 606 adult patients with neutropenic bacteremia.

Scoring systems	Total (*n* = 606)	Survivors (*n* = 249)	Non-survivors (*n* = 357)	*p*-Value
MEDS	10.90 ± 4.71	8.41 ± 4.67	12.64 ± 3.88	< 0.001**
MEWS	2.46 ± 2.05	2.06 ± 1.79	2.74 ± 2.17	< 0.001**

Chi–Square test, Fisher's exact test, Mann–Whitney test. *$p < 0.05$, **$p < 0.01$, Statistically significant. Abbreviations: MEDS, Mortality in Emergency Department Sepsis; MEWS, Modified Early Warning Score.

Univariate and Multivariate Analyses to Evaluate Mortality Risks

We performed univariate and multivariate logistic regression analyses to identify risk factors predisposing patients with adult neutropenic bacteremia to adverse clinical outcomes, with odds ratios (ORs) presented in Table 7. In univariate logistic regression analysis, absolute neutrophil count (ANC)

(ORs 0.999, $p < 0.001$), lactate (ORs 1.020, $p < 0.001$), red cell distribution width (RDW) (ORs 1.122, $p < 0.001$), albumin (ORs 0.537, $p < 0.001$), BUN/Cr (ORs 1.021, $p = 0.016$), and CRP (ORs 0.537, $p < 0.001$) were associated with increased mortality. In the multivariate logistic regression analysis, RDW (ORs 1.179, $p < 0.001$), lactate (ORs 1.020, $p < 0.001$), and ANC count levels (ORs 0.999, $p < 0.001$) were significantly associated with a heightened risk of death.

Table 7
Univariate and multivariate logistic regression analyses of mortality risk in 606 adult patients with neutropenic bacteremia.

Analyses	**Univariate**			**Multivariate[a]**		
Variables	ORs	95%CI	*p*-Value	ORs	95%CI	*p*-Value
RDW	1.122	1.058–1.191	< 0.001**	1.178	1.083–1.280	< 0.001**
ANC	0.999	0.999–1.000	< 0.001**	0.999	0.999–0.999	< 0.001**
Lactate	1.020	1.012–1.028	< 0.001**	1.016	1.005–1.026	< 0.001**
ALB	0.537	0.390–0.739	< 0.001**	0.819	0.562–1.192	0.296
BUN/Cr	1.021	1.004 – 1.038	0.016*	1.022	0.999–1.045	0.056
CRP	1.028	1.012–1.044	< 0.001**	1.010	0.990–1.026	0.335

*Univariate and Multivariate[a] logistic regression analysis. *$p < 0.05$, **$p < 0.01$, Statistically significant. ALB, Albumin; ANC, Absolute neutrophil count; BUN, Blood urea nitrogen; CRP, C-reactive protein; Cr, Creatinine; ORs, Odds ratios; RDW, red cell distribution width.

Receiver Operation Characteristic (ROC) of Scoring Systems

We performed ROC curve analysis on the original MEDS and MEWS to evaluate their accuracy in predicting mortality risk in adult patients with NB (Fig. 1). The cutoff point for the original MEDS was 10, with an AUC of 0.755, indicating a sensitivity of 73.9% and a specificity of 67.5% ($p < 0.001$). For the original MEWS, the cutoff points were 2. Its AUC was 0.588 with a sensitivity of 68.2% and a specificity of 44.5% ($p < 0.001$).

We utilized the Youden index to identify optimal cutoff points for RDW, ANC, and lactate. Each predictive factor was assigned a score of 1, based on the ORs of the dichotomized variables. Added point score into the original MEDS and MEWS scoring systems with a score of 1 if RDW > 16.0%, a score of 2 if RDW > 17.5%, a score of 1 if ANC < 250, a score of 2 if ANC < 122, a score of 1 if lactate > 45.2 mg/dL, and a score of 2 if lactate > 92.0 mg/dL. These adjustments aimed to enhance the predictive performance of the original MEDS and MEWS systems for mortality risk.

The modified MEDS (MEDS-NB) and MEWS (MEWS-NB) were evaluated, and their results were presented. The cutoff point for the MEDS-NB was 12, with an AUC of 0.784, a sensitivity of 78.2%, and a specificity of 66.3% ($p < 0.001$). For the MEWS-NB, the cutoff points were 4. Its AUC was 0.652 with a sensitivity of 63.4% and a specificity of 58.3% ($p < 0.001$). Compared to the original scoring systems, the modified systems demonstrated better predictive performance for mortality risk.

Kaplan–Meier Survival Curve of the Original and Modified Scoring Systems

We performed Kaplan–Meier survival analyses to estimate the 30-day to 5-year cumulative survival rates of adult patients with NB. The MEDS and MEDS-NB scores had cutoff points of 10 and 12, respectively (Fig. 2). The MEWS and MEWS-NB scores had cutoff points of 2 and 4, respectively (Fig. 3). These findings indicated that the modified scoring systems outperformed the original versions in predictive accuracy.

Discussion

Shapiro et al. initially developed the MEDS score, comprising nine clinical parameters: age, residence in a nursing home, presence of terminal illness, respiratory distress, lower respiratory tract infection, septic shock, platelet count, band neutrophil proportion, and altered mental status [11]. This scoring system has demonstrated significant accuracy in predicting mortality among ED patients presenting with suspected infectious conditions [12, 13].

Recent studies have validated the use of the MEDS score to predict prognosis in patients with community-acquired bacteremia in the ED. These findings support that the MEDS score can serve as a reliable diagnostic and prognostic indicator in the ED [13, 14].

In 2001, Subbe and colleagues introduced a modified Early Warning Score (MEWS), incorporating additional physiological parameters, including heart rate, respiratory rate, blood pressure, body temperature, and level of consciousness, along with optimized weighting of these parameters. The modified MEWS demonstrated an enhanced sensitivity and specificity for predicting the necessity of ICU admission and assessing the risk of in-hospital mortality [15–19].

A review of the literature revealed a paucity of studies evaluating prognostic scoring systems for bacteremia in adults with neutropenia. This study aims to validate the predictive performance of two clinically available scoring systems, the MEDS score and the MEWS, in assessing disease severity and clinical outcomes in this patient population. Additionally, we have refined these scoring systems based on multiple clinical characteristics. Compared to their original versions, the revised scoring systems were applied to predict mortality risk in adult patients with NB.

In this single-center retrospective analysis, non-surviving patients exhibited significantly elevated baseline scores on both the original MEDS and MEWS. Univariate logistic regression confirmed these

scores as robust predictors of mortality risk. Among the evaluated tools, the MEDS framework demonstrated superior performance in predicting mortality risk among adult patients with NB, achieving a highest AUC-ROC of 0.755. At the established cutoff threshold of 10 points, it yielded a sensitivity of 73.9% and specificity of 67.5%. Concurrently, the MEWS also demonstrated discriminatory ability, with an AUC-ROC of 0.588 for mortality risk stratification (Fig. 1). The existing literature indicates that adult patients with neutropenia are often immunosuppressed, making them highly susceptible to infections, particularly bacterial infections that can result in bacteremia [20].

The findings of this study revealed that the majority of blood cultures in adult patients with NB showed a single bacterial strain (monoclonal bacteremia, 87.29%; polyclonal bacteremia, 12.7%). The bacteriological profiles were largely similar between the survival and non-survival groups. Gram-negative bacteria accounted for the majority of isolates (75.41%). The three most common pathogens were *Escherichia* spp. (33.99%), *Klebsiella* spp. (18.31%), and *Pseudomonas* spp. (14.02%). Among these, only *Pseudomonas* spp. had a higher incidence of non-survivors (16.52%) than survivors (10.44%), $p = 0.045$, while other bacterial species showed no significant differences.

Several laboratory risk factors associated with mortality include various blood cell count parameters (such as hemoglobin, hematocrit, RDW, platelet count, NLCR, and PLR), as well as serum albumin, CRP, lactate levels, delta lactate (the difference between lactate at two time points), and gas analysis results (including pH and HCO3 levels). Among these factors, an increased RDW, low ANC, and high serum lactate levels showed the strongest association with mortality. Therefore, we have selected these parameters for the modified scoring systems.

Adult patients with NB who present to the ED with unstable vital signs, particularly HR and SpO2, may exhibit signs of respiratory failure and septic shock. The use of vasopressors is also a relevant factor in determining clinical prognosis and mortality [21]. Additionally, groups with a higher mortality rate tend to have shorter lengths of hospital stay and ICU duration. This may suggest that neutropenic bacteremia is associated with the manifestation of acute and severe complications.

Based on univariate and multivariate analyses of laboratory variables, we found that elevated RDW, high serum lactate, and low ANC were strongly associated with mortality (Table 7). RDW is an easily accessible laboratory parameter that has shown prognostic value across various conditions in emergency and critical care settings [29, 30]. Elevated RDW upon admission correlates with increased mortality in several diseases, particularly sepsis. Studies indicate that RDW is an independent predictor of mortality in septic patients, outperforming traditional scoring systems like Systemic Inflammatory Response Syndrome (SIRS), MEDS, and CURB-65. Integrating RDW into these clinical prediction models can enhance their accuracy, enabling clinicians to stratify patients effectively and tailor treatment strategies accordingly. Previous research has identified additional predictive factors for bloodstream infections and sepsis outcomes, including temperature, white blood cell counts, Sequential Organ Failure Assessment (SOFA) scores, heart rate, respiratory rate, and renal replacement therapy. Although RDW alone has limited diagnostic capability for sepsis, its combination with these clinical indicators may

significantly improve prediction accuracy [21, 29–32]. However, RDW's prognostic value may be limited in patients with hematologic malignancies or those undergoing chemotherapy. Its predictive accuracy appears more robust in patients without malignancies. Despite these limitations, RDW remains a simple, cost-effective tool for risk stratification in emergency departments and critical care units. Clinicians should use RDW alongside other clinical parameters to optimize patient assessment and management.

Lactate has become a crucial biomarker in septic shock management, acting as a "dashboard" for tissue perfusion assessment, and elevated lactate levels directly correlate with the shock severity. A pivotal study by Mikkelsen et al. identified lactate as an independent mortality risk factor in severe sepsis, where higher levels indicate worse prognoses [32]. Jansen et al. demonstrated that lactate-guided therapy significantly improves outcomes in critically ill patients by actively monitoring and reducing lactate through fluid resuscitation, inotropic support, or blood transfusions, effectively lowering mortality rates [33]. Further research by Jones et al. compared lactate clearance with maintaining central venous oxygen saturation as treatment goals. The study found no significant difference in mortality rates between the two groups, establishing lactate clearance (a 10–20% reduction within two hours) as a primary resuscitation target [34]. The Surviving Sepsis Campaign Guidelines emphasize the importance of promptly addressing elevated initial lactate levels (lactate > 4 mmol/L or > 36.04 mg/dL) to reduce mortality. Lactate clearance is highlighted as a more critical indicator than a single lactate measurement. If lactate levels do not decrease or worsen after aggressive resuscitation within six hours, this "lactate non-clearance" suggests a poor prognosis, with mortality rates exceeding 50–60%. So lactate is a vital indicator in septic shock management, guiding therapeutic interventions and prognostic evaluations [35].

Therefore, we applied modifications of the original MEDS and MEWS by adding scores of RDW (RDW > 16.5%, score = 1; RDW > 17.5%, score = 2), lactate (lactate > 45.2 mg/dL, score = 1; lactate > 92 mg/dL, score = 2), and ANC (ANC < 250, score = 1; ANC < 122, score = 2), to get a better performance than the original scores. The MEDS-NB (a cutoff of 12) remained the best-performance predictor of mortality, with an AUC-ROC of 0.784, a sensitivity of 78.2%, and a specificity of 66.3%. The MEWS-NB (a cutoff point of 4) simultaneously showed superior performance to the original systems, with an AUC-ROC of 0.652, a sensitivity of 63.4%, and a specificity of 58.3%. Our findings suggested that the original MEDS, MEWS, MEDS-NB, and MEWS-NB were valuable tools for predicting the mortality risk in adult patients with NB in the ED.

Limitations

This study is a single-center, retrospective investigation with a relatively small sample size and incomplete data, which may introduce unavoidable bias. Detailed records for key therapeutic determinants in bacteremia—specifically antibiotic management and fluid resuscitation—were limited in this dataset, constraining the scope and depth of our analyses. Owing to insufficient documentation of antibiotic therapy, we did not conduct a dedicated analysis of antibiotic-related effects in this study. Future work should further evaluate how antibiotic regimens influence clinical prognosis in this disease.

In the management of severe bacteremia and septic shock, the adequacy and timeliness of fluid resuscitation play a critical role in clinical outcomes. Numerous studies have examined serum lactate levels in the context of bacteremia and resuscitation from septic shock. In our investigation, we included the initial serum lactate level in the analysis; however, due to incomplete data after resuscitation, we were unable to assess lactate kinetics (e.g., post-resuscitation levels or lactate clearance), which is a notable limitation.

Abbreviations

ALK-P
Alkaline Phosphatase
ANC
Absolute Neutrophil Count
APTT
Activated Partial Thromboplastin Time
AUC
Area Under the Curve
AVPU
Alert, Verbal, Painful, and Unresponsive
BPH
Benign Prostate Hyperplasia
BT
Body Temperature
BUN
Blood Urea Nitrogen
CIs
Confidence Intervals
CKD
Chronic kidney disease
COPD
Chronic obstructive pulmonary disease
CRP
C-reactive protein
Cr
Creatinine
CVA
Cerebrovascular Accident
CVC
Central Venous Catheters
DBP

Diastolic Blood Pressure
DM
Diabetes mellitus
DNR
Do Not Resuscitate
ED
Emergency Department
FN
Febrile neutropenia
GI
Gastrointestinal
GCS
Glasgow Coma Scale
HCO3-
Bicarbonate
HR
Heart Rate
ICU
Intensive Care Units
LDH
Lactate Dehydrogenase
MAP
Mean Arterial Pressure
MEDS
Mortality in Emergency Department Sepsis
MEDS-NB
Mortality in Emergency Department Sepsis-Neutropenic Bacteremia
MEWS
Modified Early Warning Score
MEWS-NB
Modified Early Warning Score-Neutropenic Bacteremia
NB
Neutropenic Bacteremia
NLCR
Neutrophil-Lymphocyte Count Ratio
NPV
Negative Predictive Value
ORs
Odds Ratios
PLT

Platelet
PLR
Platelet-to-Lymphocyte Ratio
PPV
Positive Predictive Value
PT
Prothrombin Time
RDW
Red blood cell Distribution Width
ROC
Receiver operating characteristic
RR
Respiratory Rate
SBP
Systolic Blood Pressure
SD
Standard Deviation
SIRS
Systemic Inflammatory Response Syndrome
SOFA
Sequential Organ Failure Assessment
SpO2
Saturation of Peripheral Oxygen
TCVGH
Taichung Veterans General Hospital

Declarations

Supplementary Materials: The following supporting information is in Table S1: Parameters of scoring systems (MEWS and MEDS) [11-13,15-19].

Ethics Approval and Informed Consent

The human study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of Taichung Veterans General Hospital (IRB file code: CE23126B). Informed consent was waived because of this study's retrospective and observational nature.

Data Availability Statement

The data are available upon reasonable request to the corresponding author. Readers can access the data and material supporting the study's conclusions by contacting Sung-Yuan Hu at

song9168@pie.com.tw.

Competing interests

The authors declare no conflict of interest.

Funding

This research was supported by grants from the Taichung Veterans General Hospital (Grant numbers: TCVGH-T1147801). The funder had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Author Contributions

Conceptualization, S.-Y.H.; methodology, M.-S.H., S.-Y.H. and C.-H.S.; data curation, Y-T.C., S.-Y.H., S.-C.H., C.-A.T. and C.-H.S.; writing—original draft preparation, Y.-T.C. and S.-Y.H.; writing—review and editing, M.-S.H., S.-C.H. and S.-Y.H.; project administration, S.-Y.H.; funding acquisition, S.-Y.H. All authors have read and agreed to the published version of the manuscript.

Author details

[1]Department of Emergency Medicine, Taichung Veterans General Hospital, Taichung 40705, Taiwan.

[2]Department of Nursing, College of Health, National Taichung University of Science and Technology, Taichung 403027, Taiwan.

[3]Department of Post-Baccalaureate Medicine, College of Medicine, National Chung Hsing University, Taichung 402, Taiwan.

[4]School of Medicine, Chung Shan Medical University, Taichung 40201, Taiwan.

[5]Institute of Medicine, Chung Shan Medical University, Taichung 40201, Taiwan.

[6]School of Medicine, National Yang Ming Chiao Tung University, Taipei 11217, Taiwan.

[7]Division of Infectious Diseases, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung 40705, Taiwan.

[8]Department of Emergency Medicine, Chung Shan Medical University Hospital, Taichung 40201, Taiwan.

[9]Department of Information Management, Tunghai University, Taichung

Acknowledgments

We thank the Clinical Informatics Research and Development Center and Bio-statistics Task Force of Taichung Veterans General Hospital.

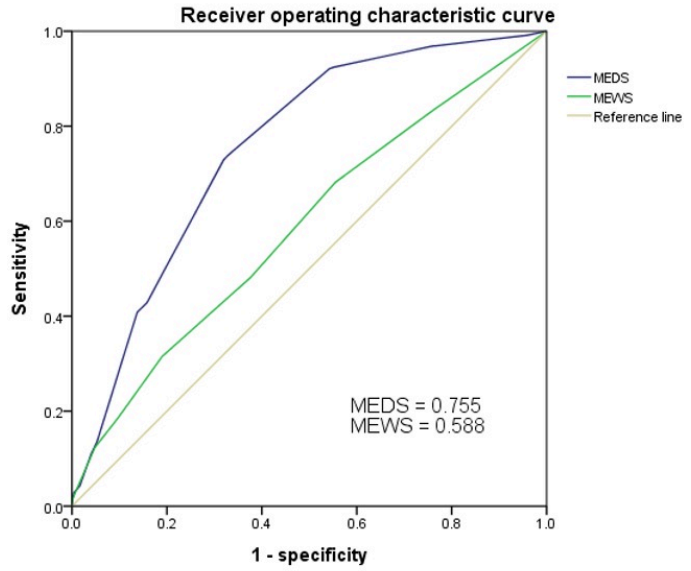
References

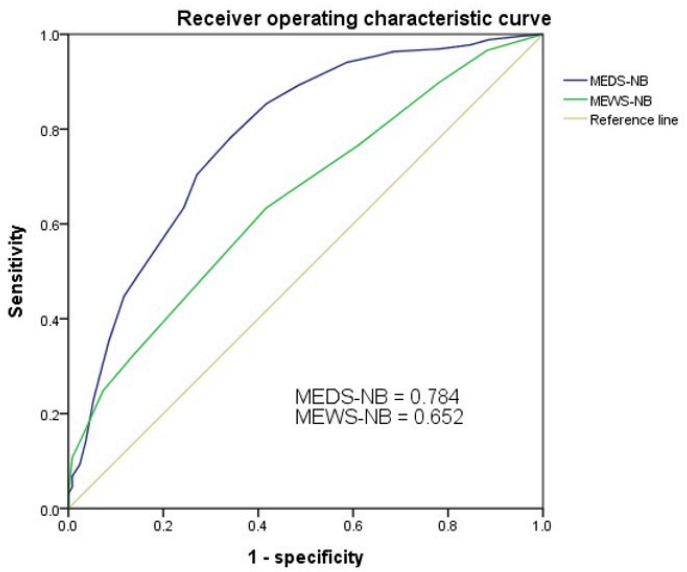
1. Sekeres MA, Taylor J. Diagnosis and Treatment of Myelodysplastic Syndromes: A Review. JAMA. 2022;328(9):872–80.
2. Gibson C, Berliner N. How we evaluate and treat neutropenia in adults. Blood. 2014;124(8):1251–8. quiz 1378.
3. Frater JL. How I investigate neutropenia. Int J Lab Hematol. 2020;42(Suppl 1):121–32.
4. Dufour C, Miano M, Fioredda F. Old and new faces of neutropenia in children. Haematologica. 2016;101(7):789–91.
5. Donadieu J, Beaupain B, Mahlaoui N, Bellanné-Chantelot C. Epidemiology of congenital neutropenia. Hematol Oncol Clin North Am. 2013;27(1):1–17. vii.
6. Farruggia P, Fioredda F, Puccio G, Porretti L, Lanza T, Ramenghi U, et al. Autoimmune neutropenia of infancy: Data from the Italian neutropenia registry. Am J Hematol. 2015;90(12):E221–2.
7. Hsieh MM, Everhart JE, Byrd-Holt DD, Tisdale JF, Rodgers GP. Prevalence of neutropenia in the U.S. population: age, sex, smoking status, and ethnic differences. Ann Intern Med. 2007;146(7):486–92.
8. Schwartzberg LS. Neutropenia: etiology and pathogenesis. Clin Cornerstone. 2006;8(Suppl 5):S5–11.
9. Villafuerte-Gutierrez P, Villalon L, Losa JE, Henriquez-Camacho C. Treatment of febrile neutropenia and prophylaxis in hematologic malignancies: a critical review and update. Adv Hematol. 2014;2014:986938.
10. Jeong IS, Park SM, Lee JM, Song JY, Lee SJ. Effect of central line bundle on central line-associated bloodstream infections in intensive care units. Am J Infect Control. 2013;41(8):710–6.
11. Shapiro NI, Wolfe RE, Moore RB, Smith E, Burdick E, Bates DW. Mortality in Emergency Department Sepsis (MEDS) score: a prospectively derived and validated clinical prediction rule. Crit Care Med. 2003;31(3):670–5.
12. Zhang G, Zhang K, Zheng X, Cui W, Hong Y, Zhang Z. Performance of the MEDS score in predicting mortality among emergency department patients with a suspected infection: a meta-analysis. Emerg Med J. 2020;37(4):232–9.
13. Hsieh CC, Yang CY, Lee CH, Chi CH, Lee CC. Validation of MEDS score in predicting short-term mortality of adults with community-onset bacteremia. Am J Emerg Med. 2020;38(2):282–7.
14. Wen CY, Hu SY, Hsieh MS, Huang SC, Shen CH, Tsai YC. Good Performance of Revised Scoring Systems in Predicting Clinical Outcomes of *Aeromonas* Bacteremia in the Emergency Department: A Retrospective Observational Study. Diagnostics (Basel). 2024;14(2):124.
15. Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified Early Warning Score in medical admissions. QJM. 2001;94(10):521–6.

16. Hester J, Youn TS, Trifilio E, Robinson CP, Babi MA, Ameli P, et al. The Modified Early Warning Score: A Useful Marker of Neurological Worsening but Unreliable Predictor of Sepsis in the Neurocritically Ill-A Retrospective Cohort Study. Crit Care Explor. 2021;3(5):e0386.
17. Kruisselbrink R, Kwizera A, Crowther M, Fox-Robichaud A, O'Shea T, Nakibuuka J, et al. Modified Early Warning Score (MEWS) Identifies Critical Illness among Ward Patients in a Resource Restricted Setting in Kampala, Uganda: A Prospective Observational Study. PLoS ONE. 2016;11(3):e0151408.
18. Kumar A, Ghabra H, Winterbottom F, Townsend M, Boysen P, Nossaman BD. The Modified Early Warning Score as a Predictive Tool During Unplanned Surgical Intensive Care Unit Admission. Ochsner J. 2020;20(2):176–81.
19. Monzon LDR, Boniatti MM. Use of the Modified Early Warning Score in intrahospital transfer of patients. Rev Bras Ter Intensiva. 2020;32(3):439–43.
20. Min KI, Byeon S. Diagnosis and management of neutropenia. Blood Res. 2025;60(1):30.
21. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181–247.
22. Stern A, Carrara E, Bitterman R, Yahav D, Leibovici L, Paul M. Early discontinuation of antibiotics for febrile neutropenia versus continuation until neutropenia resolution in people with cancer. Cochrane Database Syst Rev. 2019;1(1):CD012184.
23. Bachlitzanaki M, Aletras G, Bachlitzanaki E, Messaritakis I, Koukias S, Koulouridi A, et al. Evaluation of Febrile Neutropenia in Hospitalized Patients with Neoplasia Undergoing Chemotherapy. Microorganisms. 2023;11(10):2547.
24. Pal KV, Othus M, Ali Z, Russell K, Shaw C, Percival MM, et al. Identification of factors predicting low-risk febrile neutropenia admissions in adults with acute myeloid leukemia. Blood Adv. 2024;8(24):6161–70.
25. Lueangarun S, Leelarasamee A. Impact of inappropriate empiric antimicrobial therapy on mortality of septic patients with bacteremia: a retrospective study. Interdiscip Perspect Infect Dis. 2012;2012:765205.
26. Gustinetti G, Mikulska M. Bloodstream infections in neutropenic cancer patients: A practical update. Virulence. 2016;7(3):280–97.
27. De la Rosa-Riestra S, Martínez Pérez-Crespo PM, Pérez Rodríguez MT, Sousa A, Goikoetxea J, Reguera Iglesias JM, et al. Mortality impact of further delays in active targeted antibiotic therapy in bacteraemic patients that did not receive initial active empiric treatment: Results from the prospective, multicentre cohort PROBAC. Int J Infect Dis. 2024;145:107072.
28. Alves J, Abreu B, Palma P, Alp E, Vieceli T, Rello J. Antimicrobial Stewardship on Patients with Neutropenia: A Narrative Review Commissioned by Microorganisms. Microorganisms. 2023;11(5):1127.

29. Jo YH, Kim K, Lee JH, Kang C, Kim T, Park HM, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. Am J Emerg Med. 2013;31(3):545–8.
30. Zhang L, Yu CH, Guo KP, Huang CZ, Mo LY. Prognostic role of red blood cell distribution width in patients with sepsis: a systematic review and meta-analysis. BMC Immunol. 2020;21(1):40.
31. Noritomi DT, Soriano FG, Kellum JA, Cappi SB, Biselli PJ, Libório AB, et al. Metabolic acidosis in patients with severe sepsis and septic shock: a longitudinal quantitative study. Crit Care Med. 2009;37(10):2733–9.
32. Mikkelsen ME, Miltiades AN, Gaieski DF, Goyal M, Fuchs BD, Shah CV, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. Crit Care Med. 2009;37(5):1670–7.
33. Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med. 2010;182(6):752–61.
34. Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA. Emergency Medicine Shock Research Network (EMShockNet) Investigators. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA. 2010;303(8):739–46.
35. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47(11):1181–247.

Figures





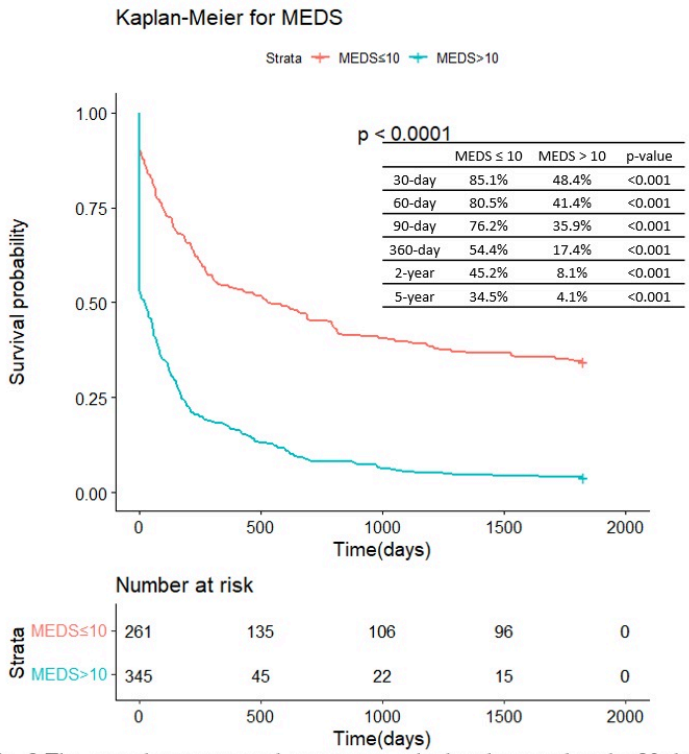
Scores	AUC	Cut-off point	Sensitivity	Specificity	PPV	NPV	Accuracy	SE	p-Value
MEDS	0.755	10	73.9%	67.5%	76.5%	64.4%	71.3%	0.021	<0.001**
MEWS	0.588	2	68.2%	44.5%	63.9%	49.3%	58.5%	0.023	<0.001**

Scores	AUC	Cut-off point	Sensitivity	Specificity	PPV	NPV	Accuracy	SE	p-Value
MEDS-NB	0.784	12	78.2%	66.3%	76.9%	67.9%	73.3%	0.019	<0.001**
MEWS-NB	0.652	4	63.4%	58.3%	68.6%	52.6%	61.3%	0.022	<0.001**

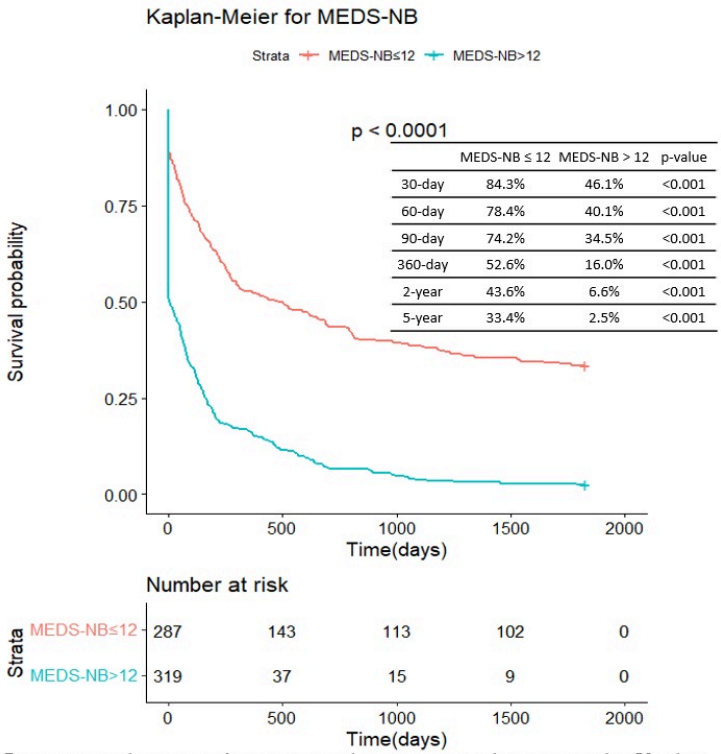
Fig. 1 The AUC of ROC of MEDS (0.755), MEWS (0.588), MEDS-NB (0.784), and MEDS-NB (0.652) showed the predictive performance of 30-day to 5-year mortality risk for adult patients with neutropenic bacteremia. AUC, Area under curve; MEDS, Mortality in Emergency Department Sepsis; MEDS-NB, Mortality in Emergency Department Sepsis-Neutropenic Bacteremia; MEWS, Modified Early Warning Score; MEWS-NB, Modified Early Warning Score-Neutropenic Bacteremia; NPV, Negative predictive value; PPV, Positive predictive value.

Figure 1

See image above for figure legend.



	MEDS ≤ 10	MEDS > 10	p-value
30-day	85.1%	48.4%	<0.001
60-day	80.5%	41.4%	<0.001
90-day	76.2%	35.9%	<0.001
360-day	54.4%	17.4%	<0.001
2-year	45.2%	8.1%	<0.001
5-year	34.5%	4.1%	<0.001



	MEDS-NB ≤ 12	MEDS-NB > 12	p-value
30-day	84.3%	46.1%	<0.001
60-day	78.4%	40.1%	<0.001
90-day	74.2%	34.5%	<0.001
360-day	52.6%	16.0%	<0.001
2-year	43.6%	6.6%	<0.001
5-year	33.4%	2.5%	<0.001

Fig. 2 The cumulative survival rates were calculated to predict the 30-day to 5-year mortality rate of patients with neutropenic bacteremia by Kaplan–Meier. The cut-off points of MEDS and MEDS-NB were 10 and 12, respectively, all $p < 0.001$. MEDS, Mortality in Emergency Department Sepsis; MEDS-NB, Mortality in Emergency Department Sepsis-Neutropenic Bacteremia.

Figure 2

See image above for figure legend.

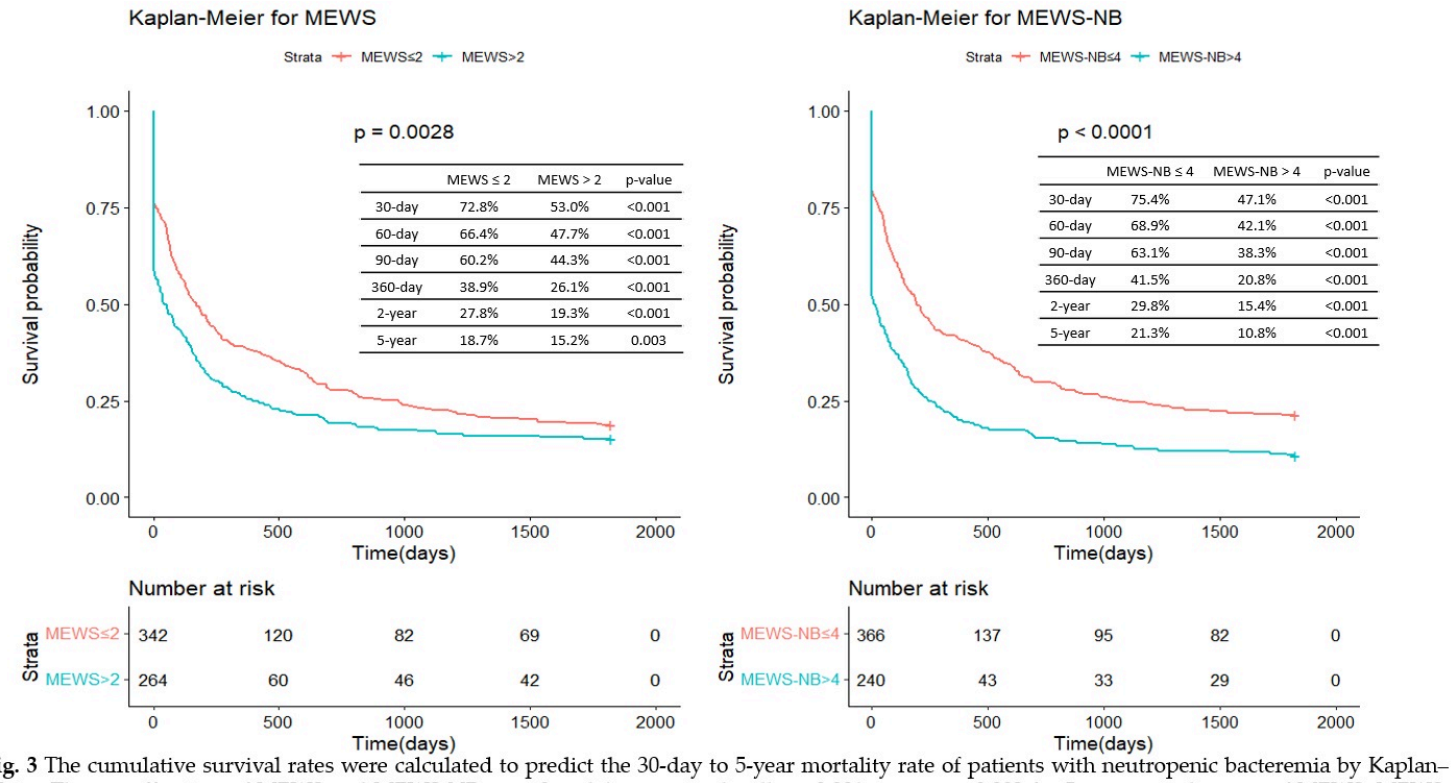


Fig. 3 The cumulative survival rates were calculated to predict the 30-day to 5-year mortality rate of patients with neutropenic bacteremia by Kaplan–Meier. The cut-off points of MEWS and MEWS-NB were 2 and 4, respectively, all $p < 0.001$ except $p = 0.003$ for 5-year mortality rate of MEWS. MEWS, Modified Early Warning Score; MEWS-NB, Modified Early Warning Score-Neutropenic Bacteremia.

Figure 3

See image above for figure legend.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementary115.05.08.docx