Indonesian Journal of Pharmacy

VOL 36 (1) 2025: 157–167 | RESEARCH ARTICLE

Decision-Making System for Extended Bacteremia Treatment in Patients with Hematologic Malignancy

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Article Info

Submitted: 17-04-2024
Revised: 05-10-2024
Accepted: 13-11-2024

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ABSTRACT

Patients with hematologic malignancy (HM) experiencing bloodstream infections by *Acinetobacter baumannii* (AB) encounter considerable mortality risks, despite 14 days of standard antibiotic therapy. This research addresses a critical clinical challenge by developing a decision-making system to identify patients with hematologic malignancy and *Acinetobacter baumannii* bloodstream infections who would benefit from extended antibiotic therapy. Retrospective cohort research was conducted on patients with hematologic malignancies (HM) who developed bloodstream infections and were treated with a 14-day course of antibiotics within the specified period from January 2019 to April 2024. The odds ratio (OR) and risk ratio (RR) were calculated to examine the relationships among clinical and demographic data. A multivariable logistic regression model has been applied and adjusted to account for various predictors. The predictive model and the "Ex-CSEPA" decision-making system were developed using logistic regression. The performance metrics, including sensitivity, specificity, positive predictive value, negative predictive value, and area under the receiver operating characteristic curve (AUC-ROC), were evaluated. The developed model demonstrated exceptional performance, achieving an accuracy of 98.7%. It exhibited a sensitivity of 99.07% and a specificity of 98.33% in predicting mortality, setting a cut-off point of 0.5 or higher as indicative of high risk for mortality after 14-day treatment. The system's ability to identify patients who would benefit from antibiotic (ATB) treatment beyond the standard 14-day period was particularly significant. The application of this predictive model in clinical practice has pushed up the potential to enhance decisions for extended-ATB duration and decrease 30-day mortality for patients with HM who are morbid with AB bloodstream infections.

Keywords: *Acinetobacter baumannii*, Decision-making system, Extended antibiotic therapy, Hematologic malignancy, Mortality prediction model.

INTRODUCTION

Hematologic malignancies (HMs) significantly elevate the vulnerability to severe and complex infections, which are major causes of death, especially when caused by multidrug-resistant organisms. *Acinetobacter baumannii* (AB) is a common hospital-acquired pathogen in patients with impaired immune response and is associated with considerably greater mortality rates. "Febrile neutropenia," a medical emergency in oncology, with a fatal outcome rate of 56-78% among patients with bloodstream infections (Yin et

al., 2023). Particularly since the emergence of multidrug-resistant bacteria, inadequate empirical antibiotic (ATB) treatment worsens the severity and mortality of HM (Itani et al., 2023). Survival and remission from the disease are adversely affected, as infection-related morbidity compromises the efficacy of chemotherapy dosing (Delgado and Guddati, 2021).

Multidrug-resistant *A. baumannii* (MDR-AB), a gram-negative nosocomial bacterium, has become more prevalent, posing a substantial risk to hospitalized HM patients and resulting in mortality rates of up to 71% (Itani et al., 2023). In Thailand, AB bacteremia affects a significant percentage of neutropenic patients; mortality rates have been recorded to reach 48% (Lertpongpiroon et al., 2018). Patients with MDR-AB infections, however, experience a staggering 92% mortality rate (Chaiwarit et al., 2005). Particularly in light of antibiotic resistance, the optimal duration of treatment for AB infections continues to be a matter of contention. Extended treatment durations should be considered in cases of multidrug resistance, as suggested by the National Comprehensive Cancer Network (NCCN), in contrast to the recommended duration of 7 to 14 days of antibiotic therapy for neutropenic bloodstream infections (NCCN, 2024). Due to the compromised condition of their bone marrow, patients with HM are especially susceptible to protracted and severe neutropenia when infected with AB (Hoffman (editor), 2018). Subsequently, this high-risk group with increased mortality risks may potentially benefit from prolonged antibiotic therapy.

The effectiveness of short courses of antibiotic therapy in managing gram-negative bloodstream infections (GN-BSI) in immunocompromised patients is supported by limited evidence. An observational study conducted by Anderson et al. (2024) evaluated the effects of short-course (7–10 days) and longer-course (10–14 days) antibiotic treatments in critically ill patients with GN-BSI. The study identified no statistically significant disparities in 30-day death, 60-day relapse, or readmission rates between the two treatment groups. Nevertheless, the longer-course group exhibited a higher incidence of adverse events. Regarding immunocompromised patients undergoing hematopoietic stem cell transplant (HSCT) and malignancy who developed GNB bacteremia, Herrera et al. (2023) assessed the efficacy of short antibiotic courses (7 days) in a prospective observational study. Comparable clinical and microbiological responses were observed in the groups treated with short-course and long-course antibiotics (7–15 days); mortality rates and bacteremia relapse were not significantly different. Significantly, individuals who received short-course-treatment experienced reduced hospitalization periods after being diagnosed with bacteremia. In contrast, retrospective cohort research conducted by Katip et al. (Katip et al., 2021) examined the effectiveness and safety of shorter (14 days) versus longer durations (over 14 days) of colistin therapy in cancer patients with Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infection. The study showed that patients undergoing long-term colistin medication saw better rates of clinical and microbiological improvement and decreased mortality after 30 days, in comparison to those receiving shorter courses. There was no notable disparity in the occurrence of kidney damage. The combined evidence indicates that a treatment period of 10-14 days appears to be adequate for gram-negative bloodstream infections. Extended-course antibiotic (Ex-ATB) therapy, often lasting 14 days, may be advantageous for managing Gram-negative bloodstream infections (GN-BSI) for certain immunosuppressed individuals, especially those with malignancy infected by multidrug-resistant (MDR) pathogens. (Anderson et al., 2024; Katip et al., 2021)

Ongoing controversy surrounds the efficacy of protracted antibiotic treatment for specific patient subgroups. Although extended periods of treatment have the potential to improve mortality rates, they concurrently elevate the likelihood of complications that are frequently related to prolonged antibiotic usage. Determining which patients would benefit from Ex-ATB is thus of paramount concern. This study aims to create mortality prediction tools specifically for patients with HMs who have AB bacteremia and have received a 14-day antibiotic regimen. These approaches are intended to facilitate the discrimination of high-risk for mortality among patients who would benefit from Ex-ATB therapy.

Different mortality prediction models were developed in previous investigations. For adults presenting to emergency departments (EDs) with bacteremia, the research investigated mortality patterns and constructed predictive models. A unique predictive model for 7-day mortality was developed, which includes characteristics such as the Pitt Bacteremia Score (PBS), age, infection

source, baseline steroid use, and metabolic profiles. The findings indicated a significant decrease in both the overall incidence and mortality rate within seven days of acquiring bacteremia between 2003 and 2016. The ED bacteremia mortality (ED-BM) model demonstrated better discriminatory ability (AUC: 0.903) than PBS (AUC: 0.848) and the BSI Mortality Risk Score (BSIMRS) (AUC: 0.885) in predicting mortality within 7 days (Chiang et al., 2021). Another instance of a mortality prediction model is additionally covered in the latest study. A predictive model for mortality due to bacteremia has been developed in a previous study, specifically for patients with COVID-19 infection. A multicentre study was conducted to examine patients with community-onset bacteremia in both the COVID-19 and pre-COVID-19 periods. The study utilized statistical and machine learning methodologies to develop and validate predictive models. The main factors influencing these predictions were alterations in consciousness between day 0 and day 3, body temperature, and a diagnosis of complicated bacteremia. The results highlight the significance of dynamic clinical factors in predicting short-term mortality and length of stay in hospitalized persons with community-onset bacteremia, especially in the setting of COVID-19 (Lee et al., 2023).

In the context of infectious disease research, current mortality predictive models frequently revolve around decision points that occur simultaneously with the emergence of symptoms, such as the day fever begins or admission to the hospital. Despite this, there is a discernible deficiency in decision-making systems regarding treatment completion, as they neglect to account for clinical characteristics following treatment and therapeutic response. To address this gap, our study focuses on investigating the decision-making process subsequent to the completion of 14-day antibiotic therapy. In light of the persistent discourse on the effectiveness of extended antibiotic treatment (Ex-ATB), this is crucial to ascertain which patients are expected to derive benefit from these therapies. This approach aspires to improve antibiotic stewardship by assisting clinicians in the prudent use of antibiotics, ultimately enhancing patient outcomes and combating antibiotic resistance.

MATERIALS AND METHODS

Study Design and Population

We conducted a retrospective cohort study from January 2019 to April 2024. The study participants were hospitalized individuals admitted to a government hospital in Chiang Mai who had been diagnosed with HM and had undergone a 14-day ATB protocol to treat *A. baumannii* bacteremia. The approval for the retrospective data collection of the study was authorized by the ethics committee of Nakornping Hospital with document number NKP 079/65, on the condition that the collected data remained anonymous and did not require informed consent.

The inclusion criteria consisted of (i) patients who were 18 years of age or older and diagnosed with HM according to ICD10 codes C081 to C096; (ii) patients with documented evidence of AB bacteremia; (iii) patients who have undergone a 14-day ATB treatment course for AB bacteremia, and (iv) patients who were admitted to the study site during the indicated timeframe. The exclusion criteria included: (i) individuals with an Eastern Cooperative Oncology Group (ECOG) score of 4 or higher; (ii) patients who passed before hemoculture results were available; and (iii) situations where there was recovery from AB infection, but death occurred due to sickness caused by other pathogens.

Upon performing exhaustive statistical analyses, we have reached the determination that a sample size of 114 patients is required to attain a statistical power of 80% at a significance level of 5% (two-sided). This result is especially relevant for a group characterized by a significant mortality rate of 92% rate (Chaiwarit et al., 2005).

Data Collection

The laboratory department of the institution provided data on *A. baumannii* bacteremia and drug susceptibility. The demographic data of the patients was extracted from the hospital information system. This data comprised age, gender, diagnosis, disease severity, comorbidities, laboratory results, treatment regimen, clinical response, 30-day mortality, 30-day recurrence, and nephrotoxicity.

Statistical Analyses and Model Development

We performed descriptive analyses on the characteristics of the participants, the profiles of the diseases, the treatment regimens, and the durations. Comparing outcomes, including 30-day mortality, required the application of univariable and multivariable risk regression models, including logistic regression and the generalized linear model. The associations were evaluated by calculating the odd ratio (OR) and risk ratio (RR).

The multivariable logistic regression model was modified to account for a range of predictors.

Combination of domain expertise and statistical techniques, feature selection methods were subsequently implemented to identify relevant variables that have the potential to affect mortality outcomes significantly. Model internal validation and calibration analysis are performed to evaluate the accuracy and concordance between predicted probability and actual results. This requires evaluating the degree of correspondence between predicted probabilities and observed outcomes via a plot. All tests were conducted using a two-tailed approach, and statistical significance was determined using a p-value threshold of less than 0.05.

RESULTS AND DISCUSSION

During the course of this investigation, 188 participants were observed to have confirmed AB and HM bloodstream infections (BSI) while receiving AB-specific antibiotic treatment. A total of 119 participants successfully completed the conventional 14-day course of antibiotics. With a mean age of 52.2 years (SD: 1.8), 63% of the participants identified as male. A low performance status score of 2–3 was observed by the majority (81%) of patients. The predominant types of HM identified were diffused large B-cell lymphoma (DLBCL), acute myeloblastic leukemia (AML), multiple myeloma (MM), acute lymphoblastic leukemia (ALL), and primary central nervous system lymphoma (PCNSL), representing 20.2%, 19.3%, 14.3%, 10.9%, and 9.6% of cases, respectively. 94% of the patients were affected by infections caused by carbapenem-resistant *Acinetobacter baumannii* (CRAB). Despite this resistance, these infections were still susceptible to colistin, which was the major antibiotic (97.1%) used in this study. The average duration until AB-specific antibiotic treatment commenced was 8.2 days (standard deviation: 0.5). The average absolute neutrophil count (ANC) on day 14 of treatmentwas 4.771 cells/mm3 (standard deviation: 746). Throughout the 14-day course, all patients demonstrated micrologic response. Clinical improvement was observed in 61 patients (51.3%) after 14 days of treatment; likewise, acute kidney injury (AKI) occurred in 74 participants (62.2%). Upon the conclusion of the designated observation period, the participants exhibited a 30-day mortality rate of 47.9% (57 patients), and 14.5% (9 patients) experienced a recurrence of infection triggered by any type of pathogen (Table I).

The logistic regression analysis identified significant correlations between 30-day mortality and a number of variables. Considerations included age, ECOG score, time to begin AB-specific ATB, Pitt's bacteremia score, Charlson comorbidity score, APACHE II score, need for mechanical ventilation, cardiac arrest, septic shock, need for vasoactive agents, mental alteration, treatment goal for cancer, and clinical improvement following a 14-day ATB course. The multivariable regression analysis revealed a correlation between the complex interaction of clinical, demographic, and treatment-related factors in predicting the risk of mortality. A prudent incorporation of collinearity analysis, statistical metrics, and clinical insights was performed during the phase of model development in order to reduce complexity without compromising predictive success. This thorough effort intended to reconcile the complexities of predictive modelling, ensuring a delicate balance between accuracy and simplicity. Five key factors were determined by a thorough selection method that included the following: ECOG score, Pitt's bacteremia score, APACHE II score, time-to-start AB-specific ATB, and clinical improvement after a 14-day treatment regimen. The aforementioned critical factors were intentionally selected to constitute the basis of a robust predictive system, with each one carrying substantial importance in accurately predicting scenarios that are relevant to clinical practice (Table II). The outcome of these exhaustive operations resulted in the development of a highly precise predictive model. The model's outstanding predictive performance was underscored by its accuracy and consistency in event estimation, as indicated by its area under the Receiver Operating Characteristic curve (AUC-ROC) of 0.9943. In addition, the model's goodness-of-fit p-value of 0.8780 and Akaike's information criteria of 32.09 provide further support for the model's validation and applicability in clinical contexts. (Table III)

To further enhance the practicability of the model in clinical settings, a detailed scoring process was conducted to establish specific thresholds for each predictor, which correlate with an increasing risk of mortality. Significant cut-off points were determined for relevant predictors, such as an ECOG score of 2 or higher, a time-to-start AB-specific ATB of 7 days or longer, a Pitt's bacteremia score of 5 or higher, an APACHE II score of 11 or higher, and the existence of clinical improvement.

Table I. Prognostic factors of hospitalized patients with hematologic malignancy systemically infected by Acinetobacter baumannii after completion of standard course ATB (14 days) were classified by mortality at 30 days of observation.

Prognostic Factors	Total n = 119	Non-Survivors n = 57	Survivors n = 62	Testing Method	p-value
Gender, n (%)					
Female	44 (37.0)	23 (40.3)	21 (33.9)	Fisher's exact	0.569
Male	75 (63.0)	34 (59.7)	41 (66.1)		
Age (year), mean (SD) *	52.2 (1.8)	56.8 (2.7)	58.0 (2.2)	Independent t-test	0.013
ECOG performance status, n (%)*					
0-1	22 (18.5)	1 (1.8)	21 (33.9)	Fisher's exact	<0.001
2-3	97 (81.5)	56 (98.2)	41 (66.1)		
Type of HM, n (%) †					
DLBCL	24 (20.2)	10 (17.5)	14 (22.6)	Fisher's exact	0.648
AML*	23 (19.3)	6 (10.5)	17 (27.4)		0.022
MM*	17 (14.3)	13 (22.8)	4 (6.5)		0.017
ALL	13 (10.9)	7 (12.3)	6 (9.7)		0.771
PCNSL	9 (7.6)	3 (5.3)	6 (9.7)		0.494
Others	33 (27.7)	18 (15.1)	15 (12.6)		0.034
ANC (cells/mm3), mean (SD) *	4,771 (746)	6,504 (1,410)	3,178 (552)	Independent t-test	0.026
Charlson Comorbidity Index, mean (SD) *	3.66 (0.2)	4.2 (0.3)	3.1 (0.2)	Independent t-test	0.006
Pitt's Bacteremia Score, mean (SD) *	5.3 (0.3)	7.4 (0.3)	3.5 (0.3)	Independent t-test	<0.001
APACHE II Score, mean (SD) *	13.7 (0.5)	15.5 (0.7)	12.0 (0.7)	Independent t-test	0.001
Time-to-Start AB-specific ATB (days), mean (SD) *	8.2 (0.5)	10.0 (0.8)	6.5 (0.7)	Independent t-test	0.001
Carbapenem-Resistant AB (CRAB), n (%)	112 (94.1)	56 (98.3)	56 (90.3)	Fisher's exact	0.116
Clinical Response, n (%)*	61 (51.3)	1 (1.75)	60 (96.8)	Fisher's exact	<0.001
Acute Kidney Injury (AKI), n (%)*	74 (62.2)	46 (80.7)	28 (45.2)	Fisher's exact	<0.001

*Significant difference with p-value less than 0.05.
†Standard deviation (SD);Eastern Cooperative Oncology Group (ECOG); diffused large B-cell lymphoma (DLBCL); acute myeloblastic leukemia (AML); multiple myeloma (MM); acute lymphoblastic leukemia (ALL); Primary central nervous system lymphoma (PCNSL); absolute neutrophil count (ANC); inter-quartile range (IQR); carbapenem-resistant Acinetobacter baumannii (CRAB); acute physiology and chronic health evaluation II (APACHE II).

Table II. The Predictive Performance of Predictors in the "Ex-CSEPA" Model

Predictor		OR††	95% CI	p-value	AUC-ROC	Coefficient	Score
ECOG performance status score	0-1	reference					0
	2-3	28.6	3.7-221.9	0.001	0.6606	1.7	1
Time-to-start AB-specific ATB	0-6	reference					0
	7 or more	7.4	3.3-16.6	<0.001	0.7306	15.9	10
Clinical Improvement	Failure	reference					0
	Improved	0.0006	0.001-0.006	<0.001	0.9751	-23.0	-14.5
Pitt's bacteremia score	0-4	reference					0
	5 or more	22.9	7.8-66.8	<0.001	0.8037	1.7	1
APACHE II score	0-10	reference					0
	11 or more	6.3	2.5-16.0	<0.001	0.6769	0.5	0.5

††Odd ratio (OR); area under the Receiver Operating Characteristic curve (AUC-ROC).

Table III. Model Predictive Performance

Model	Predictors	AUC-ROC	p-value**	AIC†††
Original Model	5	0.9943	0.8780	32.09
Scoring Model	1	0.9859	0.3515	25.42
Classified Score Model*	1	0.9870	N/A	25.52

*Cutoff of 0.5 point or more obtains sensitivity, specificity, positive predictive value, negative predictive value, false negative rate, and false positive rate of 99.07%, 98.33%, 99.07%, 98.33%, 1.67%, and 0.93%, respectively; **p-value of Goodness-of-fit test; †††Akaike's information criterion (AIC)

After establishing the threshold points, a multivariable logistic regression analysis was performed to determine the quantitative influence of each stratified group and to implement coefficient evaluation to convert the risk, which was represented by odds ratios, into a scoring system (Table II). The scoring model's predictive performance was reassessed to maintain accuracy standards. The model displayed a remarkable AUC-ROC value of 0.9859, which indicates excellent predictive capabilities. An AIC value of 25.42, considered satisfactory, and a goodness-of-fit p-value of 0.3515, indicating an adequate match to the data, supported the model's performance (Table III).

Patients were classified into low (-14.5–0 points) and high (0.5–12.5 points) risk categories based on their probability of mortality within 30 days, with corresponding rates of 1.67% and 99.07%, respectively. The model exhibited a sensitivity of 99.07% and a specificity of 98.33% when a cut-off points of 0.5 was established for predictive performance. The predictive effectiveness of the model persisted when patients were categorized based on a cut-off score of 0.5; the AUC-ROC value was 0.9870 and the AIC was 25.52. The findings suggest that the model demonstrates potential as an effective method to predict 30-day mortality rates in patients with HM and AB bacteremia by emphasizing its resilience and constancy in accurately stratifying patient risk levels (Table III).

As for the model's validity, a Cumulative Incidence of Treatment Limitation (CITL) of 0.000 is seen in the plot of expected risk versus observed risk. A value of 1.000 for the slope indicates a strong correlation between the observed risk and the expected risk, thereby emphasizing the accuracy of the model. The Area Under the Curve (AUC) value of 0.989 indicates a thorough evaluation of the model's reliability and discriminative capability in predicting clinical results (Figures 1A). For evaluation of the calibration performance of the model, we investigated the correlation between the observed outcomes and the probabilities or risks predicted by the model through modelling and evaluation of risk. This analysis provides a comprehensive overview of the model's capacity to precisely predict the probability of certain specific outcomes, therefore improving its confidence and practicality in clinical settings (Figure 1B).

The decision-tree model, named "Ex-CSEPA," has been developed based on the scoring system established with the prediction model. This decision-tree outlines the consecutive stages of the process of making decisions in accordance with the criteria of the scoring system (Figure 2). The clinical improvement should be evaluated initially in individuals with HM who have finished a 14-day course of AB-specific ATB. Individuals who achieve clinical improvement, as indicated by a score of -14.5, could be permitted to discontinue ATB treatment. Conversely, those who reveal clinical failure should be revised of the time-to-start AB-specific ATB when the infectious symptoms occurred. Late-onset specific ATB may have occurred in cases where pathogen identification was delayed, a circumstance that, according to the scoring model, is associated with an increased risk of mortality. Patients who have exceeded the 7-day threshold for initiating AB-specific treatment, which will obtain a score of 10, should be provided Ex-ATB, either with or without additional imaging and microbiological testing, to rule out co-infection or infection by another pathogen. Additionally, consideration of the potential benefits of granulocyte-colony stimulating factor (GCSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) or requesting the counsel of an infectious disease (ID) professional might be beneficial to these individuals.

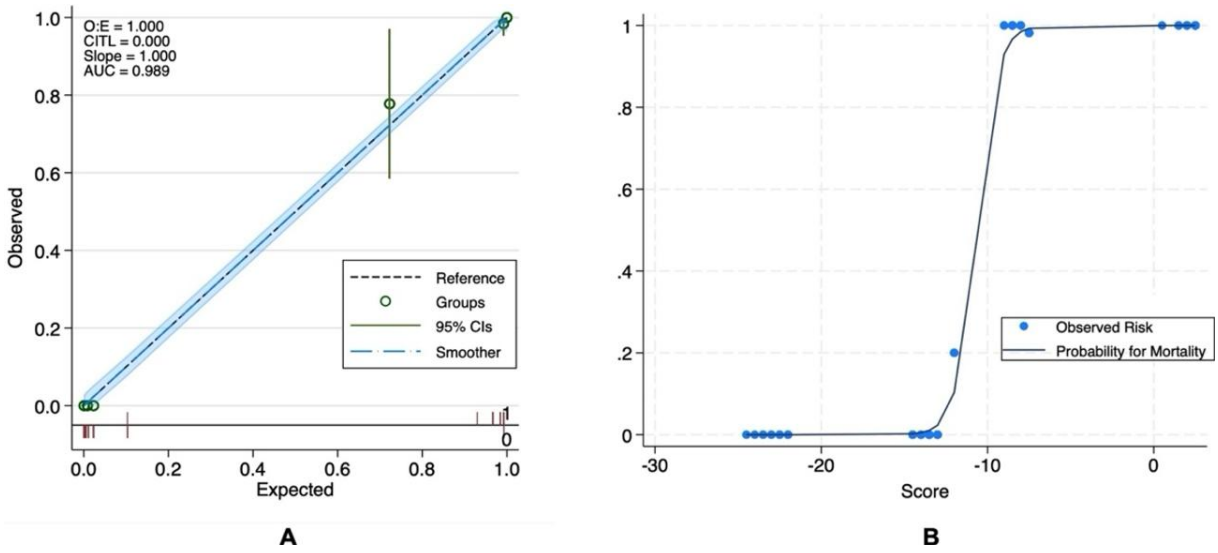

Figure 1. (A)The plot of expected risk versus observed risk demonstrates the Cumulative Incidence of Treatment Limitation (CITL) of 0.000, the slope shows the correlation between observed risk and expected risk (of 1.000, and predictive performance (AUC) of 0.989. (B) The calibration risk curve of the "Ex-CSEPA" model, a visual tool utilized in predictive modeling and risk assessment to evaluate the calibration performance of the model, shows the relationship between the actual observed outcomes and the predicted probabilities or risks generated by the model.

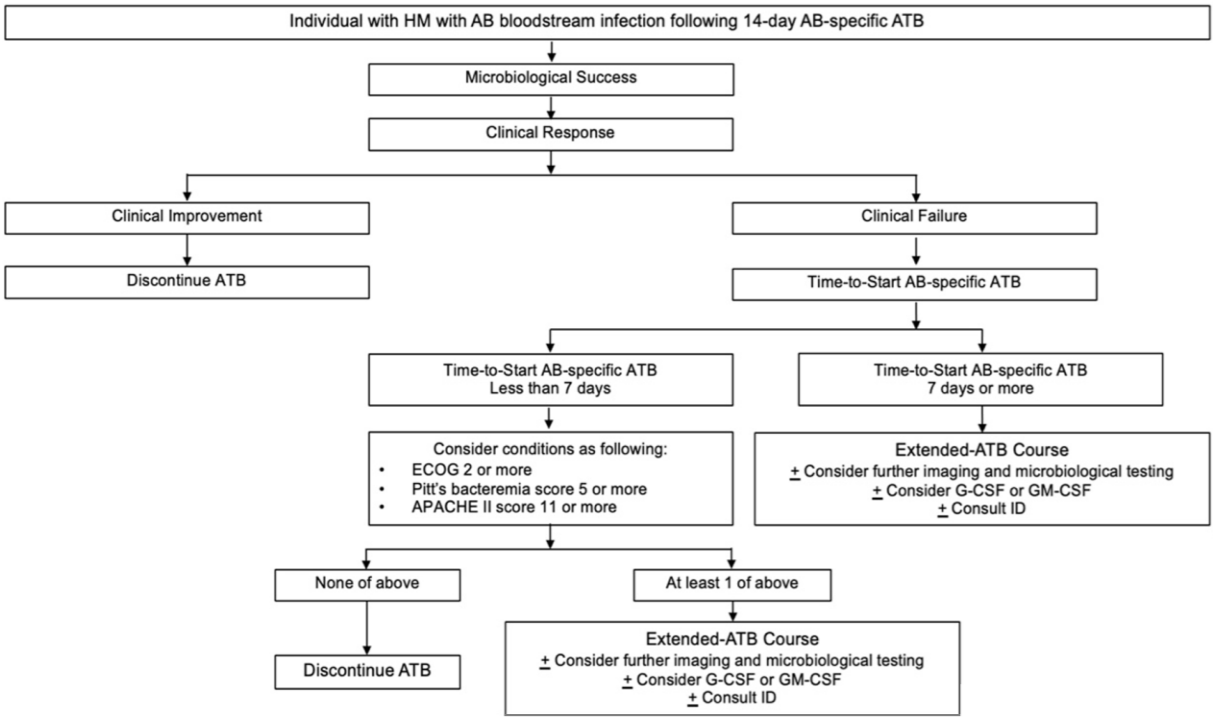

Figure 2. Decision tree of the "Ex-CSEPA" decision-making model.

Patients who received antibiotic (AB) treatment within 7 days following the onset of infection symptoms should be evaluated for the following additional conditions: an ECOG score of 2 or higher (score of 1), a Pitt's bacteria score of 5 or higher (score of 1), and an APACHE II score of 11 or higher (score of 0.5). Patients who have at least one of the aforementioned conditions should be considered using Ex-ATB and also consider further microbiological investigation, taking advantage of G-CSF or GM-CSF, and consultation with an infectious disease specialist. AB treatment should be discontinued for patients who do not have any of the conditions mentioned previously.

This study focuses on developing mortality prediction tools tailored for hematologic malignancy (HM) patients with *Acinetobacter baumannii* (AB) bacteremia who have undergone a 14-day antibiotic regimen. The aim is to identify high-risk patients who may benefit from extended-course antibiotic therapy (Ex-ATB). Unlike existing mortality prediction models, which typically centre around symptom onset or hospital admission, our study addresses the gap in decision-making systems concerning treatment completion. By examining the post-treatment clinical characteristics and response, we aim to enhance the discernment of patients suitable for Ex-ATB, given the ongoing debate surrounding its efficacy and potential complications.

Significant cut-off points were determined for relevant predictors, such as an ECOG score of 2 or higher, a time-to-start AB-specific ATB of 7 days or longer, a Pitt's bacteremia score of 5 or higher, an APACHE II score of 11 or higher, and the existence of clinical improvement. The significance of severity scores, specifically Pitt's bacteremia score and APACHE II score, in evaluating clinical conditions correlated with fatality and severity is emphasized by their incorporation in the developed predictive model. The incorporation of this component greatly improves the model's efficacy and capability to precisely detect patients who are at increased risk. The model demonstrated its strong predictive capabilities with a sensitivity of 99.07% and a specificity of 98.33% when evaluated at a threshold of 0.5. A relatively low probability of negative effects was indicated by the mean predicted risk of 0.08 (SD of 0.02) for the low-risk group. The mean predicted risk for the high-risk group, on the other hand, was considerably greater at 0.96 (standard deviation: 0.01), indicating a considerably increased probability of mortality risk. The system exhibits outstanding precision, accurately identifying individuals at a higher risk of mortality with a rate of 98.7%.

The decision-making system established through this study has been designated as the "Ex-CSEPA" model. The step-by-step procedure of making decisions in accordance with the criteria of the scoring system is delineated in this decision tree. This acronym reflects the consecutive steps involved in estimating the likelihood of a fatality depending on the specified parameters. The "Ex" in "Ex-CSEPA" stands for extended antibiotic treatment (Ex-ATB) consideration, which is the point at which the duration of antibiotic therapy is decided. The letter "C" represents clinical improvement, which is used to evaluate whether patients show an improvement in response to treatment. The letter "S" represents the starting time of AB-specific treatment, signifying the assessment of when antibiotic therapy was commenced with regard to the development of infection symptoms. The letter "P" is used to refer to Pitt's bacteremia score, which is an assessment of the severity of a BSI. Finally, the letter "A" represents the APACHE II score, an index used to evaluate the degree of sickness and predict the clinical outcome of patients who are critically ill. These components constitute the main predictors in the Ex-CSEPA model for assessing the risk of mortality.

The severity of illness demonstrates the crucial relationship between a patient's clinical condition and the potential for negative outcomes, especially mortality (Knaus et al., 1985; Rhee et al., 2009). This research defined significant cut-off points for various severity scores, including an ECOG score of 2 or higher, a Pitt's bacteremia score of 5 or higher, and an APACHE II score of 11 or higher. The model additionally encompasses clinical response following a 14-day treatment, thereby improving the predictive accuracy. These indicators function as critical metrics for assessing patient prognosis and guiding treatment decisions. The time-to-treatment argument underscores the significance of timely intervention; delays in beginning appropriate therapy may lead to worse outcomes in conditions related to bacteremia. Obstacles facilitate pathogen proliferation, thereby elevating the risk of complications involving septic shock and multi-organ failure, which correspond with increased mortality rates. Each hour of delay in administering effective antibiotics has been consistently shown to increase the risk of mortality, according to research. Proper management is vital to avoiding the development of antibiotic

resistance and maintaining the curative effects of existing therapies. The model's elevated sensitivity and specificity substantiate the importance of assessing patients' clinical condition and illness severity while ensuring timely treatment to optimize clinical decision-making and improve patient outcomes in bacteremia related to hematologic malignancies.

As for practical use in clinical settings, effective use of the decision tree necessitates the integration of a number of critical stages into routine clinical practice. Initial healthcare establishments may integrate the decision tree functionality into their electronic health record systems, thereby facilitating clinicians' access to relevant data during patient consultations. To assist clinicians in managing HM and *Acinetobacter baumannii* bloodstream infection (AB-BSI), healthcare personnel should receive training on the decision-making framework. Implementation strategies could include conducting seminars and disseminating educational materials to improve healthcare providers' comprehension of the decision tree's interpretation and application. Furthermore, consistent revisions and updates to the decision tree ought to be enabled in order to incorporate any developments in clinical research or modifications in treatment protocols. To integrate and use the decision-making system in healthcare settings, ease of use, accessibility, and compliance with clinical workflows must be considered.

Acknowledging the inherent limitations of retrospective studies and the fact that our model was constructed using data gathered during a time when colistin was the predominant treatment for AB infections is crucial. Notwithstanding this constraint, our model represents an innovative approach to estimating mortality thirty days after the onset of the signs and symptoms of infection, with particular emphasis on the day following the completion of the typical fourteen-day course of antibiotic treatment. In contrast to current instruments, including the Pitt Bacteremia Score (PBS) in conjunction with the Charlson Comorbidity Index or Chronic Disease Score, which prioritize short-term mortality and cumulative comorbidities (Vaquero-Herrero et al., 2017), or frameworks like the Emergency Department Bacteremia Mortality (ED-BM) tool (Chiang et al., 2021), which emphasizes predictors of 7-day mortality, our model broadens the predictive perspective to encompass essential post-treatment decision-making junctures in patient management. In addition, recent research on mortality prediction models for patients with concurrent COVID-19 infection and bacteremia emphasizes dynamic clinical parameters, supporting our model's attention to clinical circumstances as key predictors (Lee et al., 2023).

The model's ability to be used in other situations may be limited by its reliance on past treatment methods; instead, the approach offers an important move toward finding key decision points in patient care. Therefore, in regard to the management of AB infections. This constitutes a significant contribution to the advancement of more sophisticated and therapeutically relevant predictive strategies.

Future study projects could investigate additional avenues for improving the robustness and applicability of the decision-making system. Conducting validation studies involving patient cohorts that are larger and more diverse from the start could provide significant insights into the model's ability to generalize and maintain external validity in various healthcare settings and patient populations. Moreover, the inclusion of additional clinical factors, especially biomarkers or imaging data, could enhance the precision of the model's predictions. Furthermore, conducting prospective studies to assess the practical application of the decision-making system in clinical practice would provide valuable information about the system's accessibility, performance, and impact on patient outcomes. Additionally, the dynamic nature of antimicrobial resistance and treatment guidelines necessitates that the model be constantly updated to accommodate changes in antibiotic prescribing practices and pathogen susceptibility patterns. This is necessary to ensure that the model remains applicable and practical in modern healthcare environments.

CONCLUSION

In patients with HM, the Ex-CSEPA model provides an innovative and efficient decision-making tool for the management of AB-BSI. The model provides a precise classification of patients into high- and low-risk groups by integrating five essential clinical predictors: ECOG score, time to initiate antibiotic therapy, clinical response following a 14-day treatment, Pitt's bacteremia score, and APACHE II score. These findings empower clinicians to make more informed decisions regarding the extension of antibiotic therapy, optimizing antibiotic utilization, reducing infection recurrence, and improving patient

outcomes. The model demonstrates considerable potential for enhancing individualized treatment strategies; however, further validation and refinement are necessary to ensure its broader applicability across various clinical setting. Nevertheless, the Ex-CSEPA model represents a significant advancement in personalized AB-BSI management, offering valuable therapeutic advantages in guiding treatment decisions.

ACKNOWLEDGMENTS

This research work was partially supported by Chiang Mai University. The assistance provided by Associate Professor Dr. Dujrudee Chinwong, Assistant Professor Dr. Jukapun Yoodee, Assistant Professor Preyanate Wilairat, Miss Thanaporn Wongnava, Mr. Assawin Dadookel, and Nakornping Hospital was greatly appreciated.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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