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Burns

Predictors of Sepsis and Sepsis-related Mortality in Critically Ill Burn Patients: A Single Tertiary Care Center Experience

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Background: Clinical diagnosis of sepsis is challenging, emphasizing the importance of regular bacterial surveillance, and tailored antimicrobial therapy. This study aims to elucidate the predictors of sepsis in critically ill burn patients.

Methods: A retrospective analysis was conducted on patients admitted to the burn intensive care unit between 2016 and 2022. Demographics, type of burn, total body surface area (TBSA), presence of inhalation injury, mortality, sepsis, deep vein thrombosis, pulmonary embolism, pneumonia, cultures, and laboratory findings were collected. Descriptive statistics and survival analysis were used to analyze trends during the 7-year period.

Results: The study encompassed 196 participants. Among patient factors, men constituted 73.4% (n = 102) of those without sepsis and 86.0% (n = 49) with sepsis, with an association between sepsis and lower age (34 versus 41 years) as well as larger TBSA (41.1% versus 17.3%). Inhalation injury was a significant predictor of sepsis [35.1% (n = 20) versus 11.6% (n = 16)]. Mortality was higher in sepsis cases [17.5% (n = 10) versus 2.9% (n = 4)], as well as positive blood cultures [47.4% (n = 27) versus 2.2% (n = 3)], positive wound cultures [71.9% (n = 41) versus 12.2% (n = 17)], and positive fungal cultures [12.3% (n = 7) versus 0% (n = 0)]. Multivariable analysis identified age and TBSA as significant predictors of sepsis ($P = 0.025$, $P < 0.001$).

Conclusions: Age, TBSA affected emerge as a strong risk factor for sepsis among critically ill burn patients. It underscores the need for vigilant monitoring to improve outcomes and reduce sepsis-related mortality. *(Plast Reconstr Surg Glob Open 2024; 12:e6180; doi: 10.1097/GOX.0000000000006180; Published online 18 September 2024.)*

INTRODUCTION

Burn wound infection is one of the most frequent causes of morbidity and mortality in burn.[1] Burns that necessitate admission include those covering 10% of a child's body surface area or 15% of an adult's body surface area, and those with airway involvement; hence, these are considered major burns.[2,3] Age also plays a significant role in relation to a patient's mortality especially in those over the age of 65 years.[4] Additionally, 75% of all fatalities in patients with severe burns are brought on by sepsis.[5] According to literature, a huge systemic inflammatory response syndrome and cellular and humoral immune response depression are what lead to sepsis in burn patients.[6] A large cutaneous bacterial inoculum, the potential for gastrointestinal bacterial translocation, extended hospitalization, and invasive diagnostic and therapeutic procedures are additional risk factors for sepsis in burn patients.[7] However, the management of infections in burn patients is becoming more challenging due to the global increase in the frequency of drug-resistant microorganisms.[8] The depth of the infection cannot be determined by microbiological analysis of surface swabs and biopsies from burn wounds, which provides accurate information about the kind of infection and the bacterial

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charge.[9,10] The diagnosis of infection consequently relies on clinical factors with the use of blood and surface or tissue/biopsy cultures to identify the likely culprit.[11,12] Gram-negative pathogens make up the majority of the bacteria that have been isolated in numerous burn units.[13] *Pseudomonas aeruginosa* (74%), *Escherichia coli* (35%), *Acinetobacter baumannii* (24%), Coagulase-negative staphylococci (21%), and Enterococcus spp. (14%) are the most frequently isolated gram-negative bacteria in burn units around the world.[14,15] However, the range of microbial colonization varies between burn units, periodically and geographically. Strict aseptic procedures, the use of sterile hands and dressing materials, the wearing of masks while applying dressing changes, particular patient separation, and the use of private rooms are amongst measures that have been adopted to reduce the risk of infection.[16] Due to immune deficiencies brought on by thermal injury, malnutrition, anemia (reperfusion impeded), and immunological barrier damage, bacteremia may be symptomatic or asymptomatic.[17,18] Infection in burn patients is a major source of morbidity and mortality, and it continues to be a serious problem. The goals of this research are to identify bacteremia, sepsis, and sepsis-related mortality in critically ill burn patients. The primary aim of this study is to determine the relationship between the predictors of bacteremia, sepsis, and sepsis-related mortality in critically ill burn patients. By achieving this objective, we will gain insight into the factors associated with sepsis and mortality in burn patients as well as the most common pathogens found in burn patients.

Takeaways

Question: What are the predictors of sepsis and sepsis-related mortality in critically ill burn patients?

Findings: Age, total body surface area affected, inhalation injury, and flame burns are risk factors for sepsis among critically ill burn patients.

Meaning: These factors (age, extent of burns, respiratory tract involvement, and the nature of the burn) are significant predictors of sepsis, a severe and potentially life-threatening infection, in patients with critical burn injuries.

METHODOLOGY

Study Design and Setting

This was a single-center retrospective cohort study conducted at King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia. KAMC is an academic government-funded tertiary hospital that combines clinical care, training, academics with research, and state-of-the-art medical technologies. There are eight beds in the KAMC burn unit, specifically for patients with burn injuries.

Inclusion and Exclusion Criteria

All adults aged 18 years or older who were admitted to the burn unit from January 2016 to December 2022 were included in the study. Patients with missing essential data were excluded; however, no specific exclusion criteria were applied.

Data Collection

The required data were obtained by screening the electronic medical records via the BESTCare electronic system (ezCareTech, South Korea) of all the patients who met the inclusion criteria. The following data were collected: demographic data, including age, gender, and body mass index (BMI), comorbidities, type of burn, total body surface area (TBSA), the presence of inhalation injury, blood and wound culture results, growing organisms, including fungal organisms, antimicrobial susceptibility pattern, diagnosis of sepsis, deep vein thrombosis (DVT), pulmonary embolism (PE), and pneumonia, laboratory parameters, and survival status. To define sepsis in this article, the American Burn Association criteria for sepsis was used.[19]

Statistical Analysis

Descriptive statistics were computed to summarize participant characteristics. Categorical variables were presented as frequencies and percentages, whereas continuous variables were presented as medians with interquartile ranges (IQRs). Fisher exact tests were used to assess associations between categorical variables and sepsis, whereas independent samples Mann-Whitney U tests were used for continuous variables. Nonparametric tests were chosen for the analysis of continuous variables due to the nonnormal distribution of these variables, as assessed by Q-Q plots and the Kolmogorov-Smirnov test ($P < 0.05$). Additionally, multivariable logistic regression analysis was conducted to identify predictors of sepsis. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated to quantify the strength of associations between predictor variables and sepsis status. Significance was established at a P value of 0.05. All statistical calculations were performed using IBM SPSS, version 27.0.1.

Ethical Consideration

The study was approved by the institutional review board of King Abdullah International Medical Research Center, Ministry of National Guard-Health Affairs, Riyadh, Saudi Arabia (NRC22R/590/12). Informed consent was waived because of the retrospective nature of this study. Access to the data was restricted to the researchers. The confidentiality of all patients was protected, and no names or medical record numbers were used. Privacy and confidentiality were assured, and all the hard and soft copies of data were kept in a secure place within the Ministry of National Guard-Health Affairs premises. This study complies with the Declaration of Helsinki.

RESULTS

Patient-related Factors

Of the 196 participants, 23% were women and 77% were men, with a median BMI of 27.00 (IQR = 23.02–31.31). Most participants did not have diabetes mellitus (82.1%) or hypertension (HTN) (86.7%), and the majority

were nonsmokers (87.2%). Flame burns were the most common (57.1%), followed by scalds (17.3%) and chemical burns (10.7%). The median TBSA affected was 18.0% (IQR = 6.5–33.5). Inhalation injury was present in 18.5% of cases, and sepsis occurred in 29.1%, with a median of 2 days from admission to diagnosis (IQR = 1.00–7.00). Mortality was observed in 7.1% of patients. Positive blood cultures were found in 15.3% of cases, whereas positive wound cultures were observed in 29.6%. Fungal wound cultures were positive in 3.6% of cases (Table 1).

Laboratory Findings and Complications

The median hemoglobin level was 141.00 (IQR = 115.00–159.50), creatinine was 69.00 (IQR = 58.00–86.00), procalcitonin was 0.63 (IQR = 0.13–2.07), lactate was 2.25 (IQR = 1.43–4.01), lactate dehydrogenase (LDH) was 292.00 (IQR = 234.50–445.50), white blood cell (WBC) count was 10.80 (IQR = 7.78–14.50), erythrocyte sedimentation rate (ESR) was 52.00 (IQR = 24.00–76.00), C-reactive protein (CRP) was 114.00 (IQR = 72.00–304.00), and platelet count was 282.50 (IQR = 228.50–366.50). Pneumonia was observed in 20.4% of participants, whereas DVT was rare (0.5%). PE was also infrequent, occurring in 1.5% of cases. These findings highlight the range of laboratory abnormalities and complications experienced by burn patients (Table 2).

Factors Associated with Sepsis

Regarding gender, men constituted 73.4% of those without sepsis and 86.0% of those with sepsis ($P = 0.063$). Similarly, for comorbidities, the prevalence of DM was 20.9% among those with sepsis compared with 10.5% among those without sepsis ($P = 0.102$), and HTN was observed in 14.4% of sepsis cases versus 10.5% without sepsis ($P = 0.643$). Smoking status showed no significant association with sepsis ($P = 0.814$).

Age was significantly lower in the sepsis group (31.00, IQR = 25.00–40.00) compared with those without sepsis (38.00, IQR = 29.00-50.00) ($P = 0.008$). Similarly, patients with sepsis had a larger median TBSA of 40.0% (IQR = 20.0–55.0) compared with 12.0% (IQR = 5.0–24.2) in the nonsepsis group ($P < 0.001$).

Furthermore, significant associations were observed between sepsis and the type of burn and presence of inhalation injury ($P < 0.05$) in univariate analysis. Notably, flame burns were more strongly associated with sepsis compared with other types ($P = 0.002$). Similarly, inhalation injury emerged as a significant predictor of sepsis, with 35.1% of patients with sepsis presenting with inhalation injury compared with 11.6% of those without sepsis ($P < 0.001$). However, subsequent multivariable analysis, demonstrated in Table 3, revealed nonsignificant associations of type of burn and inhalational injury with sepsis,

Table 1. Sociodemographic Characteristics, Comorbidities, Sepsis, Mortality, and Culture Results of Participants

		N	%	Median	IQR
Age				35.00	27.00–47.50
Sex	Female	45	23.0%		
	Male	151	77.0%		
BMI				27.00	23.02–31.31
Diabetes	No	161	82.1%		
	Yes	35	17.9%		
HTN	No	170	86.7%		
	Yes	26	13.3%		
Smoker	No	171	87.2%		
	Yes	25	12.8%		
Type of burn	Flame	112	57.1%		
	Scald	34	17.3%		
	Chemical	21	10.7%		
	Contact	10	5.1%		
	Electrical	18	9.2%		
	Friction	1	0.5%		
TBSA (%)				18.0	6.5–33.5
Inhalation injury	No	159	81.5%		
	Yes	36	18.5%		
Sepsis	No	139	70.9%		
	Yes	57	29.1%		
Days from admission to sepsis diagnosis				2.00	1.00–7.00
Patient passed away	No	182	92.9%		
	Yes	14	7.1%		
Positive blood culture	No	166	84.7%		
	Yes	30	15.3%		
Positive wound culture organism	No	138	70.4%		
	Yes	58	29.6%		
Positive wound fungi culture	No	189	96.4%		
	Yes	7	3.6%		

Table 2. Laboratory Findings and Complications among the Participants

		Median	IQR	N	%
Hemoglobin (g/L)		141.00	115.00–159.50	196	
Creatinine (μmol/L)		69.00	58.00–86.00	195	
Procalcitonin (ng/mL)		0.63	0.13–2.07	47	
Lactate (mmol/L)		2.25	1.43–4.01	114	
LDH (U/L)		292.00	234.50–445.50	84	
WBC		10.80	7.78–14.50	195	
ESR (mm/h)		52.00	24.00–76.00	79	
CRP (mg/L)		114.00	72.00–304.00	39	
Platelet		282.50	228.50–366.50	196	
Pneumonia	No			156	79.6%
	Yes			40	20.4%
DVT	No			195	99.5%
	Yes			1	0.5%
PE	No			193	98.5%
	Yes			3	1.5%

Table 3. Multivariable Logistic Regression showing Predictors of Sepsis

			95% CI for AOR		
Predictors		**AOR**	Lower	Upper	***P***
Age		0.959	0.925	0.995	0.025*
Sex	Female				
	Male	10.073	0.373	30.083	0.896
BMI		0.981	0.933	10.031	0.449
Diabetes	No	Ref	Ref	Ref	Ref
	Yes	1.205	0.282	5.142	0.801
HTN	No	Ref	Ref	Ref	Ref
	Yes	4.336	0.909	20.673	.066
Smoker	No	Ref	Ref	Ref	Ref
	Yes	1.301	0.412	4.110	0.653
Type of burn					0.671
	Flame	Ref	Ref	Ref	Ref
	Scald	0.806	0.207	3.142	0.756
	Chemical	0.534	0.100	2.854	0.463
	Contact	0.732	0.072	7.476	0.793
	Electrical	2.491	0.722	8.590	0.149
	Friction	0.000	0.000		1.000
TBSA (%)		1.044	1.024	1.065	<0.001*
Inhalation injury	No	Ref	Ref	Ref	Ref
	Yes	2.078	0.771	50.597	0.148
Constant		0.623			0.675

suggesting that the significant associations observed in the univariate analysis were attributed to potential confounders such as TBSA and age.

Mortality and Culture Results

Similarly, mortality rates were significantly higher among patients with sepsis, with 17.5% of sepsis cases resulting in mortality compared with only 2.9% in the absence of sepsis ($P < 0.001$).

Regarding culture results, positive blood cultures were substantially more prevalent in patients with sepsis, accounting for 47.4% of cases, compared with a mere 2.2% among those without sepsis ($P < 0.001$). Positive wound cultures were significantly associated with sepsis, with 71.9% of sepsis cases exhibiting positive wound cultures compared with 12.2% in the absence of sepsis ($P < 0.001$). Fungal wound cultures also demonstrated a notable association with sepsis, with 12.3% of sepsis cases yielding positive results, contrasting starkly with the absence of positive fungal cultures in nonsepsis cases ($P < 0.001$).

Laboratory Findings and Complications

Pneumonia demonstrated a significant association with sepsis, with 50.9% of patients with sepsis having pneumonia compared with only 8.6% among those without sepsis ($P < 0.001$). Similarly, PE showed a significant association with sepsis, with 5.3% of sepsis cases having PE compared with none in the nonsepsis group ($P = 0.024$; Table 4).

Hemoglobin levels were significantly lower in patients with sepsis (113.00, IQR = 89.00–161.00) compared with those without sepsis (147.00, IQR = 127.00–159.00; $P < 0.001$). Although not statistically significant, trends

Table 4. Association of Sepsis with Laboratory Findings and Complications

		Sepsis								
		No				Yes				
		Median	IQR	N	Column %	Median	IQR	N	Column %	P*†
Hemoglobin (g/L) (n = 196)		147.00	127.00–159.00			113.00	89.00–161.00			<0.001‡
Creatinine (μmol/L) (n = 195)		70.00	60.00–86.00			63.00	54.00–84.00			0.249
Procalcitonin (ng/mL) (n = 47)		0.50	0.05–2.50			0.74	0.15–2.04			0.445
Lactate (mmol/L) (n = 114)		2.33	1.50–4.01			2.11	1.38–3.90			0.466
LDH (U/L) (n = 84)		282.50	230.00–451.00			292.50	245.00–415.00			0.483
WBC (n = 195)		10.20	7.70–13.50			12.00	7.90–16.80			0.089
ESR (mm/h) (n = 79)		53.50	23.50–78.00			50.00	24.00–66.00			0.984
CRP (mg/L) (n = 39)		97.50	60.00–198.00			122.00	82.00–358.00			0.223
Platelet (n = 196)		290.00	236.00–356.00			277.00	218.00–444.00			0.798
Pneumonia	No			127	91.4%			29	50.9%	<0.001‡
	Yes			12	8.6%			28	49.1%	
DVT	No			139	100.0%			56	98.2%	0.291
	Yes			0	0.0%			1	1.8%	
PE	No			139	100.0%			54	94.7%	0.024‡
	Yes			0	0.0%			3	5.3%	

*Fisher exact test.
†Independent samples Mann-Whitney U test.
‡$P < 0.05$, significant.

toward significance were observed for other parameters such as WBC count ($P = 0.089$) and CRP ($P = 0.223$; Table 4).

Predictors of Sepsis

The multivariable logistic regression analysis aimed to identify predictors of sepsis among burn patients. The results indicate that age was a significant predictor, with each unit increase associated with a slightly decreased odds of sepsis (AOR = 0.959, 95% CI = 0.925–0.995, $P = 0.025$). TBSA emerged as a significant predictor, with higher TBSA associated with increased odds of sepsis (AOR = 1.044, 95% CI = 1.024–1.065, $P < 0.001$). Among comorbidities, HTN showed a trend toward significance (AOR = 4.336, 95% CI = 0.909–20.673, $P = 0.066$), suggesting that patients with HTN may have higher odds of developing sepsis. Other factors such as gender, BMI, DM, smoking status, and the type of burn did not show significant associations with sepsis. These findings highlight age and TBSA as key predictors of sepsis risk in burn patients, emphasizing the importance of assessing these factors in clinical management and risk stratification (Table 3).

DISCUSSION

The debate over predictors of sepsis and sepsis-related mortality in critically ill burn patients centers on establishing reliable indications that can be used for early sepsis detection and, ultimately, patient outcomes. This promotes a better knowledge of sepsis in the context of burn injuries. The present study provides analysis of sepsis among critically ill patients with burns, highlighting the relationship between patient-related factors, laboratory findings, and clinical outcomes. Our study contributes to the body of current literature in several significant ways. It provides data on critically ill burn patients in Saudi Arabia, who may have more distinct genetic, environmental, and healthcare system characteristics than other groups. This aids in understanding how regional differences affect sepsis outcomes. Furthermore, it sheds light on the effectiveness of the local healthcare system, treatment procedures, and resource usage in managing sepsis in burn patients. Reports on sepsis-related mortality rates in critically ill burn patients may also provide a baseline for other tertiary care centers in comparable settings.

The predominance of flame burns (57.1%) aligns with findings from other studies indicating that this type of burn is often the most common and associated with higher morbidity.[20] The incidence of sepsis (29.1%) within an average of 9 days postadmission suggests a critical window for monitoring and intervention to prevent sepsis in burn patients, which is supported by literature emphasizing early diagnosis and management to improve outcomes.[21] The mortality rate (7.1%) falls within the expected range for burn-associated sepsis, considering the high risk of complications and death in these patients.[22]

The laboratory parameters indicate a significant inflammatory response and organ dysfunction, which are common in burn patients due to SIRS and subsequent sepsis.[21] The elevated mean levels of procalcitonin and lactate are particularly noteworthy, as they are established biomarkers for sepsis and have been shown to correlate with severity and prognosis in burn patients. The high prevalence of pneumonia (20.4%) is consistent with previous reports, highlighting respiratory complications as a leading concern in burn care.[22]

The association of sepsis with larger TBSA affected and inhalation injury is well-documented, with both factors contributing to increased susceptibility to infections and sepsis. The significant difference in age between the sepsis and nonsepsis groups (34 versus 41 years) may reflect the higher metabolic demands and stress response in younger patients, leading to a different trajectory in the development of sepsis. Although the study did not find a significant association between comorbidities like DM and HTN with sepsis, it is important to note that these conditions

can still impact the overall prognosis and management of burn patients.

The increased mortality rate in sepsis patients (17.5%) compared with nonsepsis patients (2.9%) is a stark reminder of the severity of sepsis in burn patients, which is well-documented in the literature.[21] The high incidence of positive blood cultures in sepsis patients (47.4%) emphasizes the need for vigilant monitoring and prompt antimicrobial intervention.[23] The significant correlation between positive wound cultures and sepsis (71.9%) suggests that wound management is a critical component in sepsis prevention and control.[24] The association of fungal infections with sepsis (12.3%) indicates the complexity of infection management in burn patients, where fungal pathogens represent a serious therapeutic challenge.[25] The prevalence of *A. baumanni* in blood cultures observed in our study, constituting approximately 50% of cases, aligns closely with the findings of a previously conducted study by Hu et al. Authors concluded that *A. baumanni* was the most frequently isolated organism, accounting for 22.7% of the total 225 isolates obtained from 136 burn patients.[26] *A. baumanni* is considered an opportunistic pathogen, which means it can cause infections in those with weakened immune systems or compromised skin barriers.[27] The loss of the skin's protective characteristics in burn patients makes the underlying tissues more vulnerable to microbial invasion and colonization. Moreover, *A. baumanni* has the ability to form biofilms, which are collections of microorganisms enclosed in a matrix that work together as a cooperative consortium to give microorganisms a protected state and increase resistance to different antibiotics.[28] In contrast to *A. baumanni*, another study by Kaita et al examining blood cultures from a similar population revealed a different microbial profile. In this particular study, Candida species emerged as the most frequently isolated organisms, followed by *Pseudomonas aeruginosa*, accounting for approximately 28.1% and 23.4% of cases, respectively.[29] The findings between the studies highlight the complex nature of these infections in burn patients. Although *A. baumanni* and Candida species seem to be significant organisms among burn patients, the specific microbial profile may vary across different patient factors and healthcare settings. These findings together highlight the necessity of continued research efforts and the application of focused infection control techniques.

The association of pneumonia and PE with sepsis underscores the vulnerability of burn patients to respiratory complications, which can significantly worsen the prognosis.[30,31] The lower hemoglobin levels in sepsis patients may reflect the multifactorial etiology of anemia in this population, including systemic inflammation and nutritional deficiencies.[25] The trends observed in WBC and platelet counts may indicate an ongoing inflammatory response and potential coagulopathy, which are common in sepsis and warrant further investigation.[32]

Age and TBSA are confirmed as significant predictors of sepsis, aligning with previous studies that have identified these factors as key indicators of sepsis risk in burn patients.[33,34] The trend towards significance for HTN as a predictor suggests that cardiovascular comorbidities may influence the sepsis trajectory, possibly due to their impact on the body's response to systemic inflammation.[35] The lack of significant associations with other factors such as gender, BMI, DM, smoking status, and burn type may indicate that although these factors contribute to the overall clinical picture, they do not independently predict sepsis.

Clinical Implications and Future Research

The prevalence of burn wound infection and sepsis underscores the urgent need for robust infection prevention programs in burn units. Implementation of strict aseptic protocols, regular surveillance of microbial colonization patterns, and early detection of bacteremia are crucial in mitigating the risk of infection-related morbidity and mortality. Additionally, clinicians must prioritize empiric antimicrobial selection based on local bacterial profiles and sensitivity patterns to optimize treatment outcomes and minimize the emergence of resistance. Further investigation into the relationship between microbial colonization patterns, antimicrobial susceptibility profiles, and sepsis-related mortality is warranted. Longitudinal studies examining the impact of specific bacterial strains and antimicrobial resistance mechanisms on patient outcomes could provide valuable insights into the efficacy of empiric antimicrobial therapy and guide therapeutic decision-making. Moreover, collaborative efforts between burn centers worldwide to establish standardized protocols for infection prevention and management would facilitate the development of evidence-based guidelines and improve clinical outcomes for burn patients globally.

Limitations

This study has several limitations that should be acknowledged. The retrospective nature of the study design introduces inherent biases and limitations, including the potential for incomplete or missing data, selection bias, and reliance on medical records for data collection. The study was conducted at a single center, which may limit the generalizability of the findings to broader populations or different healthcare settings. The relatively modest sample size of 196 participants may also restrict the statistical power and precision of the results, particularly for subgroup analyses or rare outcomes. The study's focus on specific laboratory parameters and clinical outcomes may overlook other potentially relevant factors influencing burn injury severity and patient outcomes, such as socioeconomic status, preexisting comorbidities, or access to healthcare resources. Despite these limitations, the study provides valuable insights into the epidemiology, clinical characteristics, and outcomes of burn injuries.

CONCLUSIONS

Our study identifies age and TBSA as significant risk factors for sepsis among critically ill burn patients. Laboratory abnormalities, including inflammatory markers and organ dysfunction, further accentuate the complexity of burn-related pathophysiology. The association

of sepsis with positive blood and wound cultures underscores the importance of vigilant surveillance and prompt antimicrobial therapy in mitigating infection-related complications. Continued research and the development of evidence-based protocols are essential to further enhance the care and survival rates of burn patients at high risk for sepsis.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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