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Original Article

The clinical and microbiological characteristics of infections in burn patients from the Formosa Fun Coast Dust Explosion

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Abstract *Background/Purpose:* Bloodstream infection is a leading cause of mortality among burn patients. This study aimed to evaluate the risk factors, causative pathogens, and the relationship between bloodstream infections and other infections among burn patients from the Formosa Fun Coast Dust Explosion.
Methods: This retrospective study evaluated the demographic and clinical characteristics, infection types, causative pathogen(s), and isolates' antibiotic susceptibilities from patients who were hospitalized between June 27 and September 31, 2015.
Results: Fifty-eight patients were admitted during the study period (36 males, mean age: 22.6 years). The mean burned total body surface area (TBSA) was 40% for all patients. Eighteen (31%) patients with mean TBSA of 80% had 66 episodes of bloodstream infections caused by 92 isolates. Twelve (18.2%) episodes of bloodstream infections were polymicrobial. *Acinetobacter baumannii* (19, 20.7%), *Ralstonia pickettii* (17, 18.5%), and *Chryseobacterium meningosepticum* (13, 14.1%) were the most common pathogens causing bloodstream infections. A high concordance rate of wound cultures with blood cultures was seen in *Staphylococcus aureus* (3, 75%) and *C. meningosepticum* (8, 61.5%) infections. However, no *Ralstonia* isolate was found in burn wounds of patients with *Ralstonia* bacteremia. A high concordance rate of central venous catheter cultures with blood cultures was noted in *Ralstonia mannitolilytica* (5, 62.5%) and *Chryseobacterium indologenes* (3, 60%) infections. Approximately 21.1% of *A. baumannii* strains were resistant to carbapenem. All *S. aureus* isolates were susceptible to methicillin.

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Conclusions: Waterborne bacteria should be considered in patients of burns with possible water contact. Empirical broad-spectrum antibiotics should be considered for patients who were hospitalized for severe sepsis, or septic shock with a large burn. Antibiotic treatment should be administered based on the specific pathogens and their detection points.

Introduction

Infection is the leading cause of mortality among burn patients. Bloodstream infections can develop because of the burn, invasive procedures, or catheter insertion. Thus, infection prevention and treatment can be difficult in burn patients, and it is important to understand the related patterns of antibiotic resistance in responsible pathogens for nosocomial infections.[1]

In 2015, the Formosa Fun Coast Dust Explosion occurred at a Taiwanese water park, and most patients used pool water to soothe their burns. Thus, we hypothesized that the causative pathogens for wound or bloodstream infections in these patients would be different from previous burn cases.[2–4] The present study aimed to evaluate the clinical characteristics, risk factors and causative pathogens of bloodstream infection, antimicrobial susceptibilities, and the relationship between bloodstream pathogens and focal infection sites. The resulting data may be useful for identifying proper antibiotic treatment for post-burn bloodstream infections, and for developing optimal treatment strategies for burn victims after a dust explosion accident.

Methods

Study subjects and antimicrobial strategy

This study was performed at the Tri-Service General Hospital (TSGH; a 1700-bed tertiary care center in northern Taiwan). All patients included in the present study were injured at the Formosa Fun Coast Dust Explosion and were admitted to the burn intensive care unit and burn ward between June 27 and September 31, 2015. Patients were excluded if they were admitted after September 31, 2015. Surveillance cultures of burn wound, sputum, urine, and blood specimens were performed at the admission, and then weekly thereafter in the patients with clinical signs of new or persistent infection. The patients' medical records and culture results in different time were retrospectively analyzed, and only the first admission was considered.

All patients underwent escharotomy or debridement to remove damaged tissue. Empirical antimicrobial treatment, *i.e.*, a fourth-generation cephalosporin plus a glycopeptide, was provided to hospitalized patients with severe sepsis or septic shock and a large burn area, and was administered for $<$7 days if there was no clinically significant pathogen detected.[1,5] Antifungal agent (fluconazole or micafungin, if fluconazole was contraindicated) was administered at 7 days after the burn, if the patient exhibited at least three specific risk factors.[6,7] This study's retrospective protocol was approved by the TSGH institutional review board (2-104-05-127), and the requirement for informed consent was waived.

Data collection and definitions

The collected data included demographic characteristics, illness severity, presence of wound infection, pneumonia, urinary tract infection, central venous catheter (CVC) infection, isolated pathogen(s), laboratory results, ventilator use, CVC use, extracorporeal membrane oxygenation at the bacteremia onset, intensive care unit (ICU) hospitalization, and 3-month mortality. Body mass index (BMI) was calculated as kg/m^2. Inhalation injury was diagnosed based on previously published criteria.[5,8] Burn severity was evaluated by the Abbreviated Burn Severity Index (ABSI),[9] which would consider the patient's sex, age, presence of inhalation injury, presence of a full-thickness burn, and burned percentage of total body surface area (TBSA).[10] The revised Baux score was calculated as the sum of the age and TBSA (a score of 17 was assigned to patients with inhalation injury and a score of 0 to those without inhalation injury).[11] The Acute Physiology and Chronic Health Evaluation II (APACHE II) score[12] was recorded at $<$24 h after the burn in those without bloodstream infection and at within 24 h prior to bloodstream infection onset in those with bloodstream infection. Sepsis, septic shock, multiple organ failure, acute respiratory distress syndrome were diagnosed as previously described.[5,13–15] Wound infection was defined as a burn wound culture with $>10^5$ bacteria/g of tissue.[5] Pneumonia, urinary tract infections, and bloodstream infections were defined as previously described.[5] CVC infection was defined as any bacteremia or fungemia in a patient with an intravascular catheter with $>$15 colony-forming units of the same organism and antimicrobial susceptibility on the catheter segment, based on semi-quantitative culture. Only the first isolated microorganism was included if the same causative microorganism was isolated multiple times under the same conditions.[16,17] However, all pathogens were included if different species or antibiograms were isolated from the same patient.[16,17]

We only evaluated infection episodes and causative pathogens that were detected at $<$60 days after the burn. The causative pathogens of bloodstream infections were analyzed at $\leq$7 days, 8–14 days, 15–21 days, 22–28 days, and $>$28 days after the burn. We also compared the pathogens of bloodstream infection with surveillance cultures collected within 7 days before the onset of bloodstream

infection. Among the patients with a recognized pathogen, such as *Corynebacteria*, *Bacillus* species, *Propionibacterium* species, coagulase-negative staphylococci [CoNS], or micrococci, in two or more blood cultures in conjunction with the presence of sepsis were included as true pathogens of bloodstream infections.[5]

Laboratory data were collected at <72 h after the burn in those without bloodstream infections and at <24 h before/after bloodstream infection onset in those with bloodstream infection. These tests included white blood cells, hemoglobin, platelets, blood urea nitrogen, creatinine, C-reactive protein, procalcitonin, lactate, aspartate aminotransferase, alanine aminotransferase, total bilirubin, albumin, triglycerides, prothrombin time, and activated partial thromboplastin time. If multiple measurements were taken, the most abnormal value was selected for the analysis.

Pathogens

All pathogens were identified using routine microbiological methods. The minimal inhibitory concentrations (MICs) for the isolates were determined by the VITEK 2 automated system (bioMérieux, Mercy l'Etoile, France), and the interpretation of susceptibility were based on the guidelines of Clinical and Laboratory Standards Institute (M100-S24).[18]

Statistical analysis

Student's *t* test or the Mann–Whitney test was used to analyze continuous variables and chi-square test with Yate's correction or Fisher's exact test was used to compare the discrete variables. The logistic regression model was used to explore risk factors for bloodstream infection, and univariate analyses were used to calculate odds ratio (OR) and 95% confidence interval (CI). All biologically plausible variables with *p*-values of ≤0.05 in the univariate analyses were considered for inclusion in the multivariate analysis. A *p*-value of <0.05 were considered statistically significant. All analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 18.0 (SPSS, Chicago, IL, USA).

Results

We identified 58 patients hospitalized for burns after the Formosa Fun Coast Dust Explosion. One patient was admitted twice and the second admission was excluded for the analysis. Sixty-six episodes of bloodstream infections were noted in 18 (31.0%) patients and 12 (18.2%) episodes of bloodstream infections were polymicrobial. Their demographic characteristics, clinical characteristics, and outcomes were summarized in Table 1.

Table 1 Demographics, clinical characteristics, and outcome of burn patients with and without bloodstream infections (BSIs).

Variables	n (%)/Mean ± SD/Median (Q1–Q3)			*p* Value
	All (n = 58)	With BSI (n = 18)	Without BSI (n = 40)	
Age in years	22.6 ± 3.9	21.6 ± 3.2	23.0 ± 4.1	0.192
Gender, Male	36 (62.1)	9 (50.0)	27 (67.5)	0.204
Body mass index	22.3 ± 3.6	23.8 ± 3.2	21.6 ± 3.6	0.032
Total body surface area (TBSA) (%)	40 (25–58)	60 (55–77)	36 (21–40)	<0.001
Second-degree TBSA (%)	18 (10–23)	10 (10–20)	18 (10–24)	0.115
Third-degree TBSA (%)	22 (5–45)	50 (40–54)	11 (0–22)	<0.001
Inhalation injury	20 (34.5)	16 (88.9)	4 (10.0)	<0.001
Severity of injury				
Abbreviated burn severity index	8 (6–10)	11 (10–12)	6.5 (5–8)	<0.001
Revised Baux score	67.5 (49–90)	97.5 (89–113)	57.5 (43–71.5)	<0.001
APACHE II score	9 (4–17)	18 (16–20)	5.0 (2.5–10.0)	<0.001
Sepsis	49 (84.5)	17 (94.4)	32 (80.0)	0.160
Shock	8 (13.8)	7 (38.9)	1 (2.5)	0.000
Multiple organ failure	1 (1.7)	1 (5.6)	0 (0)	0.133
Gastrointestinal bleeding	6 (10.3)	4 (22.2)	2 (5.0)	0.068
Acute respiratory distress syndrome	6 (10.3)	6 (33.3)	0 (0)	0.000
Burn wound infection	38 (65.5)	18 (100)	20 (50.0)	0.000
Pneumonia	23 (39.7)	18 (100)	5 (12.5)	<0.001
Urinary tract infection	5 (8.6)	4 (22.2)	1 (2.5)	0.013
Central venous catheter infection	13 (22.4)	13 (72.2)	–	–
ICU hospitalization	27 (46.6)	18 (100)	9 (22.5)	<0.001
Length of ICU stay, d (IQR)	29 (16–5)	43 (27–113)	14 (7–16)	<0.001
Length of ICU stay before bacteremia onset, d (IQR)	18 (15–24)	18 (15–24)	–	–
Ventilation days	19 (12–38)	24 (14–45)	12 (8–16)	0.010
Mortality	0 (0)	0 (0)	0 (0)	–

APACHE = acute physiology and chronic health evaluation; ICU = intensive care unit; IQR = interquartile range; SD = standard deviation.

Compared to those without bloodstream infections, the patients with bloodstream infections exhibited similar age and sex, but had significantly higher BMI ($p < 0.032$), burned TBSA ($p < 0.001$), third-degree burn of TBSA ($p < 0.001$), and more inhalation injury ($p < 0.001$). Furthermore, patients with bloodstream infections exhibited higher ABSI scores ($p < 0.001$), revised Baux scores ($p < 0.001$), APACHE II scores ($p < 0.001$), ICU stays ($p < 0.001$), mechanical ventilation durations ($p < 0.001$), shock ($p < 0.001$), and acute respiratory distress syndrome

Table 2 Clinical laboratory data and procedures of burn patients with and without bloodstream infections (BSIs).

Variables	n (%)/Mean ± SD/Median (Q1-Q3)			*p* Value
	All (n = 58)	With BSI (n = 18)	Without BSI (n = 40)	
Laboratory examinations				
White blood cells,/μL	14,395 (5360–22,750)	16,725 (12,010–21,590)	12,935 (5230–20,780)	0.156
Hemoglobin, g/dL	10.7 (9.6–14.6)	9.7 (9.1–10.5)	11.7 (9.9–15.2)	0.003
Platelet,/μL	139,000 (88,000–238,000)	188,000 (112,000–227,000)	172,500 (118,500–263,000)	0.893
Blood urea nitrogen, mg/dL	11 (7–14)	30.5 (21–43)	9 (6–12)	<0.001
Creatinine, mg/dL	0.8 (0.7–0.9)	0.7 (0.5–1.0)	0.8 (0.6–0.9)	0.392
C-reactive protein, mg/dL	9.9 (2.7–15.5)	17.9 (14.7–22.1)	11.0 (3.6–16.0)	0.035
Procalcitonin, ng/mL	1.4 (0.8–2.6)	34.3 (2.6–129.6)	1.7 (0.8–2.8)	0.022
Lactate, mg/dL	1.4 (1.0–1.8)	1.2 (0.7–1.6)	–	–
Aspartate aminotransferase, IU/L	27 (16–50)	53 (27–99)	21 (14–38)	0.002
Alanine aminotransferase, IU/L	13 (10–29)	40.5 (29.0–86.5)	12 (10–21)	0.003
Total bilirubin, mg/dL	0.8 (0.7–1.7)	1.7 (0.8–2.6)	1.0 (0.8–1.7)	0.256
Albumin, g/dL	2.4 (2.0–3.0)	3.5 (2.9–3.8)	2.6 (2.2–3.1)	0.001
Triglyceride, mg/dL	94 (66–172)	150 (103–202)	94 (91–172)	0.114
Prothrombin time, sec	12.1 (11.1–14.0)	12.3 (11.7–12.7)	11.7 (10.8–13.0)	0.171
aPTT, sec	47.7 (32.5–64.8)	36.0 (32.9–41.3)	35.7 (29.2–55.8)	0.764
Invasive procedures				
Central venous catheter	39 (67.2)	17 (94.4)	22 (55.0)	0.003
Endotracheal tube or tracheostomy	25 (43.1)	18 (100)	7 (17.5)	<0.001
Ventilation support	25 (43.1)	18 (100)	7 (17.5)	<0.001
Arterial catheter	14 (24.1)	11 (61.1)	3 (7.5)	<0.001
Thoracic drain	7 (12.1)	6 (33.3)	1 (2.5)	0.001
Hemodialysis	6 (10.3)	5 (27.8)	1 (2.5)	0.004
Extracorporeal membrane oxygenation	1 (1.7)	1 (5.6)	0 (0)	0.133
Total parental nutrition	1 (1.7)	1 (5.6)	0 (0)	0.133

aPTT = activated partial thromboplastin time; SD = standard deviation.

Table 3 Factors associated with bloodstream infections in patients injured in the Formosa Fun Coast Dust Explosion.

Variables	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*p* Value	Odds ratio (95% CI)	*p* Value
Body mass index	1.19 (1.01–1.41)	0.043		
Total body surface area (TBSA) of burn, %	1.20 (1.08–1.33)	0.001		
Third-degree burn of TBSA, %	1.15 (1.07–1.24)	0.000	1.13 (1.02–1.25)	0.016
Inhalation injury	72.00 (11.94–434.11)	<0.001		
Abbreviated burn severity index	2.76 (1.61–4.74)	0.000		
Revised Baux score	1.14 (1.06–1.24)	0.001		
APACHE II score	1.50 (1.22–1.85)	0.000		
Shock	24.82 (2.75–223.88)	0.004		
Length of ICU stay (d)	1.37 (1.03–1.83)	0.033		
Hemoglobin, g/dL	0.88 (0.74–1.05)	0.155		
Albumin, g/dL	0.15 (0.04–0.56)	0.005		
Blood urea nitrogen, mg/dL	1.17 (1.04–1.32)	0.009		
Central venous catheter	13.91 (1.69–114.75)	0.015		

APACHE II score = acute physiology and chronic health evaluation II score; CI = confidence interval; ICU = intensive care unit.

($p < 0.001$). Patients with bloodstream infections experienced more pneumonia, CVC infections, burn wound infections, and urinary tract infections. No mortality was noted within 3 months.

Patients with bloodstream infections more frequently underwent invasive produces, such as ventilator support ($p < 0.001$), endotracheal tubing or tracheostomy ($p < 0.001$), arterial catheter ($p < 0.001$) or CVC ($p = 0.003$) placement, hemodialysis ($p = 0.003$), and extracorporeal membrane oxygenation ($p = 0.133$). Moreover, patients with bloodstream infections had higher values of several laboratory parameters (Table 2). However, the multivariate analyses revealed that only third-degree burn TBSA was an independent risk factor for bloodstream infection ($p = 0.012$, OR: 1.10, 95% CI: 1.02—1.19) (Table 3).

Among our burn cases, the most common infections were burn wound infections (214, 55%) and pneumonia (66, 17%), as shown in Fig. 1A. *Acinetobacter baumannii* (222 isolates, 34%), *Pseudomonas aeruginosa* (68, 11%), and *Staphylococcus aureus* (57, 9%) were the most common microorganisms (Fig. 1B). Bacteremic pathogens involved gram-negative bacteria (85 isolates, 92.4%), gram-positive bacteria (6, 6.5%), and fungi (1, 1.1%). Among gram-negative pathogens, *A. baumannii* was the most common species (19 isolates, 20.7%), followed by *Ralstonia pickettii* (17, 18.5%), *Chryseobacterium meningosepticum* (13, 14.1%), *Stenotrophomonas maltophilia*

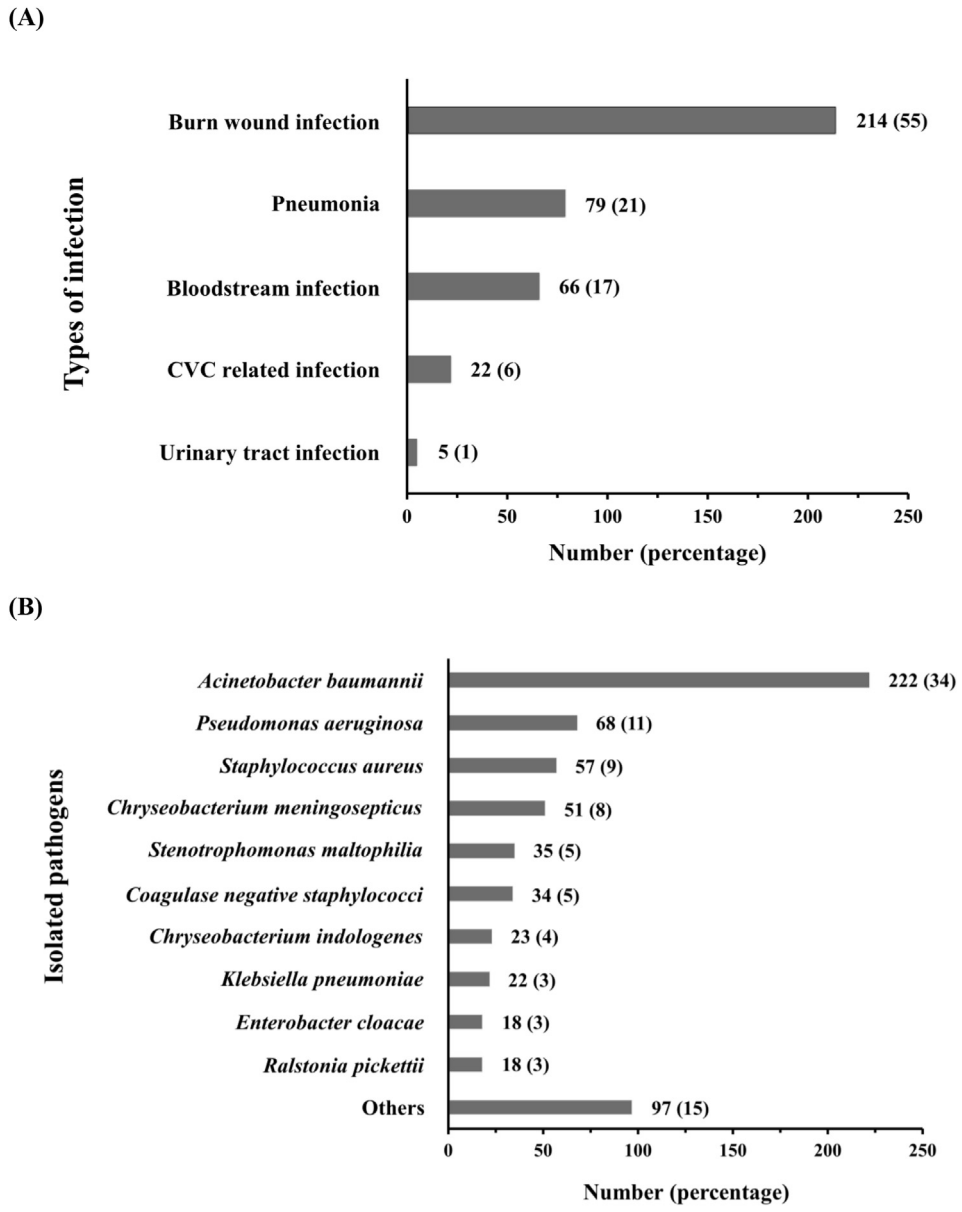

Figure 1. Types of infections (A) and causative pathogens (B) in burn patients. CVC: Central venous catheter; Others: *Aeromonas hydrophila*, *Aspergillus* spp., *Bacillus* spp., *Citrobacter diversus, Clostridium difficile, Delftia acidovorans, Enterococcus faecium, Serratia marcescens, Enterococcus faecalis, Escherichia coli, Flavobacterium species, Proteus mirabilis, Sphingomonas paucimobilis*, viridans streptococci.

(12, 13.0%), *Ralstonia mannitolilytica* (8, 8.7%), *Chryseobacterium indologenes* (5, 5.1%), and *P. aeruginosa* (4, 4.3%). Gram-positive bacteremia were caused by *S. aureus* (4 isolates, 4.3%), CoNS (1, 1.7%), and *Enterococcus faecalis* (1, 1.7%). There was one case of fungemia due to *Candida parapsilosis*.

Among the cases of bloodstream infections, *Ralstonia* isolates were the predominant microorganisms within ≤14 days after the burn (Fig. 2). *A. baumannii*, *Chryseobacterium* spp., and *S. maltophilia* were major microorganisms during 8–28 days after the burn, although their frequencies gradually declined at >28 days, with the exception of *Chryseobacterium* spp. The frequency of *S. aureus* bacteremia increased at >28 days after the burn.

Wound cultures revealed gram-negative bacteria (265 isolates, 74.4%), gram-positive bacteria (85 isolates, 23.9%) and fungi (6 isolates, 1.7%). *A. baumannii* was the most common pathogen (139 isolates, 39.0%), followed by *P. aeruginosa* (50, 14.0%), *S. aureus* (43, 12.1%), and CoNS (25, 7.0%). The fungi included *Candida* spp. (5 isolates) and *Aspergillus* spp. (1) (Fig. 3A and B).

Bloodstream infections exhibited different concordance rates with CVC cultures (25 isolates, 27.2%), wound cultures (23, 25%), and sputum cultures (12, 13%) (Table 4). No pathogens from urine cultures were in concordance with bloodstream infection pathogens. Strikingly, we did not find the isolation of *Ralstonia* spp. in burn wounds of patients with *Ralstonia* bacteremia (Table 4). *C. meningosepticum* bacteremia showed high concordance rates with wound cultures (8 isolates, 61.5%), CVC cultures (5, 38.5%), and sputum cultures (4, 30.8%). *A. baumannii* bacteremia had a high concordance rate with wound cultures (9 isolates, 47.4%) and CVC cultures (7, 36.8%). However, *R. mannitolilytica* and *C. indologenes* bacteremia were frequently in concordance with CVC cultures. *S. aureus* bacteremia exhibited a concordance with wound cultures (3, 75%).

Antimicrobial susceptibility of 92 blood isolates was summarized in Table 5. Four (21.1%) of 19 *A. baumannii* isolates were resistant to imipenem. Eighteen (72%) of 25 *Ralstonia* isolates were resistant to imipenem, and all *Ralstonia* isolates were resistant to colistin but susceptible to ciprofloxacin and levofloxacin. Most (96%) *Ralstonia* isolates were susceptible to third- and fourth-generation cephalosporin. Twelve (63.2%) of 19 *Chryseobacterium* isolates were susceptible to ciprofloxacin or levofloxacin. All *S. maltophilia* isolates were susceptible to trimethoprim-sulfamethoxazole and levofloxacin. No *S. aureus* isolates were resistant to oxacillin. The single CoNS blood isolate was resistant to oxacillin but susceptible to vancomycin. The *Enterococcus* isolate was not resistant to vancomycin and was susceptible to penicillin. We only detected one case of candidemia (*C. parapsilosis*), which was susceptible to amphotericin B, fluconazole, and voriconazole.

Discussion

Although numerous studies have evaluated cases of burn patients with or without bloodstream infections, these studies have rarely evaluated a large number of people who were burned in a single event. In the present study, the patients with bloodstream infections were relatively young (21.6 years) and exhibited a greater TBSA (60%), compared to previous studies.[19–21] However, we did not observe any fatal cases within 3 months, which is in contrast to previous reports.[19,20,22–25] For example, the reported mortality rates among patients with bloodstream infections ranged from 26% to 36%.[19–21] We observed a mean time of 18 days between admission to the onset of bloodstream infection, which agrees with published results.[19–21]

The microorganisms isolated from blood cultures after burn are different, according to time elapsed from burn injury. In the present study, the overwhelming majority of bloodstream pathogens were gram-negative bacteria (e.g., *Ralstonia* spp., *A. baumannii*, and *Chryseobacterium* spp.) and accounted for 92.4% (*vs.* gram-positive bacteria 6.6%), which is in contrast to a previous study,[19] and these isolates

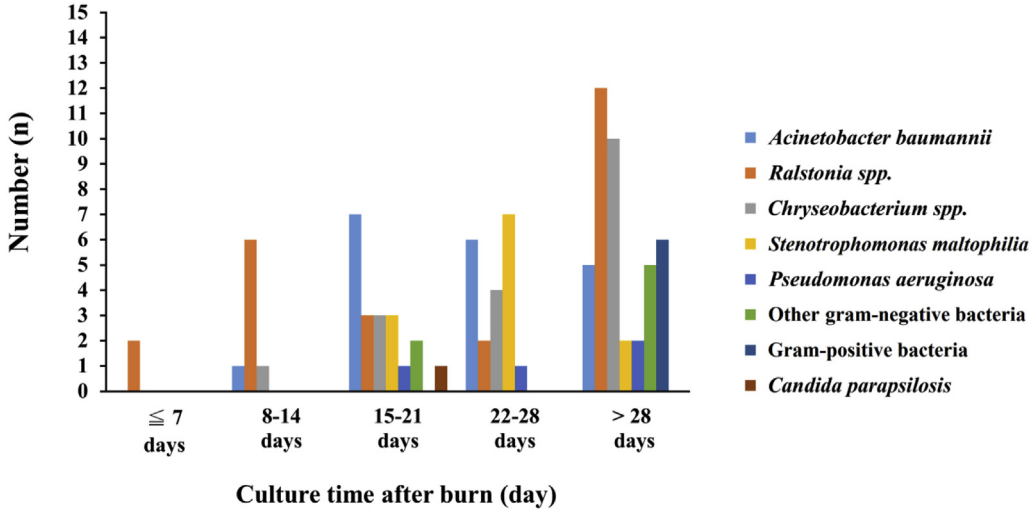

Figure 2. Species distribution of 92 bloodstream infection pathogens in different time periods after burn injury. Other gram-negative bacteria: *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Serratia marcescens*. Gram-positive bacteria: *Staphylococcus aureus* (n = 4), coagulase-negative staphylococcus (n = 1), and *Enterococcus faecalis* (n = 1).

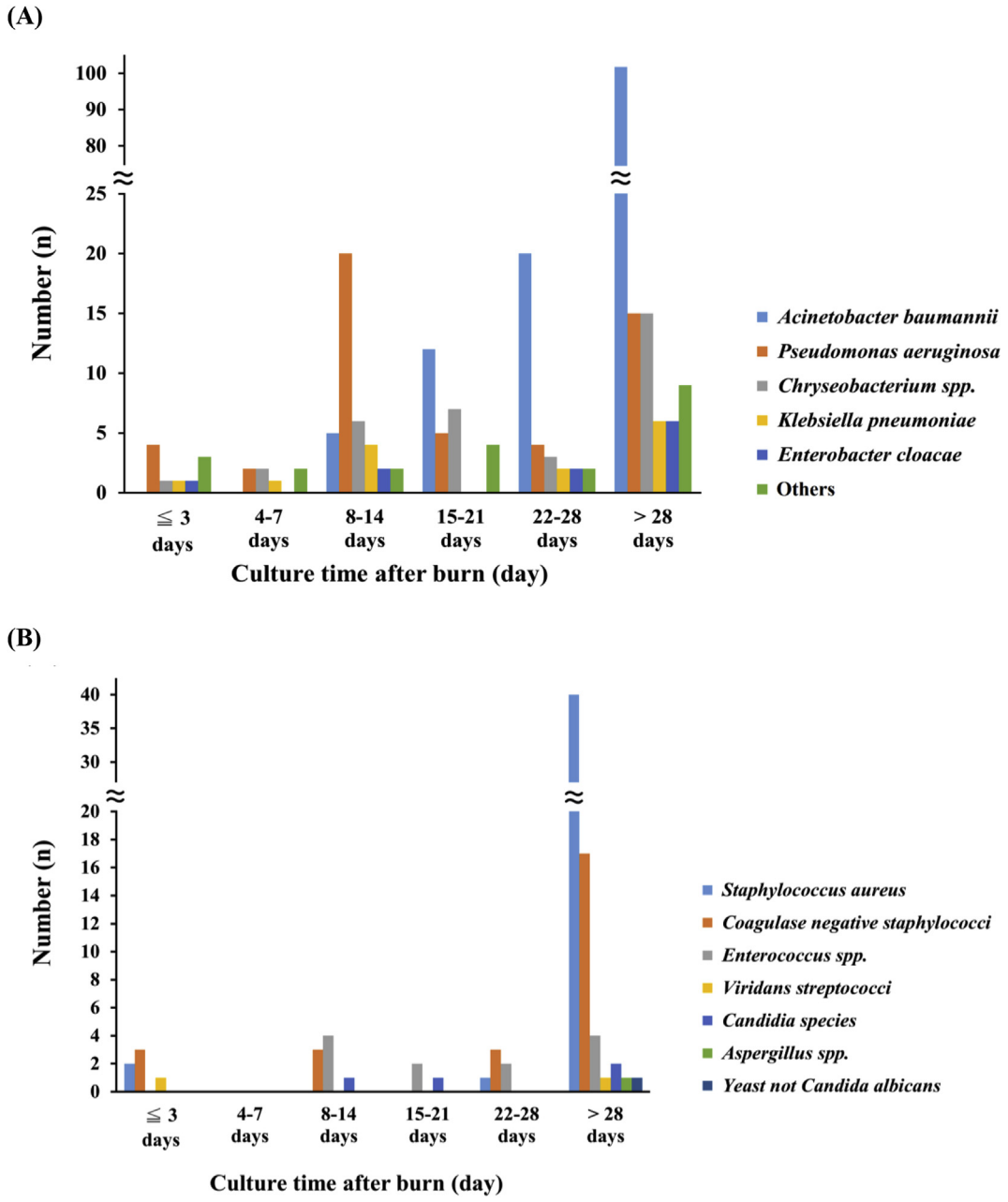

Figure 3. Species distribution of 265 isolates of gram-negative bacteria (A), 85 isolates of gram-positive bacteria, and 6 fungal isolates (B) from burn wounds in different time periods after burn injury. Others: *Aeromonas hydrophila, Citrobacter diversus, Escherichia coli, Serratia marcescens, Flavobacterium species, Klebsiella pneumoniae, Proteus mirabilis, Stenotrophomonas maltophilia.*

were typically observed within two weeks after the burn. During 15—28 days after burn, *A. baumannii* was the most common causative pathogen, followed by *Chryseobacterium* spp. and *S. maltophilia*. *R. mannitolilytica* was most frequently isolated early after the burn (mean: 14.5 days) and their detection rate gradually decreased over time. *P. aeruginos*a bacteremia (4.4%; the fifth common pathogen) was less common, compared to the rates from other studies,[23,26—30] and was only observed at >14 days after the burn. However, *P. aeruginosa* was commonly isolated from wound infections, especially at <14 days after the burn. These trends in the early infection period may be related to the fact that all patients were injured in the same water park accident, and that most patients poured pool water on their burns.

Among our cases of gram-positive bacteremia, *S. aureus* bacteremia was less frequently found (4, 4.3%) than those previously reported (14.4%—74%),[19,20,31] and all occurred at >28 days after the burn. Similarly CoNS and *E. faecalis* were relatively uncommon (1 isolate each, 1.1%), compared to the reports of Still et al. (11%),[32] Lee et al. (12.3%),[20] and Ronat et al. (8%).[20] Moreover, we only detected one case of fluconazole-susceptible *C. parapsilosis* fungemia, which was noted at the third week after

Table 4 The concordance rate of positive cultures of central venous catheter (CVC), sputum, and wound in patients with bloodstream infections.

Pathogens	Isolate number (%)			
	Blood	CVC	Wound	Sputum
Gram-negative bacteria				
Acinetobacter baumannii	19	7 (36.8)	9 (47.4)	6 (31.6)
Ralstonia pickettii	17	2 (11.8)	0 (0)	0 (0)
Chryseobacterium meningosepticus	13	5 (38.5)	8 (61.5)	4 (30.8)
Stenotrophomonas maltophilia	12	1 (8.3)	1 (8.3)	1 (8.3)
Ralstonia mannitolilytica	8	5 (62.5)	0 (0)	0 (0)
Chryseobacterium indologenes	5	3 (60.0)	1 (20.0)	0 (0)
Pseudomonas aeruginosa	4	0 (0)	1 (25.0)	1 (25.0)
Serratia marcescens	4	0 (0)	0 (0)	0 (0)
Chryseobacterium gleum	1	0 (0)	0 (0)	0 (0)
Enterobacter cloacae	1	0 (0)	0 (0)	0 (0)
Klebsiella pneumoniae	1	1 (100)	0 (0)	0 (0)
Gram-positive bacteria				
Staphylococcus aureus	4	1 (25.0)	3 (75.0)	0 (0)
Coagulase-negative staphylococci	1	0 (0)	0 (0)	0 (0)
Enterococcus faecalis	1	0 (0)	0 (0)	0 (0)
Fungus				
Candida parapsilosis	1	0 (0)	0 (0)	0 (0)
Total	92	25 (27.2)	23 (25.0)	12 (13.0)

burn. In contrast, previous studies reported more cases of fungemia, often candidemia, and higher mortality rates during prolonged follow-ups after burns.[6,33] In this context, several centers administer fluconazole as fungal prophylaxis,[34,35] and we also provided antifungal agents for burn patients with more than three specific risk factors[29]: older age, >40% TBSA, inhalation injury,[6,34] neutropenia, uncontrolled diabetes mellitus,[36] or gastric ulcers (either pre-existing or acquired during intensive care).[37,38] This approach appears to be effective, since there was only one episode of candidemia.

Here, wound cultures exhibited a high degree of concordance with *C. meningosepticum* and *S. aureus* bacteremia, wound and CVC cultures with *A. baumannii* bacteremia, and CVC cultures with *R. mannitolilytica* and *C. indologenes* bacteremia. This information may help predict the original site of infection related to subsequent bloodstream infection due to specific pathogens. However, only two patients had these waterborne pathogens isolated from their initial burn wound, *i.e., Chryseobacterium* spp. and *A. baumannii*. Moreover, *Ralstonia* bacteremia was often regarded as primary bacteremia without the same pathogens found other sites. However, the rarity of the isolation of waterborne pathogens in burn wounds was possibly due to initial wound debridement when the patients arrived at the hospital. Besides, these waterborne pathogens are not indigenous bacteria in the skin. Transient bacteremia associated with burn wounds manipulation in these cases was less likely because of the persistence of bloodstream infections for more than 1 week after initial onset.

All *A. baumannii* isolates were susceptible to colistin, and such a finding was in accordance with published studies.[19,39] However, imipenem-resistant *A. baumannii* blood isolates were noted in 21%, which was less than those in published studies,[19,20,39] and most of *A. baumannii* blood isolates were detected in the third and fourth week after the burn. In contrast, approximate 60% of *Chryseobacterium* isolates were susceptible to ciprofloxacin and levofloxacin, but 94.7% resistant to third- and fourth-generation cephalosporin and imipenem. We did not detect any methicillin-resistant *S. aureus*, methicillin-resistant CoNS, or vancomycin-resistant enterococci.

The genus *Ralstonia* is an aerobic, non-fermentative, oxidase-positive, gram-negative bacillus commonly isolated from various environmental samples, such as river and pond water, soil and activated sludge, and from clinical samples, such as respiratory secretions of cystic fibrosis patients.[40–42] However, little is known regarding their antibiotic resistance profile. The effective antibiotics included sulfamethoxazole/trimethoprim, cefepime, and quinolones.[40–42] All of our *Ralstonia* isolates were susceptible to ciprofloxacin and levofloxacin, 96% susceptible to third- and fourth-generation cephalosporins, but 72% resistant to imipenem.

A high prevalence of multidrug-resistant bacteremic pathogens causing bloodstream infections has been noted in burn patients.[20,30] This is a serious cause for concern, as there is a high risk of cross-contamination when the skin barrier is broken (*e.g.*, cases without early excision, debridement, and grafting, and burned TBSA of >40%). Although it would be difficult to completely prevent infections due to multidrug-resistant pathogens among burn patients, these infections might be minimized by implementing isolation, aggressive infection control, appropriate antimicrobial therapy, debridement, early excision, and grafting.[20,28]

Species types of the pathogens support our hypothesis that the healthcare-associated infections were typically due to waterborne bacteria, such as *Ralstonia* spp., *A. baumannii*, *Chryseobacterium* spp., and *P. aeruginosa*.[3,43,44] As these pathogens can grow in various water sources,[41,45] waterborne bacteria should be considered at <14 days after burn, if there is exposure to water. Empirical broad-spectrum antibiotics, such as a fourth-generation cephalosporin plus a glycopeptide, should be considered for hospitalized burn patients with severe sepsis or septic shock and a large burn area. However, this treatment may be used for less than 7 days, if there is no pathogen detected,[1,5] and should be de-escalated as soon as possible, based on culture results and antimicrobial susceptibility results. Antifungal agents may be appropriate at 1 week after the burn, if the patient have

Table 5 Time frame of bloodstream infections and antimicrobial susceptibility of bacteremic gram-negative isolates.

Pathogens	Susceptibility, isolate number (%)					
	≦7 days	8—14 days	15—21 days	22—28 days	>28 days	Total
Acinetobacter baumannii	**n = 0**	**n = 1**	**n = 7**	**n = 6**	**n = 5**	**n = 19**
Ampicillin-sulbactam	—	1 (100)	5 (71.4)	5 (83.3)	4 (80.0)	15 (78.9)
Piperacillin-tazobactam	—	1 (100)	4 (57.1)	3 (60.0)	4 (80.0)	12 (63.2)
Ceftazidime	—	1 (100)	4 (57.1)	4 (66.7)	4 (80.0)	13 (68.4)
Ceftriaxone	—	0 (0)	2 (28.6)	1 (16.7)	2 (40.0)	5 (26.3)
Cefepime	—	1 (100)	4 (57.1)	4 (66.7)	4 (80.0)	13 (68.4)
Imipenem	—	1 (100)	5 (71.4)	5 (83.3)	4 (80.0)	15 (78.9)
Amikacin	—	1 (100)	5 (71.4)	5 (83.3)	4 (80.0)	15 (78.9)
Ciprofloxacin	—	1 (100)	4 (57.1)	4 (66.7)	4 (80.0)	13 (68.4)
Levofloxacin	—	1 (100)	4 (57.1)	4 (66.7)	4 (80.0)	13 (68.4)
Colistin	—	1 (100)	7 (100)	6 (100)	5 (100)	19 (100)
***Ralstonia* species**	**n = 2**	**n = 6**	**n = 3**	**n = 2**	**n = 12**	**n = 25**
Ampicillin	0 (0)	2 (33.3)	0 (0)	1 (50.0)	2 (16.7)	5 (20.0)
Ceftazidime	0 (0)	0 (0)	0 (0)	1 (50.0)	2 (16.7)	3 (12.0)
Ceftriaxone	2 (100)	5 (83.3)	3 (100)	2 (100)	12 (100)	24 (96.0)
Cefepime	2 (100)	5 (83.3)	3 (100)	2 (100)	12 (100)	24 (96.0)
Imipenem	1 (50.0)	2 (33.3)	0 (0)	1 (50.0)	3 (25.0)	7 (28.0)
Amikacin	0 (0)	0 (0)	0 (0)	0 (0.0)	0 (0)	0 (0)
Ciprofloxacin	2 (100)	6 (100.0)	3 (100)	2 (100)	12 (100)	25 (100)
Levofloxacin	2 (100)	6 (100.0)	3 (100)	2 (100)	12 (100)	25 (100)
Colistin	0 (0)	0 (0.0)	0 (0)	0 (0)	0 (0)	0 (0)
***Chryseobacterium* species**	**n = 0**	**n = 1**	**n = 3**	**n = 4**	**n = 11**	**n = 19**
Ampicillin	—	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ceftazidime	—	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ceftriaxone	—	1 (100)	0 (0)	0 (0)	0 (0)	1 (5.3)
Cefepime	—	1 (100)	0 (0)	0 (0)	1 (9.1)	2 (10.5)
Imipenem	—	1 (100)	0 (0)	0 (0)	0 (0)	1 (5.3)
Amikacin	—	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ciprofloxacin	—	1 (100)	0 (0)	3 (75.0)	8 (72.7)	12 (63.2)
Levofloxacin	—	1 (100)	0 (0)	3 (75.0)	8 (72.7)	12 (63.2)
Colistin	—	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Stenotrophomonas maltophilia	**n = 0**	**n = 0**	**n = 3**	**n = 7**	**n = 2**	**n = 12**
Trimethoprim-sulfamethoxazole	—	—	3 (100)	7 (100)	2 (100)	12 (100)
Levofloxacin	—	—	3 (100)	7 (100)	2 (100)	12 (100)
[a]**Others**	**n = 0**	**n = 0**	**n = 3**	**n = 1**	**n = 6**	**n = 10**
Ampicillin-sulbactam	—	—	0 (0)	0 (0)	0 (0)	0 (0)
Piperacillin-tazobactam	—	—	3 (100)	1 (100)	6 (100)	10 (100)
Ceftazidime	—	—	3 (100)	1 (100)	3 (50.0)	7 (70.0)
Ceftriaxone	—	—	2 (66.7)	0 (0)	3 (50.0)	5 (50.0)
Cefepime	—	—	3 (100)	1 (100)	4 (66.7)	8 (80.0)
Imipenem	—	—	3 (100)	1 (100)	6 (100)	10 (100)
Amikacin	—	—	2 (66.7)	1 (100)	6 (100)	9 (90.0)
Ciprofloxacin	—	—	3 (100)	1 (100)	5 (83.3)	9 (90.0)
Levofloxacin	—	—	3 (100)	1 (100)	4 (66.7)	8 (80.0)
Colistin	—	—	2 (66.7)	1 (100)	3 (50.0)	6 (60.0)

[a] Other gram-negative bacteria included *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Serratia marcescens*, and *Pseudomonas aeruginosa*.

specific risk factors,[37,38] and should be used for ≤7 days, if there is no fungal pathogen found. Nosocomial bloodstream infection due to multidrug-resistant organisms increased at >14 days after burn. Therefore, to reduce the risk of multidrug-resistant infections, aggressive escharotomy or debridement, contact precaution, and infection control measures should be implemented as early as possible.

Conflicts of interest

All authors declare no conflicts of interest.

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