Clinical Characteristics and Mortality Associated with Blood Culture Positivity in Adult Inpatients with Sepsis: A 15-Year Cohort Study of 48,706 Patients at a Tertiary Medical Center in Taiwan Hsiu-Yin Chiang, MS, PhD¹; Pei-Shan Chen, MS¹; Chih-Yu Chi, MD^{2,3}; Chin-Chi Kuo, MD, PhD^{1,4,5}

¹Big Data Center, China Medical University Hospital, Taichung, Taiwan; ²Department of Internal Medicine, China Medical University Hospital, Taichung, Taiwan; ³School of Medicine, College of Medicine, China Medical University, Taichung, Taiwan; ⁴Kidney Institute, China Medical University Hospital, Taichung, Taiwan; ⁵Department of Medical Research, China Medical University Hospital

BACKGROUND

- Culture-negative (CN) sepsis occurs in 30% to 60% of patients with sepsis. (Phua 2013; Yang 2013; Armstrong-Briley 2015; Gupta 2016; Kethireddy 2018; Sigakis 2019)
- Published studies of CN and culture-positive (CP) sepsis did not use the current Sepsis-III definition. Current knowledge regarding the role of culture positivity in sepsis is limited.

STUDY AIMS

- Describe the trend of sepsis and in-hospital mortality.
- Study the characteristics and all-cause mortality associated with culture positivity.

METHODS

Study Setting

- Study population: 48,706 adult (\geq 18 years old) inpatients with first-time sepsis who had been admitted to China Medical University Hospital (CMUH) between 2003 – 2017.
- Sepsis: We used an electronic medical records (EMR)-based surveillance of Sepsis-III definition. (Rhee 2017)



Exposures and Outcome

- Data were abstracted from the EMR. Mortality data were obtained from Taiwan's National Death Registry.
- Exposures: Blood CP (BCP) sepsis were those whose blood cultures grew non-commensal organisms for ≥ 1 blood draw and those whose blood cultures grew common commensal organisms for ≥ 2 blood draws. Blood CN (BCN) sepsis were those that did not meet BCP criteria. (CDC NHSN definition)
- Outcome: All-cause mortality (in-hospital, 7-day, 30-day, 1year) following index sepsis date.

Statistical Analysis

Cox proportional hazard model, built using the significant variables in the univariable analysis, was used to evaluate the role of BCP on all-cause mortality.

RESULTS

Flowchart of the selection process of 48,706 adult Figure 1 inpatients with sepsis during 2003-2017 at CMUH.



RESULTS cont.

- The in-hospital mortality for all sepsis significantly decreased from 30.2% to 14.5%.
- The overall trend of in-hospital mortality was consistently higher in BCP sepsis than in BCN sepsis.

Figure 3. In-hospital mortality of adult inpatients with sepsis.



Table 1. Baseline demographic and clinical characteristics.

Characteristics	All Sepsis (N=48,706)	Blood Cult			
		Positive (BCP)	Negative (BCN)	P value	
		(N=7,402)	(N=41,304)		
Age in year, median (IQR)	66 (53 <i>,</i> 78)	67 (55, 77.8)	66 (52, 78)	< 0.001	
Male , N (%)	29343 (60.2)	4006 (54.1)	25337 (61.3)	< 0.001	
Comorbidities, N (%)					
Diabetes mellitus	12544 (25.8)	2173 (29.4)	10371 (25.1)	< 0.001	
Cardiovascular disease	14143 (29)	1841 (24.9)	12302 (29.8)	< 0.001	
CKD Stage 3 to 5	42.312 (86.9)	6235 (84.2)	36077 (87.3)	< 0.001	
$(eGFR < 60 mL/min/1.73m^2)$					
Liver cirrhosis	3690 (7.6)	755 (10.2)	2935 (7.1)	< 0.001	
Chronic lung disease	5305 (10.9)	622 (8.4)	4683 (11.3)	< 0.001	
Systemic antibiotic use in 14 days, N (%)	7838 (16.1)	1047 (14.1)	6791 (16.4)	< 0.001	
Baseline biochemical in -/+ 2 days, N (%)					
Procalcitonin, ng/mL	1.8 (0.4, 9.8)	8.9 (2 <i>,</i> 34.4)	1.3 (0.3, 6.5)	< 0.001	
hs-CRP, mg/dL	7.5 (2.3, 17.9)	13.8 (4.9, 24.2)	6.9 (2, 16.6)	< 0.001	
Blood urea nitrogen, mg/dL	21.5 (13, 40)	26 (16, 46.5)	21 (13, 38)	< 0.001	
Albumin, g/dL	3 (2.5, 3.5)	2.8 (2.4, 3.3)	3 (2.6, 3.5)	< 0.001	
Vital signs, median (IQR)					
Ear temperature, °C	37.1 (36.4, 38)	37.8 (36.7, 38.9)	37 (36.3, 37.9)	< 0.001	
Heart rate, per min	101 (85, 118)	107 (90, 123)	100 (84, 116)	< 0.001	
Systolic blood pressure, mmHg	126 (107, 147)	122 (103, 144)	126 (108, 147)	< 0.001	
Diastolic blood pressure, mmHg	73 (62 <i>,</i> 85)	70 (59 <i>,</i> 83)	74 (62.2 <i>,</i> 86)	< 0.001	
Respiratory rate, per min	20 (19, 22)	20 (20, 22)	20 (19, 22)	< 0.001	
APACHE II for ICU patients, median (IQR)	13 (8, 19)	13 (9, 20)	13 (8, 19)	0.002	
Organ dysfunction criteria , N (%)					
Vasopressor	19677 (40.4)	3233 (43.7)	16444 (39.8)	< 0.001	
Invasive mechanical ventilation	21194 (43.5)	2239 (30.2)	18955 (45.9)	< 0.001	
Doubled sCr or ≥ 50% declined eGFR	15088 (31)	2797 (37.8)	12291 (29.8)	< 0.001	
Bilirubin ≥ 2 mg/dL & 100% increase	8904 (18.3)	1713 (23.1)	7191 (17.4)	< 0.001	
Platelet < 100 cells/uL & ≥ 50% decline	10236 (21)	1987 (26.8)	8249 (20)	< 0.001	
Lactate ≥ 2 mmol/L	20503 (42.1)	3645 (49.2)	16858 (40.8)	< 0.001	
Site of infection, N (%)					
Genitourinary	6934 (20.2)	1984 (31.1)	4950 (17.7)	< 0.001	
Respiratory	13067 (38.1)	1239 (19.4)	11826 (42.3)	< 0.001	
Digestive	6041 (17.6)	1445 (22.6)	4596 (16.5)	< 0.001	







Hsiu-Yin Chiang, MS, PhD Assistant Investigator Big Data Center. China Medical E-mail: t32031@mail.cmuh.org.tw Tel: +886-4-22052121 ext. 2910

RESULTS cont.

BCP sepsis were more likely to: be older, have diabetes, have cirrhosis, have higher inflammatory markers, have organ dysfunction, have genitourinary or digestive as infection source, have higher mortality.

BCN sepsis were more likely to:

be male, have CVD, have CKD stage 3 to 5, have chronic lung disease, receive systemic antibiotic in 14 days prior, have mechanical ventilation, have respiratory as infection source, be admitted to ICU.

Table 2. Outcomes of the adult inpatients with sepsis.

		•	-	
	All Sepsis — (N=48,706)	Blood Cult	_	
Outcomes		Positive (BCP)	Negative (BCN)	P value
		(N=7,402)	(N=41,304)	
Length of hospital stay , day, median (IQR)	13 (7, 25)	13 (7, 24)	13 (7, 25)	0.509
ICU admission, N (%)	25182 (51.7)	3130 (42.3)	22052 (53.4)	< 0.001
Mortality, N (%)	28769 (59.1)	4362 (58.9)	24407 (59.1)	0.795
In-hospital	9699 (19.9)	1624 (21.9)	8075 (19.6)	< 0.001
7-day mortality	2851 (5.9)	529 (7.1)	2322 (5.6)	< 0.001
30-day mortality	8386 (17.2)	1398 (18.9)	6988 (16.9)	< 0.001
1-year mortality	19116 (39.2)	2961 (40)	16155 (39.1)	0.149

After adjusting for confounders, BCP sepsis was significantly associated with 7-day mortality (aHR 1.21; 95% CI 1.08, 1.37).

Table 3. Hazard ratio (HR) and 95% confidence interval (CI) for mortality associated with BCP sepsis.

	Crude Model		Model 1 ^a		Model 2 ^b	
Mortality	Adjusted HR (95% Cl)	P-value	Adjusted HR (95% Cl)	P-value	Adjusted HR (95% Cl)	P-value
In-hospital	1.14 (1.08 - 1.21)	<0.001	1.06 (1.01 - 1.12)	0.032	0.99 (0.93 - 1.06)	0.862
7-day	1.28 (1.17 - 1.41)	<0.001	1.18 (1.07 - 1.30)	0.001	1.21 (1.08 - 1.37)	0.001
30-day	1.13 (1.07 - 1.20)	<0.001	1.06 (1.00 - 1.12)	0.068	0.97 (0.91 - 1.05)	0.475
1-year	1.04 (1.00 - 1.09)	0.028	0.98 (0.94 - 1.02)	0.325	0.93 (0.89 - 0.98)	0.005

a. Adjusted for age, gender, recent hospitalization status, hospital-acquired, diabetes, CVD, CKD stage, chronic lung disease, steroids use and antibiotic use. (N = 48,573).

b. Further adjusted for hs-CRP, BUN, sodium, heart rate, organ dysfunction criteria, site of infection. (N = 32,674). Abbreviations: APACHE, acute physiologic and chronic health evaluation; BUN, blood urea nitrogen; CKD, chronic kidney disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; hs-CRP, high sensitivity C-reactive protein; ICU, intensive care unit; IQR, interquartile range; sCr, serum creatinine.

DISCUSSION

- Consistent with Rhee et al's findings, sepsis prevalence increased while mortality decreased, indicating improvement of sepsis management in 15 years.
- BCN sepsis accounted for 85% of sepsis, which is comparable to Sigakis et al' results (89%).
- BCN sepsis had more ICU admission than had BCP sepsis, possibly because respiratory infection requiring mechanical ventilation were more common in BCN sepsis.
- The adjusted risk of 7-day mortality was 21% higher in BCP sepsis than that in BCN sepsis.
- Further investigation should: 1) evaluate the effect of BCP sepsis in outcome separately by site of infection; 2) study the treatment responses in BCN and BCP sepsis.