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Original Article

Hematological parameters in patients with bloodstream infection: A retrospective observational study

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Abstract

Introduction: To date, the relationship between the causative pathogens and the changes of hematological parameters was rarely referred and deserves further investigation.

Methodology: A total of 825 adult patients, including 134 negative blood cultures patients and 691 bloodstream infection (BSI) patients, were screened for eligibility in this study. Receiver operating characteristic curves and binary logistic regression models were used to assess the power of hematological parameters to distinguish patients with BSI caused by different pathogens.

Results: Except for platelet-to-lymphocyte ratio (PLR) and platelet larger cell count (P-LCC), the other hematological parameters investigated in the study were significantly different in patients with BSI caused by different pathogens, including Candida. The specific combinations of lymphocyte count (LYM), platelet count (PLT), neutrophil-to-lymphocyte ratio (NLR), mean platelet volume (MPV), MPV-to-PLT ratio (MPV/PLT), platelet larger cell ratio (P-LCR), and C-reactive protein (CRP) can improve the ability to distinguish various BSI from negative blood cultures. The highest area under the curve of was 0.753 (95% CI 0.709-0.797) for positive blood cultures, 0.715 (95% CI 0.658-0.771) for Gram-positive pathogens BSI, 0.777 (95% CI 0.730-0.824) for Gram-negative pathogens BSI, 0.797 (95% CI 0.747-0.846) for Escherichia coli BSI, 0.943 (95% CI 0.899-0.987) for Enterobacter aerogenes BSI, 0.830 (95% CI 0.740-0.921) for Pseudomonas aeruginosa BSI, and 0.767 (95% CI 0.695-0.839) for Staphylococcus aureus BSI.

Conclusions: The specific combinations of hematological parameters can improve the power to distinguish patients with BSI caused by different pathogens. Attention to these parameters can be easily integrated into daily medical activities, without extra costs.

Key words: bloodstream infection; blood cultures; hematological parameters; differential ability.

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Introduction

Blood is usually sterile. However, once enter the blood, pathogens can interact with neutrophils, lymphocytes, monocytes, and platelets, leading to bacteremia and sepsis [1], known as bloodstream infection (BSI). Of course, this process also involves humoral immunity, cellular immunity, and endothelial activation mediated by antibodies, complement proteins, and interleukins [2]. Venous access devices and ports often increase the risk of BSI, especially in hematological and tumor patients in intensive care unit [3]. The mortality rate of BSI is about 25%, and up to 54% when developed to severe sepsis [4]. Currently, the most common pathogen is *Staphylococcus*, followed by *Enterobacteriaceae*, *Pseudomonas*, *Enterococcus*, *Acinetobacter*, and *Candida* [5,6].

Generally speaking, except for *Salmonella*, in a bacterial infection, the neutrophil count (NEU) will increase. By contrast, persistent lymphocytopenia was described in patients with Gram-positive and Gram-negative bacteremia [7]. Nevertheless, the changes of platelet count (PLT) and other platelet-related parameters in pathogens infection, particularly, BSI caused by different pathogens, are still ambiguity [8-11]. Platelets are classically known for their critical role in thrombosis, hemostasis, and wound repair. However, emerging evidence indicates that platelets also have a complex role in tumor growth, autoimmune disease, inflammation, and infection [12]. As the first cell at the site of injury, platelets act as primitive immune cells by interacting with invading pathogens, inducing platelet activation. Once activated, platelets release preformed granules that contain diverse bioactive molecules, including cytokines, chemokines [13], and antimicrobial molecules [14]. Besides, activated platelets can also promote the activation of dendritic

cells and monocytes, enhancing adaptive immune responses [15]. Moreover, during BSI, platelets detect pathogens via their Toll-like receptors [16], glomming onto neutrophils. In response, the neutrophils release neutrophil extracellular traps (NETs), webs of DNA, ensnaring pathogens [17,18]. Platelets are needed for the recruitment of neutrophils to tissues of inflammation and infection [19]. Additionally, pathogens that enter the bloodstream will produce diverse extracellular proteins and toxins, resulting in platelet activation or inhibition of platelet activation [20]. Taken together, it is apparent that the interaction between platelets and pathogens not only has important consequences for the pathophysiological response to pathogenic infection but also affect PLT and other platelet-related parameters.

To date, the relationship between the causative pathogens and the changes of hematological parameters was rarely referred and deserves further investigation. Given the protective role of neutrophils, lymphocytes, and platelets in immunity against pathogens, in this retrospective observational study, we sought to systematically investigate the changes of hematological parameters and their differential ability in patients with BSI caused by different pathogens.

Methodology

Study design and data collection

This retrospective observational study was conducted using laboratory and clinical data collected from the microbial information system, laboratory information system, and laboratory electronic medical record system of the Second Hospital of Anhui Medical University, a 2,200-bed tertiary teaching hospital in Hefei (8.0 million inhabitants), Anhui province, China. Since the vast majority of our daily blood cultures were negative, to balance the sample size between groups, we collected data between February 2011 and June 2019 for positive blood cultures and May 2019 to June 2019 (randomly selected) for negative blood cultures.

The inclusion criteria were as follows: (1) age of at least 18 years; (2) clinical suspicion of BSI; and (3) C-reactive protein (CRP), hematological tests, and blood culture ordered, simultaneously. The exclusion criteria were as follows: (1) concomitant hematological diseases; (2) cancer; (3) preexisting immunodeficiency; (4) receiving chemotherapy such as glucocorticoids; (5) chronic liver disease; (6) splenomegaly; and (7) massive hemorrhage.

Instrument and reagent

Serum CRP concentration was detected by Dimension EXL with LM automatic biochemistry analyzer (Siemens Healthcare Diagnostics, Newark, DE). Hematological parameters, such as NEU, lymphocyte count (LYM), PLT, mean platelet volume (MPV), platelet distribution width (PDW), and platelet larger cell ratio (P-LCR), were determined on Sysmex XE2100 hematology analyzer (Sysmex Corporation, Kobe). Subsequently, plateletcrit (PCT), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), mean platelet volume-to-platelet count ratio (MPV/PLT), and platelet larger cell count (P-LCC) were calculated. Blood cultures were incubated in BACTEC FX automatic blood culture system (Becton Dickinson, Sparks, MD). The suspected positive bottles were removed and subjected to culturing tests by using Colombian blood agar plate, chocolate agar plate, and anaerobe 5% sheep blood agar plate [10]. Identification of microorganisms was performed with VITEKII Compact system (BioMérieux, Marcy L'Etoile) and matrix-assisted laser desorption/ionization time-of-flight Microflex LT mass spectrometer (Bruker Daltonics, Hamburg). When no bacterial growth was detected for five days, the result was considered negative.

Statistical analysis

Statistical analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL). Firstly, all variables were tested for normal distribution by the Kolmogorov-Smirnov test. In accordance with the result of this test, the statistical significance of differences was tested using the Student's *t*-test or Mann-Whitney *U* test (two groups' comparison). In the case of multigroup comparison, One-Way ANOVA (LSD) or nonparametric (Kruskal-Wallis) test was applied. Through the above steps, we examined the relationship between all independent variables and dependent variable, consequently, some independent variables that may be meaningless were filtered out. Then, binary logistic regression analysis was conducted. Odds ratios (OR) and 95% CI were calculated to determine the strength of the association between hematological parameters and BSI pathogens. Besides, receiver operating characteristic (ROC) curves were constructed to investigate area under the curve (AUC), 95% confidence intervals (CI), sensitivity, specificity, and cut-off value of hematological parameters [21]. Continuous variables were reported as mean values ± standard deviation (SD) or median with interquartile range (IQR), while categorical variables

Table 1. Demographic and laboratory characteristics of all patients included.

Characteristics	Negative blood cultures	Positive blood cultures	Mann-Whitney *U* test (*Z* value)	Student's *t*-test (*t* value)	*P* value
Number of patients	134	691	–	–	–
Males, number (%)	67 (50.0%)	360 (52.10%)	–	–	–
Age (years)	53.00 (28.00-69.00)	61.00 (46.00-72.00)	- 3.44	–	***0.001***
NEU (10^9/L)	6.95 (4.48-10.14)	9.16 (6.21-13.15)	- 4.38	–	***< 0.001***
LYM (10^9/L)	1.06 (0.72-1.35)	0.75 (0.48-1.16)	- 4.96	–	***< 0.001***
PLT (10^9/L)	207.41 ± 94.48	148.00 (100.00-209.00)	- 5.60	–	***< 0.001***
MPV (fL)	10.06 ± 1.15	10.78 ± 1.51	–	- 6.19	***< 0.001***
PDW (%)	15.90 (13.00-16.30)	16.10 (13.52-15.80)	- 3.25	–	***0.001***
PCT	0.20 ± 0.08	0.16 (0.12-0.22)	- 3.89	–	***< 0.001***
NLR	7.58 (4.12-11.69)	12.12 (6.79-21.27)	- 6.38	–	***< 0.001***
PLR	183.15 (132.64-272.56)	194.80 (123.63-313.64)	- 0.15	–	0.88
MPV/PLT (fL 10^{-5} μL^{-1})	5.10 (3.80-7.25)	7.20 (4.80-10.70)	- 5.56	–	***< 0.001***
P-LCR (%)	27.02 ± 8.42	31.74 ± 10.23	–	- 5.42	***< 0.001***
P-LCC (10^9/L)	53.23 ± 22.14	47.72 (33.18-63.00)	- 1.55	–	0.12
CRP (g/L)	58.70 (24.40-114.65)	122.75 (64.08-205.31)	- 7.15	–	***< 0.001***

Data are shown as number (%), mean (standard deviation, SD), or median (interquartile range, IQR) as appropriate. BSI: bloodstream infection; CRP: C-reactive protein; LYM: lymphocyte count; MPV: mean platelet volume; MPV/PLT: mean platelet volume-to-platelet count ratio; NEU: neutrophil count; NLR: neutrophil-to-lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLT: platelet count; PLR: platelet-to-lymphocyte ratio; P-LCC: platelet larger cell count; P-LCR: platelet larger cell ratio.

were expressed as count and percentage. Two-sided $p < 0.05$ was considered to represent a statistically significant difference.

Ethics statement

Ethical approval was not required as all data used in this study were acquired retrospectively from the microbial information system, laboratory information system, and laboratory electronic medical record system.

Results

Demographic and laboratory characteristics of study subjects

A total of 825 patients were included in the study. Blood cultures were positive in 691 patients. The demographic characteristics of all patients are summarized in Table 1. As for gender distribution, there was no significant difference between positive and negative blood cultures. Nevertheless, patients with positive blood cultures were older than those with negative blood cultures ($p = 0.001$). Furthermore,

Table 2. Demographic and laboratory characteristics of patients with negative, Gram-positive, Gram-negative, and *Candida* blood cultures.

Characteristics	Blood Cultures				*P* value
	Negative	Gram-positive	Gram-negative	*Candida*	
Number of patients	134	278	393	20	–
Males, number (%)	67 (50.0%)	171 (61.5%)	181 (46.0%)	8 (40.0%)	–
Age (years)	53.00 (28.00-69.00)	54.33 ± 18.42	62.00 (51.00-74.00)	60.00 ± 14.77	***< 0.001***
NEU (10^9/L)	6.95 (4.48-10.14)	7.86 (5.24-12.04)	9.91 (6.76-13.76)	11.04 ± 10.26	***< 0.001***
LYM (10^9/L)	1.06 (0.72-1.35)	0.85 (0.56-1.34)	0.68 (0.45-1.00)	0.73 ± 0.52	***< 0.001***
PLT (10^9/L)	207.41 ± 94.48	168.00 (107.00-239.50)	134.00 (93.50-186.50)	194.10 ± 117.32	***< 0.001***
MPV (fL)	10.06 ± 1.15	10.61 ± 1.51	10.93 ± 1.49	10.23 ± 1.54	***< 0.001***
PDW (%)	15.90 (13.00-16.30)	15.90 (13.18-16.80)	16.20 (14.00-16.80)	14.28 ± 2.96	**0 001**
PCT	0.20 ± 0.08	0.18 (0.12-0.25)	0.15 (0.11-0.20)	0.20 ± 0.11	***< 0.001***
NLR	7.58 (4.12-11.69)	9.46 (5.39-15.77)	14.15 (8.34-24.34)	14.39 (8.13-27.10)	***< 0.001***
PLR	183.15 (132.64-272.56)	192.74 (120.54-323.66)	194.80 (124.20-304.37)	354.71 ± 237.45	0.16
MPV/PLT	5.10 (3.80-7.25)	6.40 (4.30-10.00)	7.60 (5.20-11.30)	6.93 ± 4.80	***< 0.001***
P-LCR (%)	27.02 ± 8.42	30.27 ± 9.81	33.04 ± 10.10	27.76 ± 8.06	***< 0.001***
P-LCC (10^9/L)	53.23 ± 22.14	50.35 (33.16-69.20)	47.84 ± 20.55	47.96 ± 23.62	0.07
CRP (g/L)	58.70 (24.40-114.65)	101.00 (52.42-182.06)	153.32 ± 97.88	138.45 ± 77.37	***< 0.001***

Data are shown as number (%), mean (standard deviation, SD), or median (interquartile range, IQR) as appropriate. BSI: bloodstream infection; CRP: C-reactive protein; LYM: lymphocyte count; MPV: mean platelet volume; MPV/PLT: mean platelet volume-to-platelet count ratio; NEU: neutrophil count; NLR: neutrophil-to-lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLT: platelet count; PLR: platelet-to-lymphocyte ratio; P-LCC: platelet larger cell count; P-LCR: platelet larger cell ratio.

patients with isolated Gram-negative pathogens were older than that with Gram-positive pathogens ($p < 0.001$) and negative blood culture ($p < 0.001$) (Table 2). Moreover, patients with *E. coli* BSI were older than those with *S. aureus* BSI ($p < 0.001$) and negative blood culture ($p < 0.001$) (Table 3).

Changes of hematological parameters in negative and positive blood cultures

Other than PLR ($p = 0.881$) and P-LCC ($p = 0.122$), the other hematological parameters were significantly different between the two groups. NEU, MPV, PDW, PCT, MPV/PLT, P-LCR, and P-LCR were higher in patients with positive blood cultures, while PCT, LYM, and PLT were lower (Table 1).

Table 3. Demographic and laboratory characteristics of patients with negative blood cultures and different pathogens positive blood cultures.

	Blood Cultures							
Characteristics	**Negative**	***S. epidermidis***	***S. haemolyticus***	***S. aureus***	***E. faecalis***	***E. faecium***	***Candida***	***P* value**
Number of patients	134	106	28	92	27	25	20	–
Males, number (%)	67 (50.0%)	61 (57.5%)	22 (78.6%)	59 (64.1%)	17 (63.0%)	12 (48.0%)	8 (40.0%)	–
Age (years)	53.00 (28.00-69.00)	56.70 ± 19.21	55.54 ± 20.62	52.28 ± 16.76	49.89 ± 16.62	55.28 ± 19.85	60.00 ± 14.77	***≤ 0.001***
NEU (10^9/L)	6.95 (4.48-10.14)	7.58 (5.42-11.62)	8.47 ± 5.11	9.16 ± 5.32	8.63 ± 4.34	11.17 ± 6.82	11.04 ± 10.26	***≤ 0.001***
LYM (10^9/L)	1.06 (0.72-1.35)	0.93 (0.58-1.53)	1.06 ± 0.49	0.90 ± 0.57	0.89 ± 0.70	0.92 ± 0.46	0.73 ± 0.52	***≤ 0.001***
PLT (10^9/L)	207.41 ± 94.48	222.57 ± 115.51	145.43 ± 70.03	162.01 ± 85.46	160.48 ± 97.76	202.96 ± 158.97	194.10 ± 117.32	***≤ 0.001***
MPV (fL)	10.06 ± 1.15	10.37 ± 1.43	10.76 ± 1.31	10.67 ± 1.61	10.88 ± 1.68	10.99 ± 1.44	10.23 ± 1.54	***≤ 0.001***
PDW (%)	15.90 (13.00-16.30)	15.75 (13.02-16.58)	14.50 ± 3.52	16.10 (13.92-16.98)	15.61 ± 3.25	15.26 ± 2.31	14.28 ± 2.96	***0.01***
PCT	0.20 ± 0.08	0.22 ± 0.11	0.16 ± 0.06	0.15 (0.11-0.22)	0.17 ± 0.10	0.23 ± 0.16	0.20 ± 0.11	***≤ 0.001***
NLR	7.58 (4.12-11.69)	8.38 (4.46-15.16)	10.29 ± 8.55	10.48 (6.81-16.21)	14.24 ± 11.77	15.11 ± 13.52	14.39 (8.13-27.10)	***≤ 0.001***
PLR	183.15 (132.64-272.56)	266.64 ± 202.12	168.10 ± 114.48	192.96 (116.76-306.33)	290.05 ± 287.04	246.18 ± 181.24	354.71 ± 237.45	0.18
MPV/PLT	5.10 (3.80-7.25)	5.10 (3.10-7.78)	8.81 ± 4.82	7.30 (4.83-10.38)	12.73 ± 14.65	8.49 ± 7.22	6.93 ± 4.80	***≤ 0.001***
P-LCR (%)	27.02 ± 8.42	29.91 ± 9.76	31.33 ± 9.14	29.09 ± 9.61	32.71 ± 11.95	31.10 ± 8.61	27.76 ± 8.06	***≤ 0.001***
P-LCC (10^9/L)	53.23 ± 22.14	58.60 ± 25.92	43.65 ± 18.61	51.15 ± 24.35	53.27 ± 33.90	56.94 ± 32.47	47.96 ± 23.62	0.25
CRP (g/L)	58.70 (24.40-114.65)	110.89 ± 86.35	119.86 ± 75.13	146.45 ± 106.06	103.41 ± 78.87	110.14 ± 85.46	138.45 ± 77.37	***≤ 0.001***

Table 3 (continued). Demographic and laboratory characteristics of patients with negative blood cultures and different pathogens positive blood cultures.

	Blood Cultures						
Characteristics	***E. coli***	***K. pneumoniae***	***E. aerogenes***	***E. cloacae***	***P. aeruginosa***	***A. baumannii***	***P* value**
Number of patients	235	80	11	20	30	17	–
Males, number (%)	82 (34.9%)	48 (60.0%)	5 (45.4%)	12 (60.0%)	19 (63.3%)	15 (88.2%)	–
Age (years)	63.00 (50.00-74.00)	60.46 ± 14.55	54.09 ± 13.49	65.90 ± 11.90	63.77 ± 16.34	52.88 ± 18.48	***≤ 0.001***
NEU (10^9/L)	10.06 (7.09-14.09)	11.06 ± 6.16	12.17 ± 12.21	9.59 ± 4.37	11.38 ± 9.00	9.70 ± 6.47	***≤ 0.001***
LYM (10^9/L)	0.66 (0.46-0.94)	0.80 ± 0.53	0.50 ± 0.19	0.78 ± 0.40	0.90 ± 0.56	1.07 ± 0.67	***≤ 0.001***
PLT (10^9/L)	145.82 ± 78.64	143.40 ± 83.54	127.54 ± 45.86	134.15 ± 61.58	161.43 ± 105.41	182.76 ± 118.23	***≤ 0.001***
MPV (fL)	10.92 ± 1.52	11.08 ± 1.49	10.80 ± 1.22	10.88 ± 1.64	10.82 ± 1.27	10.59 ± 1.54	***≤ 0.001***
PDW (%)	16.10 (14.50-16.70)	16.40 (13.90-17.00)	16.41 ± 1.41	15.84 ± 2.39	15.01 ± 2.88	14.69 ± 3.46	***0.01***
PCT	0.16 (0.12-0.20)	0.16 ± 0.08	0.14 ± 0.04	0.16 ± 0.04	0.18 ± 0.10	0.19 ± 0.11	***≤ 0.001***
NLR	14.70 (9.47-24.78)	14.26 (8.37-25.19)	23.57 ± 19.44	16.31 ± 11.55	9.43 (5.27-18.28)	10.45 ± 7.22	***≤ 0.001***
PLR	194.80 (128.00-297.29)	219.29 ± 143.96	305.31 ± 194.01	224.93 ± 167.37	252.65 ± 219.14	202.45 ± 122.98	0.18
MPV/PLT	7.50 (5.30-10.90)	8.10 (5.50-12.75)	9.35 ± 3.59	8.28 ± 3.20	9.81 ± 7.32	9.21 ± 7.66	***≤ 0.001***
P-LCR (%)	32.51 ± 10.22	34.68 ± 9.41	35.27 ± 8.38	33.19 ± 12.66	32.48 ± 9.47	31.59 ± 11.06	***≤ 0.001***
P-LCC (10^9/L)	47.12 ± 19.67	48.58 ± 20.59	44.72 ± 13.84	46.32 ± 19.66	51.29 ± 25.97	51.46 ± 27.60	0.25
CRP (g/L)	160.59 ± 98.12	154.56 ± 101.60	143.48 ± 61.40	96.69 ± 85.02	159.26 ± 98.73	102.46 ± 79.70	***≤ 0.001***

Data are shown as number (%), mean (standard deviation, SD), or median (interquartile range, IQR) as appropriate. BSI: bloodstream infection; CRP: C-reactive protein; LYM: lymphocyte count; MPV: mean platelet volume; MPV/PLT: mean platelet volume-to-platelet count ratio; NEU: neutrophil count; NLR: neutrophil-to-lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLT: platelet count; PLR: platelet-to-lymphocyte ratio; P-LCC: platelet larger cell count; P-LCR: platelet larger cell ratio.

Table 4. Changes of hematological parameters in patients with negative, Gram-positive, Gram-negative, and *Candida* blood cultures.

Comparison			Hematological parameters	
			↑	↓
Negative	*vs.*	Gram-positive	PLT	CRP, MPV, MPV/PLT, NLR, P-LCR
		Gram-negative	PLT, LYM, PCT	CRP, NEU, PDW, MPV, MPV/PLT, NLR, P-LCR
		Candida	LYM	NLR
Gram-positive	*vs.*	Gram-negative	PLT, LYM, PCT	CRP, NEU, MPV/PLT, NLR, P-LCR

CRP: C-reactive protein; LYM: lymphocyte count; MPV: mean platelet volume; MPV/PLT: mean platelet volume-to-platelet count ratio; NEU: neutrophil count; NLR: neutrophil-to-lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLT: platelet count; PLR: platelet-to-lymphocyte ratio; P-LCC: platelet larger cell count; P-LCR: platelet larger cell ratio; ↑: the value of hematological parameters increase; ↓: the value of hematological parameters decrease.

Changes of hematological parameters in negative, Gram-positive, Gram-negative, and Candida blood cultures

Similarly, other than PLR (p = 0.158) and P-LCC (p = 0.075), the other hematological parameters were significantly different among the four groups (Table 2). Compare to negative blood cultures, Gram-negative pathogens BSI have higher values of CRP, NEU, PDW, MPV, MPV/PLT, NLR, and P-LCR, but lower values of PLT, LYM, and PCT (Supplementary Figure 1); Gram-positive pathogens BSI have higher values of CRP, MPV, MPV/PLT, NLR, and P-LCR, but the lower value of PLT (Supplementary Figure 1a, 1c, 1d, 1e); *Candida* BSI have higher value of NLR, whereas a lower value of LYM (Supplementary Figure 1b, 1e). Furthermore, compared to Gram-positive pathogens BSI, Gram-negative pathogens BSI have higher values of CRP, NEU, MPV/PLT, NLR, and P-LCR, while lower values of PLT, LYM, and PCT (Supplementary Figure 1a, 1b, 1d, 1e). See Table 4 for more details.

Changes of hematological parameters in negative blood cultures and different pathogens BSI

Likewise, other than PLR (p = 0.178) and P-LCC (p = 0.254), the other hematological parameters were significantly different among negative blood cultures and different pathogens BSI (Table 3). Compare to negative blood cultures, *E. coli* BSI has higher values of CRP, NEU, MPV, MPV/PLT, NLR, and P-LCR, but lower values of PLT, LYM, and PCT (Supplementary

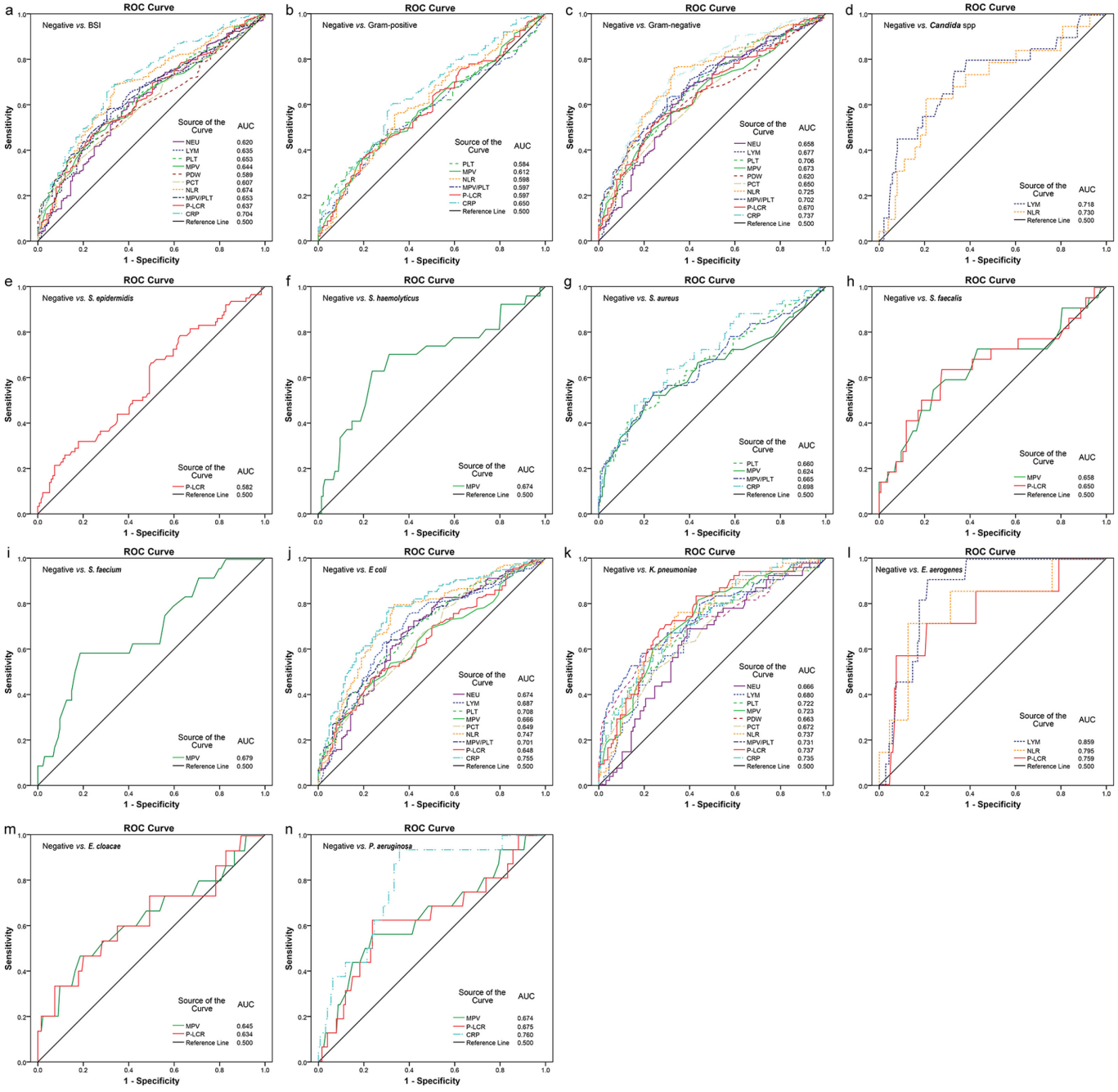
Table 5. Changes of hematological parameters in patients with negative blood cultures and different pathogens positive blood cultures.

Comparison			Hematological parameters	
			↑	↓
Negative	*vs.*	*S. epidermidis*	–	P-LCR
		S. haemolyticus	–	MPV
		S. aureus	PLT	CRP, MPV, MPV/PLT
		E. faecalis	–	MPV, P-LCR
		E. faecium	–	MPV
		E. coli	PLT, LYM, PCT	CRP, NEU, MPV, MPV/PLT, NLR, P-LCR
		K. pneumoniae	PLT, LYM, PCT	CRP, NEU, PDW, MPV, MPV/PLT, NLR, P-LCR
		E. aerogenes	LYM	NLR, P-LCR
		E. cloacae	–	MPV, P-LCR
		P. aeruginosa	–	CRP, MPV, P-LCR
		Candida	–	NLR
S. epidermidis	*vs.*	*S. aureus*	PLT, PCT	MPV/PLT
		E. coli	PLT, LYM, PCT	CRP, MPV, MPV/PLT, NLR
		K. pneumoniae	PLT, PCT	MPV, MPV/PLT, NLR, P-LCR
		E. aerogenes	LYM	–
S. haemolyticus	*vs.*	*E. coli*	–	NLR
		E. aerogenes	LYM	–
S. aureus	*vs.*	*E. coli*	–	P-LCR
		K. pneumoniae	–	P-LCR
Candida	*vs.*	*E. coli*	–	MPV
		K. pneumoniae	–	MPV, P-LCR

CRP: C-reactive protein; LYM: lymphocyte count; MPV: mean platelet volume: MPV/PLT: mean platelet volume-to-platelet count ratio; NEU: neutrophil count; NLR: neutrophil-to-lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLT: platelet count; PLR: platelet-to-lymphocyte ratio; P-LCC: platelet larger cell count; P-LCR: platelet larger cell ratio; ↑: the value of hematological parameters increase; ↓: the value of hematological parameters decrease.

Figures 2, 3, 4, 5, 6); *K. pneumoniae* BSI has higher values of CRP, NEU, PDW, MPV, MPV/PLT, NLR, and P-LCR, while lower values of PLT, LYM, and PCT (Supplementary Figures 2, 3 4, 5, 6); *E. aerogenes* BSI has higher values of NLR, and P-LCR, whereas lower value of LYM (Supplementary Figures 3, 6); *E. cloacae* BSI has higher values of MPV, and P-LCR (Supplementary Figures 4, 6); *P. aeruginosa* BSI has higher values of CRP, MPV, and P-LCR (Supplementary Figures 2, 4, 6); *S. epidermidis* BSI has higher value of P-LCR (Supplementary Figure 6); *S. haemolyticus* BSI has higher value of MPV (Supplementary Figure 4); *S. aureus* BSI has higher values of CRP, MPV ($p = 0.002$), and MPV/PLT, while lower value of PLT (Supplementary Figures 2, 4, 5); *E. faecalis* BSI has higher values of MPV, and P-LCR

Figure 1. ROC curves of hematological parameters for differentiating negative blood cultures from positive blood cultures (**a**), Gram-positive pathogens bloodstream infection (BSI) (**b**), Gram-negative pathogens BSI (**c**), *Candida* BSI (**d**), *S. epidermidis* BSI (**e**), *S. haemolyticus* BSI (**f**), *S. aureus* BSI (**g**), *E. faecalis* BSI (**h**), *E. faecium* BSI (**i**), *E. coli* BSI (**j**), *K. pneumoniae* BSI (**k**), *E. aerogenes* BSI (**l**), *E. cloacae* BSI (**m**), and *P. aeruginosa* BSI (**n**).



(Supplementary Figures 4, 6); *E. faecium* BSI has higher value of MPV (Supplementary Figure 4); *Candida* BSI only has higher value of NLR (Supplementary Figure 6).

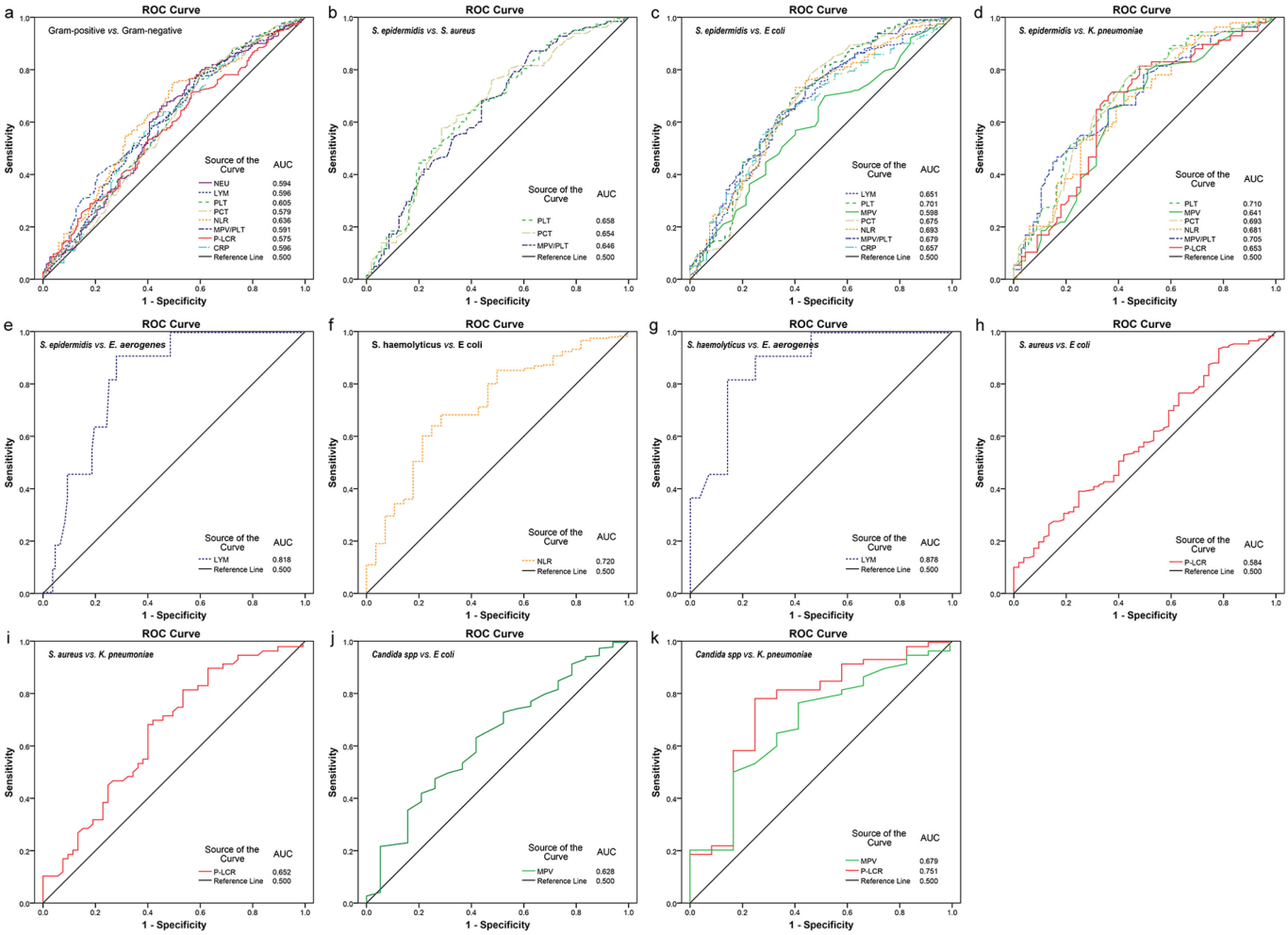
More importantly, compared to *S. epidermidis* BSI, *E. coli* BSI has higher values of CRP, MPV, MPV/PLT, and NLR, but lower values of PLT, LYM, and PCT (Supplementary Figures 2-6); *K. pneumoniae* BSI has higher values of MPV, MPV/PLT, NLR, and P-LCR, whereas lower values of PLT, and PCT (Supplementary Figures 2, 4, 5, 6); *E. aerogenes* BSI only has a lower value of LYM (Supplementary Figure 3); *S. aureus* BSI has a higher value of MPV/PLT, while lower values of PLT, and PCT (Supplementary Figures 2, 5).

Besides, compared to *S. haemolyticus* BSI, *E. coli* BSI has a higher value of NLR (Supplementary Figure 6); *E. aerogenes* BSI has a lower value of LYM (Supplementary Figure 3). Moreover, compared to *S. aureus* BSI, both *E. coli* BSI and *K. pneumoniae* BSI have a higher value of P-LCR (Supplementary Figure 6). Similarly, compare to *Candida* BSI, both *E. coli* BSI and *K. pneumoniae* BSI have a higher value of MPV (Supplementary Figure 4); besides, *K. pneumoniae* BSI has a higher value of P-LCR as well (Supplementary Figure 6). See Table 5 for more details.

Differential ability of hematological parameters

ROC curves were constructed to evaluate the power of hematological parameters to distinguish patients with BSI caused by different pathogens. The AUC, optimal cutoff value, sensitivity, and specificity of each hematological parameter are presented in Supplementary Table 1. The related ROC curves are presented in Figures 1 and Figure 2.

Figure 2. ROC curves of hematological parameters for Gram-positive pathogens bloodstream infection (BSI) vs. Gram-negative pathogens BSI (**a**), *S. epidermidis* BSI vs. *S. aureus* BSI (**b**), *S. epidermidis* BSI vs. *E. coli* BSI (**c**), *S. epidermidis* BSI vs. *K. pneumoniae* BSI (**d**), *S. epidermidis* BSI vs. *E. aerogenes* BSI (**e**), *S. haemolyticus* BSI vs. *E. coli* BSI (**f**), *S. haemolyticus* BSI vs. *E. aerogenes* BSI (**g**), *S. aureus* BSI vs. *E. coli* BSI (**h**), *S. aureus* BSI vs. *K. pneumoniae* BSI (**i**), *Candida* BSI vs. *E. coli* BSI (**j**), *Candida* BSI vs. *K. pneumoniae* BSI (**k**).



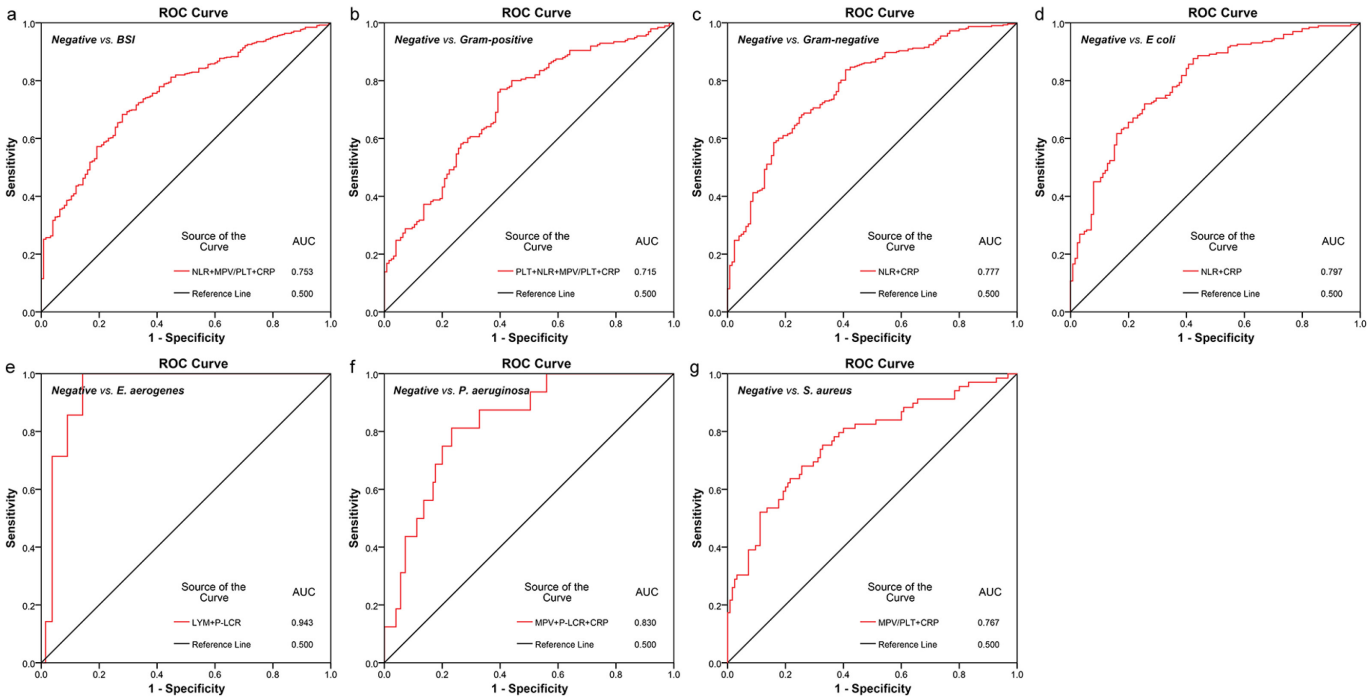
Furthermore, we performed univariate logistic regression analysis to examine the associations of each hematological parameter with different pathogens BSI, and calculated the standardized regression coefficient (β) and the odds ratio (OR) for each blood cell parameter. See Supplementary Table 2 for more details. The combined ROC curves of relevant hematological parameters were shown in Figure 3. The combinations of relevant hematological parameters can increase the differential ability to different pathogens BSI.

Discussion

Blood culture is the most definitive way to confirm BSI. Nonetheless, this gold standard needs at least one day to get the result and may be influenced by many factors [22]. Besides, partly due to differences in both pathogen and host, individual clinical responses to BSI vary greatly [23]. To date, early recognition, rapid microbiological diagnosis, as well as prompt initiation of appropriate antibiotics are always the goals of clinicians who confront probable BSI [24]. Therefore, there is an urgent need for efficient and rapid detection of BSI. For this purpose, it is important to explore BSI comprehensively and deeply, especially the relationship between the causative pathogens and the changes of hematological parameters.

Previous studies have shown that, during BSI, secreted immunomodulatory proteins of pathogen activate platelets and the coagulation system [25-27]. Consequently, the platelet-leukocyte aggregates formed [28] and adhere to endothelium [29,30]. Eventually, the platelets are activated, aggregated, and consumed [31]. Additionally, it has been demonstrated that platelets with higher MPV values have a larger surface area and more granules, which is associated with their activation [32]. Furthermore, MPV, MPV/PLT, and PLR were considered as diagnostic adjunct tests for BSI [33-36]. Nevertheless, Johansson et al. have reported that there was no association between bacterial species and the occurrence of thrombocytopenia [37]. However, each species of bacterium, and even individual strains, have different mechanisms for interacting with platelets [18]. Actually, the immune responses of the host to Gram-positive pathogens are fundamentally different from Gram-negative pathogens [38,39]. Therefore, the kinds of causative pathogens should be taken into account. Opposite to our results, Djordjevic and coauthors reported [9] that patients with Gram-positive BSI have significantly lower values of MPV/PLT and PLR than those with negative blood cultures. Comparing to Gram-positive BSI and negative blood cultures, patients with Gram-negative BSI have the highest values of PLR. It should be noted that the population

Figure 3. ROC curves of the specific combination of hematological parameters for differentiating negative blood cultures from positive blood cultures (**a**), Gram-positive pathogens bloodstream infection (BSI) (**b**), Gram-negative pathogens BSI (**c**), *E. coli* BSI (**d**), *E. aerogenes* BSI (**e**), *P. aeruginosa* BSI (**f**), *S. aureus* BSI (**g**).



included in that research were patients with critically ill BSI and severe trauma. Altogether, to some extent, platelet-related parameters may reflect the distinction of platelet activation in BSI caused by different pathogens.

Although in a study by Wu et al., no significant differences were found in WBC, PLT, and CRP between BSI and negative blood cultures [11], while most of the previous studies have shown that the immune responses to BSI have obvious characteristics, such as the increase of NEU, NLR, PDW, and CRP [40], as well as the decrease of LYM [41]. These are consistent with our results. Furthermore, NLR and MPV were found to reflect the severity of BSI, as well as an independent predictor of death [9,42]. Currently, we provided the first retrospective observational study to systematically investigate the changes of more kinds of hematological parameters and their differential ability in patients with BSI caused by different pathogens, including *Candida* spp. Notably, our results provided some fundamental data, most of which were reported for the first time.

It is undeniable that our present study has some limitations. Firstly, the study was conducted at a single center, and the findings may not be readily suitable to patients with different demographic characteristics. Secondly, we excluded patients suffering from the severe underlying disease. Thirdly, patients with positive blood cultures were significantly older than those with negative blood cultures. Although this may be because older patients are more prone to BSI than younger patients, age-matched groups can better reflect the effects of different pathogens on hematological parameters. Fourthly, except for retrospective observational design, implementation of strict inclusion and exclusion criteria led to a lower number of patients with BSI caused by *S. haemolyticus*, *E. faecalis*, *E. faecium*, *E. aerogenes*, *E. cloacae*, *P. aeruginosa*, *A. baumannii*, and *Candida*. To explore the changes of hematological parameters and their differential ability in patients with BSI caused by more kinds of pathogens, further larger prospective studies are warranted.

Conclusions

Taken together, the specific combinations of hematological parameters can improve the power to distinguish patients with BSI caused by different pathogens. Attention to these parameters can be easily integrated into daily medical activities, without extra costs.

Acknowledgements

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Annex – Supplementary Items

Supplementary Figure 1. Hematological parameters among and between negative, Gram-positive, Gram-negative, and *Candida* blood cultures. (**a**) platelet count (PLT) and C-reactive protein (CRP); (**b**) neutrophil count (NEU) and lymphocyte count (LYM); (**c**) platelet distribution width (PDW) and mean platelet volume (MPV); (**d**) plateletcrit (PCT) and mean platelet volume-to-platelet count ratio (MPV/PLT); (**e**) neutrophil-to-lymphocyte ratio (NLR) and platelet larger cell ratio (P-LCR). Comparisons should be read from left to right. The estimate is located at the intersection of the column-defining blood cultures and the row-defining blood cultures. Significant results are bolded and underscored. Green means that, in comparison, the former is lower than the latter. Red means that, in comparison, the former is higher than the latter.

a

Negative	Z = -4.454 **$P < 0.001$**	Z = -7.946 **$P < 0.001$**	Z = -2.476 P = 0.080
Z = -3.031 **$P = 0.015$**	Gram-positive	Z = -3.737 **$P = 0.001$**	Z = -0.889 P = 1.000
Z = -6.912 **$P < 0.001$**	Z = -4.756 **$P < 0.001$**	Gram-negative	Z = -0.178 P = 1.000
Z = -1.001 P = 1.000	Z = -0.340 P = 1.000	Z = -1.969 P = 0.293	*Candida* spp

Group PLT CRP

b

Negative	Z = -2.477 P = 0.080	Z = -5.973 **$P < 0.001$**	Z = -3.354 **$P = 0.005$**
Z = -2.139 P = 0.195	Gram-positive	Z = -4.301 **$P < 0.001$**	Z = -2.348 P = 0.113
Z = -5.500 **$P < 0.001$**	Z = -4.150 **$P < 0.001$**	Gram-negative	Z = -0.901 P = 1.000
Z = -1.500 P = 0.801	Z = -0.582 P = 1.000	Z = -0.831 P = 1.000	*Candida* spp

Group NEU LYM

c

Negative	Z = -3.780 **$P = 0.001$**	Z = -5.834 **$P < 0.001$**	Z = -0.502 P = 1.000
Z = -2.131 P = 0.199	Gram-positive	Z = -2.376 P = 0.105	Z = -1.168 P = 1.000
Z = -3.835 **$P = 0.001$**	Z = -2.028 P = 0.255	Gram-negative	Z = -1.989 P = 0.280
Z = -0.116 P = 1.000	Z = -1.071 P = 1.000	Z = -1.773 P = 0.457	*Candida* spp

Group PDW MPV

d

Negative	Z = -3.369 **$P = 0.005$**	Z = -6.708 **$P < 0.001$**	Z = -0.456 P = 1.000
Z = -2.029 P = 0.255	Gram-positive	Z = -4.018 **$P < 0.001$**	Z = -1.069 P = 1.000
Z = -4.918 **$P < 0.001$**	Z = -3.528 **$P = 0.003$**	Gram-negative	Z = -2.484 P = 0.078
Z = -0.548 P = 1.000	Z = -0.339 P = 1.000	Z = -1.547 P = 0.731	*Candida* spp

Group PCT MPV/PLT

e

Negative	**$P = 0.004$**	**$P < 0.001$**	P = *0.805*
Z = -3.081 **$P = 0.012$**	Gram-positive	**$P = 0.003$**	P = 0.403
Z = -7.875 **$P < 0.001$**	Z = -5.918 **$P < 0.001$**	Gram-negative	P = 0.075
Z = -3.473 **$P = 0.003$**	Z = -2.196 P = 0.168	Z = -0.195 P = 1.000	*Candida* spp

Group NLR P-LCR

Supplementary Figure 2. Platelet count (PLT) and C-reactive protein (CRP) values among and between negative blood cultures and bloodstream infection (BSI) caused by different pathogens. Comparisons should be read from left to right. The estimate is located at the intersection of the column-defining blood cultures and the row-defining blood cultures. Significant results are bolded and underscored. Green means that, in comparison, the former is lower than the latter. Red means that, in comparison, the former is higher than the latter.

Negative	Z = -2.592 P = 0.744	Z = -2.103 P = 1.000	Z = -4.880 **P < 0.001**	Z = -1.267 P = 1.000	Z = -1.625 P = 1.000	Z = -8.006 **P < 0.001**	Z = -5.553 **P < 0.001**	Z = -2.420 P = 1.000	Z = -0.842 P = 1.000	Z = -3.907 **P = 0.007**	Z = -1.083 P = 1.000	Z = -2.476 P = 1.000
Z = -0.126 P = 1.000	*S. epidermidis*	Z = -0.652 P = 1.000	Z = 2.163 P = 1.000	Z = -0.193 P = 1.000	Z = -0.087 P = 1.000	Z = 4.109 **P = 0.003**	Z = 2.814 P = 0.382	Z = -1.384 P = 1.000	Z = 0.570 P = 1.000	Z = 2.219 P = 1.000	Z = 0.182 P = 1.000	Z = -1.272 P = 1.000
Z = -3.253 P = 0.089	Z = -3.258 P = 0.087	*S. haemolyticus*	Z = 0.651 P = 1.000	Z = 0.663 P = 1.000	Z = 0.461 P = 1.000	Z = 1.449 P = 1.000	Z = 1.056 P = 1.000	Z = -0.791 P = 1.000	Z = 0.950 P = 1.000	Z = 1.114 P = 1.000	Z = 0.619 P = 1.000	Z = -0.607 P = 1.000
Z = -3.905 **P = 0.007**	Z = 3.826 **P = 0.010**	Z = 0.682 P = 1.000	*S. aureus*	Z = -1.518 P = 1.000	Z = -1.297 P = 1.000	Z = -1.396 P = 1.000	Z = -0.658 P = 1.000	Z = -0.440 P = 1.000	Z = -1.862 P = 1.000	Z = -0.758 P = 1.000	Z = -1.340 P = 1.000	Z = -0.185 P = 1.000
Z = -2.544 P = 0.854	Z = -2.566 P = 0.803	Z = 0.516 P = 1.000	Z = -0.037 P = 1.000	*E. faecalis*	Z = -0.222 P = 1.000	Z = 2.339 P = 1.000	Z = 1.928 P = 1.000	Z = -1.326 P = 1.000	Z = 0.301 P = 1.000	Z = 1.837 P = 1.000	Z = 0.011 P = 1.000	Z = -1.200 P = 1.000
Z = -1.524 P = 1.000	Z = -1.567 P = 1.000	Z = 1.249 P = 1.000	Z = -0.872 P = 1.000	Z = -0.737 P = 1.000	*E. faecium*	Z = 2.210 P = 1.000	Z = 1.725 P = 1.000	Z = -1.174 P = 1.000	Z = 0.527 P = 1.000	Z = 1.656 P = 1.000	Z = 0.213 P = 1.000	Z = -1.031 P = 1.000
Z = -6.377 **P < 0.001**	Z = 6.040 **P < 0.001**	Z = 0.072 P = 1.000	Z = -1.314 P = 1.000	Z = 0.756 P = 1.000	Z = 1.703 P = 1.000	*E. coli*	Z = -0.580 P = 1.000	Z = -0.074 P = 1.000	Z = -2.740 P = 0.479	Z = -0.027 P = 1.000	Z = -2.076 P = 1.000	Z = -0.422 P = 1.000
Z = -5.236 **P < 0.001**	Z = 5.106 **P < 0.001**	Z = 0.291 P = 1.000	Z = -1.381 P = 1.000	Z = 0.912 P = 1.000	Z = 1.779 P = 1.000	Z = -0.382 P = 1.000	*K. pneumoniae*	Z = -0.144 P = 1.000	Z = -2.261 P = 1.000	Z = -0.304 P = 1.000	Z = -1.700 P = 1.000	Z = -0.155 P = 1.000
Z = -2.927 P = 0.267	Z = -2.950 P = 0.248	Z = -0.680 P = 1.000	Z = -1.220 P = 1.000	Z = -1.066 P = 1.000	Z = -1.619 P = 1.000	Z = -0.738 P = 1.000	Z = -0.554 P = 1.000	*E. aerogenes*	Z = 1.551 P = 1.000	Z = 0.050 P = 1.000	Z = 1.262 P = 1.000	Z = -0.224 P = 1.000
Z = -3.218 P = 0.101	Z = 3.232 P = 0.096	Z = 0.326 P = 1.000	Z = -0.984 P = 1.000	Z = 0.795 P = 1.000	Z = 1.464 P = 1.000	Z = -0.348 P = 1.000	Z = -0.127 P = 1.000	Z = 0.390 P = 1.000	*E. cloacae*	Z = -2.123 P = 1.000	Z = 0.266 P = 1.000	Z = -1.450 P = 1.000
Z = -2.964 P = 0.237	Z = 2.974 P = 0.229	Z = 0.294 P = 1.000	Z = -0.332 P = 1.000	Z = 0.233 P = 1.000	Z = 0.984 P = 1.000	Z = -0.437 P = 1.000	Z = -0.659 P = 1.000	Z = 0.906 P = 1.000	Z = -0.559 P = 1.000	*P. aeruginosa*	Z = 1.680 P = 1.000	Z = -0.338 P = 1.000
Z = -1.569 P = 1.000	Z = 1.609 P = 0.229	Z = 0.885 P = 1.000	Z = -0.473 P = 1.000	Z = 0.429 P = 1.000	Z = 0.228 P = 1.000	Z = -1.140 P = 1.000	Z = -1.258 P = 1.000	Z = -1.329 P = 1.000	Z = 1.114 P = 1.000	Z = 0.641 P = 1.000	*A. baumannii*	Z = -1.130 P = 1.000
Z = -1.001 P = 1.000	Z = -1.052 P = 1.000	Z = -1.489 P = 1.000	Z = -1.170 P = 1.000	Z = -1.006 P = 1.000	Z = -0.307 P = 1.000	Z = -1.933 P = 1.000	Z = -1.999 P = 1.000	Z = -1.806 P = 1.000	Z = -1.680 P = 1.000	Z = -1.242 P = 1.000	Z = -0.497 P = 1.000	*Candida*

Group PLT CRP

Supplementary Figure 3. Neutrophil count (NEU) and lymphocyte count (LYM) values among and between negative blood cultures and bloodstream infection (BSI) caused by different pathogens. Comparisons should be read from left to right. The estimate is located at the intersection of the column-defining blood cultures and the row-defining blood cultures. Significant results are bolded and underscored. Green means that, in comparison, the former is lower than the latter. Red means that, in comparison, the former is higher than the latter.

Negative	Z = -0.693 P = 1.000	Z = -0.178 P = 1.000	Z = -3.090 P = 0.156	Z = -2.893 P = 0.298	Z = -1.258 P = 1.000	Z = -5.805 **P < 0.001**	Z = -4.198 **P = 0.002**	Z = -4.042 **P = 0.004**	Z = -2.339 P = 1.000	Z = -2.063 P = 1.000	Z = -0.468 P = 1.000	Z = -3.354 P = 0.062
Z = -1.584 P = 1.000	*S. epidermidis*	Z = -0.250 P = 1.000	Z = 2.304 P = 1.000	Z = -2.413 P = 1.000	Z = -0.827 P = 1.000	Z = 4.600 **P < 0.001**	Z = 3.396 P = 0.053	Z = -3.718 **P = 0.016**	Z = 1.930 P = 1.000	Z = 1.579 P = 1.000	Z = 0.117 P = 1.000	Z = -2.929 P = 0.266
Z = -0.457 P = 1.000	Z = -0.522 P = 1.000	*S. haemolyticus*	Z = 1.767 P = 1.000	Z = 2.125 P = 1.000	Z = 0.862 P = 1.000	Z = 2.958 P = 0.241	Z = 2.533 P = 0.882	Z = -3.459 **P = 0.042**	Z = 1.798 P = 1.000	Z = 1.445 P = 1.000	Z = 0.272 P = 1.000	Z = -2.620 P = 0.685
Z = -1.636 P = 1.000	Z = 0.109 P = 1.000	Z = 0.586 P = 1.000	*S. aureus*	Z = -0.876 P = 1.000	Z = -0.640 P = 1.000	Z = -1.707 P = 1.000	Z = -1.143 P = 1.000	Z = -2.663 P = 0.605	Z = -0.576 P = 1.000	Z = -0.008 P = 1.000	Z = -1.128 P = 1.000	Z = -1.563 P = 1.000
Z = -1.046 P = 1.000	Z = -0.068 P = 1.000	Z = 0.466 P = 1.000	Z = -0.004 P = 1.000	*E. faecalis*	Z = -1.211 P = 1.000	Z = 0.090 P = 1.000	Z = 0.077 P = 1.000	Z = -1.839 P = 1.000	Z = 0.168 P = 1.000	Z = 0.729 P = 1.000	Z = 1.581 P = 1.000	Z = -0.657 P = 1.000
Z = -2.153 P = 1.000	Z = -1.183 P = 1.000	Z = 1.359 P = 1.000	Z = -1.097 P = 1.000	Z = -0.895 P = 1.000	*E. faecium*	Z = 1.685 P = 1.000	Z = 1.393 P = 1.000	Z = -2.747 P = 0.469	Z = 0.955 P = 1.000	Z = 0.527 P = 1.000	Z = 0.488 P = 1.000	Z = -1.767 P = 1.000
Z = -5.583 **P < 0.001**	Z = 3.405 P = 0.052	Z = 2.548 P = 0.845	Z = -3.113 P = 0.144	Z = 1.889 P = 1.000	Z = 0.643 P = 1.000	*E. coli*	Z = -0.272 P = 1.000	Z = -2.073 P = 1.000	Z = -0.291 P = 1.000	Z = -1.092 P = 1.000	Z = -2.022 P = 1.000	Z = -0.754 P = 1.000
Z = -3.991 **P = 0.005**	Z = 2.417 P = 1.000	Z = 2.136 P = 1.000	Z = -2.240 P = 1.000	Z = 1.543 P = 1.000	Z = 0.414 P = 1.000	Z = -0.312 P = 1.000	*K. pneumoniae*	Z = -2.098 P = 1.000	Z = -0.130 P = 1.000	Z = -0.824 P = 1.000	Z = -1.769 P = 1.000	Z = -0.844 P = 1.000
Z = -1.031 P = 1.000	Z = -0.371 P = 1.000	Z = -0.642 P = 1.000	Z = -0.319 P = 1.000	Z = -0.287 P = 1.000	Z = -0.403 P = 1.000	Z = -0.911 P = 1.000	Z = -0.748 P = 1.000	*E. aerogenes*	Z = 1.884 P = 1.000	Z = 2.415 P = 1.000	Z = 2.965 P = 0.236	Z = -1.235 P = 1.000
Z = -1.635 P = 1.000	Z = 0.763 P = 1.000	Z = 1.015 P = 1.000	Z = -0.691 P = 1.000	Z = 0.581 P = 1.000	Z = 0.256 P = 1.000	Z = -0.911 P = 1.000	Z = -0.688 P = 1.000	Z = 0.183 P = 1.000	*E. cloacae*	Z = -0.498 P = 1.000	Z = 1.334 P = 1.000	Z = -0.770 P = 1.000
Z = -2.120 P = 1.000	Z = 1.075 P = 1.000	Z = 1.268 P = 1.000	Z = -0.983 P = 1.000	Z = 0.783 P = 1.000	Z = 0.151 P = 1.000	Z = -0.909 P = 1.000	Z = -0.634 P = 1.000	Z = 0.297 P = 1.000	Z = -0.125 P = 1.000	*P. aeruginosa*	Z = 0.975 P = 1.000	Z = -1.342 P = 1.000
Z = -1.107 P = 1.000	Z = 0.303 P = 1.000	Z = 0.618 P = 1.000	Z = -0.241 P = 1.000	Z = 0.208 P = 1.000	Z = 0.585 P = 1.000	Z = -1.271 P = 1.000	Z = -1.044 P = 1.000	Z = 0.099 P = 1.000	Z = 0.324 P = 1.000	Z = 0.472 P = 1.000	*A. baumannii*	Z = -2.072 P = 1.000
Z = -1.500 P = 1.000	Z = -0.630 P = 1.000	Z = -0.904 P = 1.000	Z = -0.560 P = 1.000	Z = -0.471 P = 1.000	Z = -0.365 P = 1.000	Z = -1.051 P = 1.000	Z = -0.817 P = 1.000	Z = -0.097 P = 1.000	Z = -0.103 P = 1.000	Z = -0.237 P = 1.000	Z = -0.226 P = 1.000	*Candida*

Group NEU LYM

Supplementary Figure 4. Platelet distribution width (PDW) and mean platelet volume (MPV) values among and between negative blood cultures and bloodstream infection (BSI) caused by different pathogens. Comparisons should be read from left to right. The estimate is located at the intersection of the column-defining blood cultures and the row-defining blood cultures. Significant results are bolded and underscored. Green means that, in comparison, the former is lower than the latter. Red means that, in comparison, the former is higher than the latter.

Negative	$P = 0.100$	**$P = 0.022$**	**$P = 0.002$**	**$P = 0.007$**	**$P = 0.004$**	**$P < 0.001$**	**$P < 0.001$**	$P = 0.118$	**$P = 0.023$**	**$P = 0.013$**	$P = 0.167$	$P = 0.635$
$Z = -1.062$ $P = 1.000$	*S. epidermidis*	$P = 0.214$	$P = 0.151$	$P = 0.103$	$P = 0.060$	**$P = 0.002$**	**$P = 0.001$**	$P = 0.370$	$P = 0.166$	$P = 0.149$	$P = 0.577$	$P = 0.690$
$Z = -0.039$ $P = 1.000$	$Z = -0.605$ $P = 1.000$	*S. haemolyticus*	$P = 0.784$	$P = 0.757$	$P = 0.574$	$P = 0.593$	$P = 0.316$	$P = 0.939$	$P = 0.778$	$P = 0.873$	$P = 0.707$	$P = 0.219$
$Z = -2.723$ $P = 0.505$	$Z = 1.624$ $P = 1.000$	$Z = 1.663$ $P = 1.000$	*S. aureus*	$P = 0.511$	$P = 0.344$	$P = 0.181$	$P = 0.068$	$P = 0.791$	$P = 0.573$	$P = 0.637$	$P = 0.830$	$P = 0.224$
$Z = -1.145$ $P = 1.000$	$Z = -0.475$ $P = 1.000$	$Z = 0.858$ $P = 1.000$	$Z = -0.602$ $P = 1.000$	*E. faecalis*	$P = 0.794$	$P = 0.904$	$P = 0.531$	$P = 0.879$	$P = 0.997$	$P = 0.881$	$P = 0.520$	$P = 0.131$
$Z = -1.282$ $P = 1.000$	$Z = -0.642$ $P = 1.000$	$Z = 0.984$ $P = 1.000$	$Z = -0.390$ $P = 1.000$	$Z = -0.152$ $P = 1.000$	*E. faecium*	$P = 0.822$	$P = 0.775$	$P = 0.731$	$P = 0.818$	$P = 0.684$	$P = 0.392$	$P = 0.087$
$Z = -3.362$ $P = 0.060$	$Z = 1.942$ $P = 1.000$	$Z = 1.776$ $P = 1.000$	$Z = -0.026$ $P = 1.000$	$Z = 0.633$ $P = 1.000$	$Z = 0.403$ $P = 1.000$	*E. coli*	$P = 0.385$	$P = 0.802$	$P = 0.924$	$P = 0.748$	$P = 0.380$	**$P = 0.047$**
$Z = -3.556$ **$P = 0.029$**	$Z = 2.463$ $P = 1.000$	$Z = 2.240$ $P = 1.000$	$Z = -0.865$ $P = 1.000$	$Z = 1.196$ $P = 1.000$	$Z = 0.962$ $P = 1.000$	$Z = -1.041$ $P = 1.000$	*K. pneumoniae*	$P = 0.559$	$P = 0.596$	$P = 0.418$	$P = 0.212$	**$P = 0.021$**
$Z = -1.885$ $P = 1.000$	$Z = -1.447$ $P = 1.000$	$Z = -1.648$ $P = 1.000$	$Z = -0.731$ $P = 1.000$	$Z = -1.017$ $P = 1.000$	$Z = -0.887$ $P = 1.000$	$Z = -0.764$ $P = 1.000$	$Z = -0.324$ $P = 1.000$	*E. aerogenes*	$P = 0.884$	$P = 0.976$	$P = 0.716$	$P = 0.311$
$Z = -2.138$ $P = 1.000$	$Z = 1.559$ $P = 1.000$	$Z = 1.783$ $P = 1.000$	$Z = -0.630$ $P = 1.000$	$Z = 0.971$ $P = 1.000$	$Z = 0.811$ $P = 1.000$	$Z = -0.677$ $P = 1.000$	$Z = -0.106$ $P = 1.000$	$Z = 0.206$ $P = 1.000$	*E. cloacae*	$P = 0.890$	$P = 0.552$	$P = 0.168$
$Z = -0.792$ $P = 1.000$	$Z = 0.131$ $P = 1.000$	$Z = 0.584$ $P = 1.000$	$Z = -0.941$ $P = 1.000$	$Z = 0.274$ $P = 1.000$	$Z = 0.417$ $P = 1.000$	$Z = -0.998$ $P = 1.000$	$Z = -1.529$ $P = 1.000$	$Z = 1.218$ $P = 1.000$	$Z = -1.216$ $P = 1.000$	*P. aeruginosa*	$P = 0.608$	$P = 0.170$
$Z = -0.422$ $P = 1.000$	$Z = 0.102$ $P = 1.000$	$Z = 0.327$ $P = 1.000$	$Z = -0.996$ $P = 1.000$	$Z = 0.412$ $P = 1.000$	$Z = 0.535$ $P = 1.000$	$Z = -1.001$ $P = 1.000$	$Z = -1.447$ $P = 1.000$	$Z = 1.257$ $P = 1.000$	$Z = 1.238$ $P = 1.000$	$Z = 0.176$ $P = 1.000$	*A. baumannii*	$P = 0.462$
$Z = -0.116$ $P = 1.000$	$Z = -0.671$ $P = 1.000$	$Z = -0.123$ $P = 1.000$	$Z = -1.592$ $P = 1.000$	$Z = -0.902$ $P = 1.000$	$Z = -1.019$ $P = 1.000$	$Z = -1.669$ $P = 1.000$	$Z = -2.099$ $P = 1.000$	$Z = -1.655$ $P = 1.000$	$Z = -1.720$ $P = 1.000$	$Z = -0.654$ $P = 1.000$	$Z = -0.413$ $P = 1.000$	*Candida*

Group PDW MPV

Supplementary Figure 5. Plateletcrit (PCT) and mean platelet volume-to-platelet count ratio (MPV/PLT) values among and between negative blood cultures and bloodstream infection (BSI) caused by different pathogens. Comparisons should be read from left to right. The estimate is located at the intersection of the column-defining blood cultures and the row-defining blood cultures. Significant results are bolded and underscored. Green means that, in comparison, the former is lower than the latter. Red means that, in comparison, the former is higher than the latter.

Negative	$Z = -0.282$ $P = 1.000$	$Z = -3.254$ $P = 0.089$	$Z = -3.954$ **$P = 0.006$**	$Z = -2.956$ $P = 0.243$	$Z = -1.752$ $P = 1.000$	$Z = -6.000$ **$P < 0.001$**	$Z = -5.511$ **$P < 0.001$**	$Z = -2.807$ $P = 0.390$	$Z = -2.797$ $P = 0.402$	$Z = -2.536$ $P = 0.876$	$Z = -1.752$ $P = 1.000$	$Z = -0.456$ $P = 1.000$
$Z = -0.868$ $P = 1.000$	*S. epidermidis*	$Z = -3.009$ $P = 0.205$	$Z = 3.496$ **$P = 0.037$**	$Z = -2.718$ $P = 0.513$	$Z = -1.553$ $P = 1.000$	$Z = 5.232$ **$P < 0.001$**	$Z = 5.003$ **$P < 0.001$**	$Z = -2.668$ $P = 0.595$	$Z = 2.607$ $P = 0.712$	$Z = 2.307$ $P = 1.000$	$Z = 1.588$ $P = 1.000$	$Z = -0.296$ $P = 1.000$
$Z = -2.815$ $P = 0.380$	$Z = -3.277$ $P = 0.082$	*S. haemolyticus*	$Z = 0.652$ $P = 1.000$	$Z = 0.231$ $P = 1.000$	$Z = 1.063$ $P = 1.000$	$Z = 0.122$ $P = 1.000$	$Z = 0.457$ $P = 1.000$	$Z = -0.631$ $P = 1.000$	$Z = 0.052$ $P = 1.000$	$Z = 0.557$ $P = 1.000$	$Z = 0.708$ $P = 1.000$	$Z = -1.958$ $P = 1.000$
$Z = -3.216$ $P = 0.101$	$Z = 3.835$ **$P = 0.010$**	$Z = 0.692$ $P = 1.000$	*S. aureus*	$Z = -0.336$ $P = 1.000$	$Z = -0.672$ $P = 1.000$	$Z = -0.937$ $P = 1.000$	$Z = -1.575$ $P = 1.000$	$Z = -1.130$ $P = 1.000$	$Z = -0.615$ $P = 1.000$	$Z = -0.037$ $P = 1.000$	$Z = -0.294$ $P = 1.000$	$Z = -1.752$ $P = 1.000$
$Z = -2.156$ $P = 1.000$	$Z = -2.633$ $P = 0.661$	$Z = 0.511$ $P = 1.000$	$Z = -0.060$ $P = 1.000$	*E. faecalis*	$Z = -0.839$ $P = 1.000$	$Z = 0.186$ $P = 1.000$	$Z = 0.738$ $P = 1.000$	$Z = -0.801$ $P = 1.000$	$Z = 0.258$ $P = 1.000$	$Z = 0.326$ $P = 1.000$	$Z = 0.509$ $P = 1.000$	$Z = -1.745$ $P = 1.000$
$Z = -0.494$ $P = 1.000$	$Z = -0.985$ $P = 1.000$	$Z = 1.728$ $P = 1.000$	$Z = -1.444$ $P = 1.000$	$Z = -1.232$ $P = 1.000$	*E. faecium*	$Z = 1.270$ $P = 1.000$	$Z = 1.713$ $P = 1.000$	$Z = -1.413$ $P = 1.000$	$Z = 1.007$ $P = 1.000$	$Z = 0.523$ $P = 1.000$	$Z = 0.232$ $P = 1.000$	$Z = -0.922$ $P = 1.000$
$Z = -4.386$ **$P = 0.001$**	$Z = 5.002$ **$P < 0.001$**	$Z = 0.540$ $P = 1.000$	$Z = -0.331$ $P = 1.000$	$Z = 0.141$ $P = 1.000$	$Z = 1.740$ $P = 1.000$	*E. coli*	$Z = -0.958$ $P = 1.000$	$Z = -0.799$ $P = 1.000$	$Z = -0.166$ $P = 1.000$	$Z = -0.621$ $P = 1.000$	$Z = -0.766$ $P = 1.000$	$Z = -2.364$ $P = 1.000$
$Z = -4.043$ **$P = 0.004$**	$Z = 4.607$ **$P < 0.001$**	$Z = 0.068$ $P = 1.000$	$Z = -0.878$ $P = 1.000$	$Z = 0.554$ $P = 1.000$	$Z = 2.008$ $P = 1.000$	$Z = -0.716$ $P = 1.000$	*K. pneumoniae*	$Z = -0.390$ $P = 1.000$	$Z = -0.331$ $P = 1.000$	$Z = -1.135$ $P = 1.000$	$Z = -1.185$ $P = 1.000$	$Z = -2.709$ $P = 0.526$
$Z = -2.449$ $P = 1.000$	$Z = -2.769$ $P = 0.439$	$Z = -0.564$ $P = 1.000$	$Z = -1.082$ $P = 1.000$	$Z = -0.940$ $P = 1.000$	$Z = -1.843$ $P = 1.000$	$Z = -0.987$ $P = 1.000$	$Z = -0.667$ $P = 1.000$	*E. aerogenes*	$Z = 0.552$ $P = 1.000$	$Z = 1.040$ $P = 1.000$	$Z = 1.133$ $P = 1.000$	$Z = -2.094$ $P = 1.000$
$Z = -2.008$ $P = 1.000$	$Z = 2.420$ $P = 1.000$	$Z = 0.295$ $P = 1.000$	$Z = -0.241$ $P = 1.000$	$Z = 0.162$ $P = 1.000$	$Z = 1.266$ $P = 1.000$	$Z = -0.083$ $P = 1.000$	$Z = -0.285$ $P = 1.000$	$Z = 0.757$ $P = 1.000$	*E. cloacae*	$Z = -0.550$ $P = 1.000$	$Z = 0.696$ $P = 1.000$	$Z = -1.826$ $P = 1.000$
$Z = -1.656$ $P = 1.000$	$Z = 2.145$ $P = 1.000$	$Z = 0.899$ $P = 1.000$	$Z = -0.420$ $P = 1.000$	$Z = 0.387$ $P = 1.000$	$Z = 0.856$ $P = 1.000$	$Z = -0.658$ $P = 1.000$	$Z = -1.026$ $P = 1.000$	$Z = 1.225$ $P = 1.000$	$Z = -0.508$ $P = 1.000$	*P. aeruginosa*	$Z = 0.227$ $P = 1.000$	$Z = -1.444$ $P = 1.000$
$Z = -1.368$ $P = 1.000$	$Z = 1.771$ $P = 1.000$	$Z = 0.736$ $P = 1.000$	$Z = -0.295$ $P = 1.000$	$Z = 0.295$ $P = 1.000$	$Z = 0.782$ $P = 1.000$	$Z = -0.471$ $P = 1.000$	$Z = -0.790$ $P = 1.000$	$Z = 1.094$ $P = 1.000$	$Z = 0.415$ $P = 1.000$	$Z = 0.039$ $P = 1.000$	*A. baumannii*	$Z = -1.056$ $P = 1.000$
$Z = -0.548$ $P = 1.000$	$Z = -0.994$ $P = 1.000$	$Z = -1.535$ $P = 1.000$	$Z = -1.216$ $P = 1.000$	$Z = -1.071$ $P = 1.000$	$Z = -0.081$ $P = 1.000$	$Z = -1.460$ $P = 1.000$	$Z = -1.735$ $P = 1.000$	$Z = -1.711$ $P = 1.000$	$Z = -1.125$ $P = 1.000$	$Z = -0.719$ $P = 1.000$	$Z = -0.670$ $P = 1.000$	*Candida*

Group PCT MPV/PLT

Supplementary Figure 6. Neutrophil-to-lymphocyte ratio (NLR) and platelet larger cell ratio (P-LCR) values among and between negative blood cultures and bloodstream infection (BSI) caused by different pathogens. Comparisons should be read from left to right. The estimate is located at the intersection of the column-defining blood cultures and the row-defining blood cultures. Significant results are bolded and underscored. Green means that, in comparison, the former is lower than the latter. Red means that, in comparison, the former is higher than the latter.

Negative	**P = 0.047**	P = 0.113	P = 0.190	**P = 0.011**	P = 0.079	**P < 0.001**	**P < 0.001**	**P = 0.028**	**P = 0.019**	**P = 0.021**	P = 0.092	P = 0.806
Z = -1.413 P = 1.000	*S. epidermidis*	P = 0.618	P = 0.649	P = 0.240	P = 0.631	P = 0.065	**P = 0.006**	P = 0.163	P = 0.236	P = 0.306	P = 0.554	P = 0.496
Z = -0.469 P = 1.000	Z = -0.405 P = 1.000	*S. haemolyticus*	P = 0.442	P = 0.676	P = 0.945	P = 0.660	P = 0.242	P = 0.378	P = 0.605	P = 0.734	P = 0.942	P = 0.360
Z = -3.328 P = 0.068	Z = 1.873 P = 1.000	Z = 1.636 P = 1.000	*S. aureus*	P = 0.142	P = 0.431	**P = 0.027**	**P = 0.002**	P = 0.113	P = 0.149	P = 0.191	P = 0.390	P = 0.679
Z = -2.237 P = 1.000	Z = -1.337 P = 1.000	Z = 1.388 P = 1.000	Z = -0.097 P = 1.000	*E. faecalis*	P = 0.589	P = 0.928	P = 0.412	P = 0.541	P = 0.883	P = 0.941	P = 0.735	P = 0.166
Z = -2.513 P = 0.935	Z = -1.636 P = 1.000	Z = 1.635 P = 1.000	Z = -0.429 P = 1.000	Z = -0.272 P = 1.000	*E. faecium*	P = 0.536	P = 0.151	P = 0.325	P = 0.526	P = 0.654	P = 0.882	P = 0.359
Z = -8.001 **P < 0.001**	Z = -5.833 **P < 0.001**	Z = 3.844 **P = 0.009**	Z = -3.378 P = 0.057	Z = 1.940 P = 1.000	Z = 1.515 P = 1.000	*E. coli*	P = 0.137	P = 0.460	P = 0.796	P = 0.991	P = 0.733	P = 0.115
Z = -5.698 **P < 0.001**	Z = 4.196 **P = 0.002**	Z = 3.222 P = 0.099	Z = -2.319 P = 1.000	Z = 1.497 P = 1.000	Z = 1.125 P = 1.000	Z = -0.472 P = 1.000	*K. pneumoniae*	P = 0.879	P = 0.591	P = 0.387	P = 0.281	**P = 0.029**
Z = -3.500 **P = 0.036**	Z = -2.886 P = 0.304	Z = -2.811 P = 0.385	Z = -2.029 P = 1.000	Z = -1.750 P = 1.000	Z = -1.521 P = 1.000	Z = -0.751 P = 1.000	Z = -0.911 P = 1.000	*E. aerogenes*	P = 0.637	P = 0.514	P = 0.411	P = 0.108
Z = -2.890 P = 0.301	Z = 2.088 P = 1.000	Z = 2.033 P = 1.000	Z = -0.981 P = 1.000	Z = 0.749 P = 1.000	Z = 0.485 P = 1.000	Z = -0.744 P = 1.000	Z = -0.449 P = 1.000	Z = 1.079 P = 1.000	*E. cloacae*	P = 0.833	P = 0.657	P = 0.158
Z = -2.073 P = 1.000	Z = 1.136 P = 1.000	Z = 1.222 P = 1.000	Z = -1.152 P = 1.000	Z = 0.201 P = 1.000	Z = 0.475 P = 1.000	Z = -2.308 P = 1.000	Z = -1.805 P = 1.000	Z = 1.927 P = 1.000	Z = -0.950 P = 1.000	*P. aeruginosa*	P = 0.793	P = 0.198
Z = -0.728 P = 1.000	Z = 0.014 P = 1.000	Z = 0.292 P = 1.000	Z = -0.997 P = 1.000	Z = 0.919 P = 1.000	Z = 1.145 P = 1.000	Z = -2.702 P = 0.538	Z = -2.312 P = 1.000	Z = 2.353 P = 1.000	Z = 1.532 P = 1.000	Z = 0.761 P = 1.000	*A. baumannii*	P = 0.326
Z = -3.473 **P < 0.001**	Z = -2.661 P = 0.607	Z = -2.510 P = 0.941	Z = -1.548 P = 1.000	Z = -1.222 P = 1.000	Z = -0.950 P = 1.000	Z = -0.144 P = 1.000	Z = -0.110 P = 1.000	Z = -0.707 P = 1.000	Z = -0.442 P = 1.000	Z = -1.434 P = 1.000	Z = -1.955 P = 1.000	*Candida*

Group NLR P-LCR

Supplementary Table 1. Performance of hematological parameters in diagnosing bloodstream infection (BSI) caused by different pathogens.

Comparison	Hematological parameters	AUC	95% CI	Sensitivity (%)	Specificity (%)	Cut-off
Negative vs. BSI	NEU	0.620	0.585-0.653	61.4	60.4	7.66
	LYM	0.635	0.601-0.668	66.7	59.0	0.96
	PLT	0.653	0.619-0.685	38.4	87.3	121.00
	MPV	0.644	0.609-0.678	51.1	76.0	10.70
	PDW	0.589	0.554-0.624	28.7	93.2	16.60
	PCT	0.607	0.572-0.641	35.9	81.2	0.14
	NLR	0.674	0.641-0.706	65.3	66.4	9.01
	MPV/PLT	0.653	0.618-0.686	44.6	80.4	7.70
	P-LCR	0.637	0.597-0.676	48.4	75.9	31.90
	CRP	0.704	0.669-0.739	65.2	68.8	89.40
Negative vs. Gram-positive	PLT	0.584	0.535-0.632	32.0	87.3	121.00
	MPV	0.612	0.563-0.660	48.2	76.0	10.70
	NLR	0.598	0.549-0.646	54.0	66.4	9.01
	MPV/PLT	0.597	0.547-0.645	45.6	75.2	7.20
	P-LCR	0.597	0.540-0.653	38.5	79.7	33.30
	CRP	0.650	0.596-0.701	56.0	68.8	89.40
Negative vs. *Candida*	LYM	0.718	0.639-0.787	75.0	66.4	0.84
	NLR	0.730	0.652-0.798	65.0	80.6	13.38
Negative vs. Gram-negative	NEU	0.658	0.616-0.699	65.6	63.4	8.02
	LYM	0.677	0.635-0.717	72.8	59.0	0.96
	PLT	0.706	0.665-0.745	44.0	86.6	122.00
	MPV	0.673	0.630-0.715	54.0	75.9	10.70
	PDW	0.620	0.575-0.663	43.8	82.0	16.30

	PCT	0.650	0.607-0.692	78.0	44.4	0.20
	NLR	0.725	0.684-0.762	73.0	66.4	9.01
	MPV/PLT	0.702	0.660-0.742	63.1	68.4	6.40
	P-LCR	0.670	0.622-0.715	54.1	75.9	31.90
	CRP	0.737	0.695-0.777	70.4	68.8	89.40
Gram-positive vs. Gram-negative	NEU	0.594	0.556-0.631	64.9	52.9	8.08
	LYM	0.596	0.558-0.634	78.4	39.6	1.05
	PLT	0.605	0.567-0.642	81.4	37.4	203.00
	PCT	0.579	0.540-0.618	78.0	39.6	0.20
	NLR	0.636	0.598-0.672	63.4	60.4	11.17
	MPV/PLT	0.591	0.551-0.629	78.0	37.8	5.00
	P-LCR	0.575	0.528-0.621	54.8	59.2	31.80
	CRP	0.596	0.554-0.638	61.7	58.8	111.60
Negative vs. *S. epidermidis*	P-LCR	0.582	0.510-0.651	66.7	49.6	25.60
Negative vs. *S. haemolyticus*	MPV	0.674	0.595-0.746	63.0	75.9	10.70
Negative vs. *S. aureus*	PLT	0.660	0.594-0.721	40.2	87.3	121.00
	MPV	0.624	0.556-0.688	50.0	75.9	10.70
	MPV/PLT	0.665	0.599-0.727	52.3	75.2	7.20
	CRP	0.698	0.629-0.761	63.0	69.6	94.10
Negative vs. *S. faecalis*	MPV	0.658	0.579-0.731	63.0	70.7	10.60
	P-LCR	0.650	0.569-0.724	63.6	72.2	31.00
Negative vs. *S. faecium*	MPV	0.679	0.599-0.751	58.3	81.2	11.00
Negative vs. *E coli*	NEU	0.674	0.624-0.722	68.1	63.4	8.02
	LYM	0.687	0.637-0.734	76.2	59.0	0.95
	PLT	0.708	0.659-0.754	43.8	86.6	122.00
	MPV	0.666	0.613-0.715	49.8	77.4	10.80
	PCT	0.649	0.596-0.699	78.1	44.4	0.20
	NLR	0.747	0.699-0.790	77.4	66.4	9.01
	MPV/PLT	0.701	0.650-0.749	63.7	68.4	6.40
	P-LCR	0.648	0.590-0.702	48.8	76.7	32.10
	CRP	0.755	0.705-0.801	75.0	68.8	89.4
Negative vs. *K. pneumoniae*	NEU	0.666	0.598-0.729	68.8	61.2	7.85
	LYM	0.680	0.613-0.742	76.2	55.2	0.99
	PLT	0.722	0.657-0.781	62.5	70.2	156.00
	MPV	0.723	0.657-0.782	63.6	75.9	10.70
	PDW	0.663	0.595-0.727	50.6	82.0	16.30
	PCT	0.672	0.604-0.735	50.6	75.2	0.14
	NLR	0.737	0.672-0.794	72.5	65.7	8.93
	MPV/PLT	0.731	0.666-0.790	54.6	81.2	7.80
	P-LCR	0.737	0.669-0.797	68.3	72.9	31.20
	CRP	0.735	0.667-0.795	55.7	81.6	133.70
Negative vs. *E. aerogenes*	LYM	0.859	0.791-0.911	90.9	78.4	0.650
	NLR	0.795	0.720-0.858	72.7	87.3	16.85
	P-LCR	0.759	0.679-0.827	71.4	79.0	32.90
Negative vs. *E. cloacae*	MPV	0.645	0.563-0.721	50.0	81.2	11.00
	P-LCR	0.634	0.551-0.712	46.7	79.7	33.30
Negative vs. *P. aeruginosa*	MPV	0.674	0.596-0.746	59.3	75.9	10.70
	P-LCR	0.675	0.594-0.749	68.4	75.9	31.90
	CRP	0.760	0.683-0.827	86.4	64.0	81.30
Negative vs. *Candida*	NLR	0.730	0.652-0.798	65.0	80.6	13.38
S. epidermidis vs. S. aureus	PLT	0.658	0.587-0.724	51.1	74.5	144.00
	PCT	0.654	0.582-0.721	58.0	71.2	0.16
	MPV/PLT	0.646	0.574-0.714	87.5	36.5	4.20
S. epidermidis vs. E coli	LYM	0.651	0.598-0.702	63.0	65.1	0.78
	PLT	0.701	0.649-0.749	70.6	61.3	175.00
	MPV	0.598	0.542-0.652	73.0	47.1	10.00
	PCT	0.675	0.621-0.726	78.1	53.8	0.20

	NLR	0.693	0.641-0.741	74.5	60.4	9.67
	MPV/PLT	0.679	0.625-0.730	74.9	55.8	5.30
	CRP	0.657	0.598-0.712	65.2	64.2	111.60
S. epidermidis vs. K. pneumoniae	PLT	0.710	0.639-0.774	78.8	55.7	184.00
	MPV	0.641	0.566-0.711	80.5	49.0	10.10
	PCT	0.693	0.620-0.759	81.8	51.9	0.21
	NLR	0.681	0.609-0.748	68.8	60.4	9.67
	MPV/PLT	0.705	0.633-0.770	77.9	55.8	5.30
	P-LCR	0.653	0.563-0.736	71.7	62.1	30.50
S. epidermidis vs. *E. aerogenes*	LYM	0.818	0.736-0.883	90.9	71.7	0.65
S. haemolyticus vs. *E coli*	NLR	0.720	0.662-0.774	68.5	71.4	10.94
S. haemolyticus vs. *E. aerogenes*	LYM	0.878	0.734-0.961	81.8	85.7	0.59
S. aureus vs. *E coli*	P-LCR	0.584	0.515-0.650	93.9	21.2	17.70
S. aureus vs. *K. pneumoniae*	P-LCR	0.652	0.557-0.740	68.3	59.6	31.50
Candida vs. E coli	MPV	0.628	0.563-0.690	63.3	57.9	10.20
Candida vs. *K. pneumoniae*	MPV	0.679	0.576-0.771	76.6	57.9	10.20
	P-LCR	0.751	0.635-0.846	78.3	75.0	28.70

BSI: bloodstream infection; CRP: C-reactive protein; LYM: lymphocyte count; MPV: mean platelet volume; MPV/PLT: mean platelet volume-to-platelet count ratio; NEU: neutrophil count; NLR: neutrophil-to-lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLT: platelet count; P-LCR: platelet larger cell ratio; AUC: the area under the curve; CI: confidence intervals.

Supplementary Table 2. Univariate odds ratios of hematological parameters in diagnosing bloodstream infection (BSI) caused by different pathogens.

Comparison	Hematological parameters	Standard β value	OR	95% CI		*P* value
				Lower bound	Upper bound	
Negative *vs.* BSI	NEU	- 0.002	0.998	0.942	1.057	0.938
	LYM	- 0.020	0.980	0.667	1.442	0.920
	PLT	< 0.001	0.999	0.979	1.020	0.925
	MPV	0.184	1.202	0.267	5.414	0.810
	PDW	- 0.021	0.979	0.847	1.131	0.775
	PCT	6.026	41.424	< 0.001	94.541	0.620
	NLR	0.040	1.041	1.005	1.077	***0.025***
	MPV/PLT	19.955	46.378	7.590	283.316	***0.029***
	P-LCR	- 0.019	0.981	0.806	1.195	0.894
	CRP	0.008	1.008	1.005	1.011	***< 0.001***
Negative *vs.* Gram-positive	PLT	0.005	1.005	1.001	1.009	***0.023***
	MPV	0.829	2.292	0.665	7.898	0.189
	NLR	0.026	1.026	1.001	1.052	***0.043***
	MPV/PLT	16.851	20.817	10.467	41.381	***0.023***
	P-LCR	- 0.099	0.906	0.762	1.078	0.265
	CRP	0.006	1.006	1.003	1.009	***< 0.001***
Negative *vs. Candida*	LYM	- 0.852	0.427	0.112	1.630	0.213
	NLR	0.035	1.036	0.988	1.086	0.146
Negative *vs.* Gram-negative	NEU	0.023	1.024	0.956	1.096	0.502
	LYM	- 0.068	0.935	0.577	1.515	0.784
	PLT	0.004	1.004	0.980	1.029	0.723
	MPV	- 0.096	0.909	0.177	6.674	0.909
	PDW	- 0.068	0.934	0.786	1.109	0.436
	PCT	- 2.605	0.074	< 0.001	74.321	0.853
	NLR	0.045	1.046	1.005	1.088	***0.027***
	MPV/PLT	14.963	3.151	0.060	16.591	0.099
	P-LCR	0.056	1.058	0.852	1.313	0.610

	CRP	0.009	1.009	1.006	1.013	***< 0.001***
Gram-positive *vs.* Gram-negative	NEU	0.041	1.041	0.993	1.092	0.095
	LYM	- 0.104	0.901	0.617	1.316	0.590
	PLT	0.006	1.006	0.989	1.023	0.494
	PCT	- 10.210	< 0.001	< 0.001	11.253	0.246
	NLR	0.008	1.009	0.988	1.030	0.429
	MPV/PLT	- 1.384	0.251	0.002	27.866	0.565
	P-LCR	0.033	1.034	0.986	1.083	0.167
	CRP	0.002	1.002	0.999	1.004	0.184
Negative *vs. S. epidermidis*	P-LCR	0.027	1.027	0.990	1.066	0.150
Negative *vs. S. haemolyticus*	MPV	0.514	1.672	1.150	2.432	***0.007***
Negative *vs. S. aureus*	PLT	0.003	1.003	0.997	1.010	0.284
	MPV	- 0.016	0.984	0.715	1.354	0.923
	MPV/PLT	24.860	6.258	1.202	32.592	***0.006***
	CRP	0.009	1.009	1.005	1.013	***< 0.001***
Negative *vs. S. faecalis*	MPV	- 0.274	0.760	0.069	8.359	0.823
	P-LCR	0.102	1.108	0.800	1.534	0.538
Negative *vs. S. faecium*	MPV	0.606	1.833	1.256	2.676	***0.002***
Negative *vs. E coli*	NEU	0.026	1.026	0.951	1.107	0.507
	LYM	- 0.033	0.967	0.552	1.695	0.908
	PLT	- 0.005	0.995	0.966	1.026	0.757
	MPV	0.108	1.114	0.251	4.939	0.887
	PCT	3.927	50.750	< 0.001	432.115	0.810
	NLR	0.045	1.046	1.002	1.091	***0.038***
	MPV/PLT	7.803	2.449	< 0.001	13.741	0.325
	P-LCR	0.008	1.008	0.838	1.212	0.936
	CRP	0.010	1.010	1.006	1.014	***< 0.001***
Negative *vs. K. pneumoniae*	NEU	0.024	1.024	0.906	1.158	0.702
	LYM	- 0.219	0.803	0.272	2.373	0.691
	PLT	0.012	1.012	0.978	1.048	0.493
	MPV	- 1.273	0.280	0.024	3.253	0..309
	PDW	-0.049	0.953	0.713	1.272	0.742
	PCT	- 7.555	0.001	< 0.001	19.531	0.714
	NLR	0.039	1.040	0.978	1.105	0.209
	MPV/PLT	19.922	4.490	0.019	106.119	0.102
	P-LCR	0.257	1.292	0.930	1.797	0.127
	CRP	0.008	1.008	1.003	1.013	***0.001***
Negative *vs. E. aerogenes*	LYM	- 4.562	0.010	< 0.001	0.613	***0.028***
	NLR	0.018	1.019	0.965	1.075	0.501
	P-LCR	0.119	1.127	1.021	1.244	***0.018***
Negative *vs. E. cloacae*	MPV	- 1.079	0.340	0.019	6.144	0.465
	P-LCR	0.210	1.234	0.840	1.814	0.285
Negative *vs. P. aeruginosa*	MPV	4.132	62.276	1.977	196.130	***0.019***
	P-LCR	- 0.493	0.611	0.391	0.953	***0.030***
	CRP	0.013	1.013	1.006	1.020	***< 0.001***
S. epidermidis vs. S. aureus	PLT	- 0.007	0.993	0.982	1.005	0.250
	PCT	- 0.422	0.655	< 0.001	4.078	0.940
	MPV/PLT	- 2.671	0.069	< 0.001	675.769	0.569
S. epidermidis vs. E coli	LYM	- 0.069	0.933	0.626	1.392	0.734
	PLT	- 0.002	0.998	0.976	1.020	0.827
	MPV	0.078	1.081	0.688	1.699	0.735
	PCT	- 4.405	0.012	< 0.001	8.224	0.703
	NLR	0.009	1.009	0.987	1.032	0.428
	MPV/PLT	- 1.065	0.345	< 0.001	280.870	0.755
	CRP	0.004	1.004	1.001	1.007	***0.021***
S. epidermidis vs. K. pneumoniae	PLT	0.020	1.020	0.990	1.051	0.189
	MPV	- 0.761	0.467	0.067	3.282	0.444

	PCT	- 25.161	< 0.001	< 0.001	1.612	0.130
	NLR	0.029	1.030	0.995	1.066	0.093
	MPV/PLT	-2.488	0.083	< 0.001	6.233	0.718
	P-LCR	0.192	1.211	0.934	1.570	0.148
S. epidermidis vs. E. aerogenes	LYM	- 3.425	0.033	0.003	0.387	***0.007***
S. haemolyticus vs. E coli	NLR	0.084	1.088	1.030	1.149	***0.003***
S. haemolyticus vs. E. aerogenes	LYM	- 5.901	0.003	< 0.001	0.254	***0.011***
S. aureus vs. E coli	P-LCR	0.031	1.032	1.000	1.064	0.052
S. aureus vs. K. pneumoniae	P-LCR	0.063	1.065	1.021	1.111	***0.004***
Candida vs. E coli	MPV	0.338	1.403	0.988	1.992	0.058
Candida vs. K. pneumoniae	MPV	- 3.378	0.034	0.001	1.046	0.053
	P-LCR	0.538	1.713	1.077	2.727	***0.023***

BSI: bloodstream infection; CRP: C-reactive protein; LYM: lymphocyte count; MPV: mean platelet volume; MPV/PLT: mean platelet volume-to-platelet count ratio; NEU: neutrophil count; NLR: neutrophil-to-lymphocyte ratio; PCT: plateletcrit; PDW: platelet distribution width; PLT: platelet count; P-LCR: platelet larger cell ratio; OR: odds ratios; CI: confidence intervals.