Predictive scoring models for persistent gram-negative bacteremia that reduce the need for follow-up blood cultures: a retrospective observational cohort study

Jongtak Jung
Seoul National University Bundang Hospital
Kyoung-Ho Song (khsongmd@gmail.com)
Seoul National University Bundang Hospital https://orcid.org/0000-0002-4517-3840
Kang Il Jun
Seoul National University College of Medicine
Chang Kyoung Kang
Seoul National University College of Medicine
Nak-Hyun Kim
Seoul National University Bundang Hospital
Pyoeng Gyun Choe
Seoul National University College of Medicine
Wan Beom Park
Seoul National University College of Medicine
Ji Hwan Bang
Seoul National University College of Medicine
Eu Suk Kim
Seoul National University Bundang Hospital
Sang-Won Park
Seoul National University College of Medicine
Nam Joong Kim
Seoul National University College of Medicine
Myoung-don Oh
Seoul National University College of Medicine
Hong Bin Kim
Seoul National University Bundang Hospital

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Abstract

Background: Although the risk factors for positive follow-up blood cultures (FUBCs) in gram-negative bacteremia (GNB) have not been investigated extensively, FUBC has been routinely carried out in many acute care hospitals. We attempted to identify the risk factors and develop a predictive scoring model for positive FUBC in GNB cases.

Methods: All adults with GNB in a tertiary care hospital were retrospectively identified during a 2-year period, and GNB cases were assigned to eradicable and non-eradicable groups based on whether removal of the source of infection was possible. We performed multivariate logistic analyses to identify risk factors for positive FUBC and built predictive scoring models accordingly.

Results: Out of 1,473 GNB cases, FUBCs were carried out in 1,268 cases, and 122 produced positive results. In patient with eradicable source of infection, we assigned points according to the coefficients from the multivariate logistic regression analysis: Extended spectrum beta-lactamase producing microorganism (+1 point), Catheter-related bloodstream infection(+1), unfavorable treatment response (+1), and quick sequential organ failure assessment score of 2 points or more (+1), administration of effective antibiotics (-1), and adequate source control (-2). In non-eradicable source of infection, assigned points were end-stage renal disease on hemodialysis (+1), unfavorable treatment response (+1) and the administration of effective antibiotics (-2). The areas under the curves were 0.861 (95% confidence interval [95CI] 0.806-0.916) and 0.792 (95CI, 0.724-0.861), respectively. When we applied a cut-off of 0, the specificities and negative predictive values (NPVs) in the eradicable and non-eradicable sources of infection groups were 95.6/92.6% and 95.5/95.0%, respectively.

Conclusions: FUBC is commonly carried out in GNB cases, but the rate of positive results is less than 10%. In our simple predictive scoring model, zero scores—which were easily achieved following the administration of effective antibiotics and/or adequate source control in both groups—had high NPVs. We expect that the model reported herein will reduce the necessity for FUBCs in GNB cases.

Background

Although the positive rate of detection from follow-up blood cultures (FUBCs) in gram-negative bacteremia (GNB) is relatively low (5.8–10.9%) [1–3], and the risk factors for persistent GNB have not been investigated extensively, FUBCs have been routinely conducted in cases of GNB in many acute care hospitals [1–4]. Unnecessary routine blood cultures are invasive, and false positives due to contamination increase medical costs and time spent in hospitals [2, 5]. The authors of a previous study identified the risk factors for persistent bacteremia, and fever was found to be the only risk factor associated with GNB [1]. Owing to the rarity of persistent GNB, the previous study had limitations, including an insufficient number of persistent GNB cases.

Recently, several studies have reported that a shorter course of antibiotics in uncomplicated GNB (hemodynamically stable patients who have received effective antibiotics and adequate source control)

[6, 7] does not produce an inferior prognosis compared to a longer course. Further, a recent randomized control study showed that a 7-day course of antibiotic therapy in uncomplicated GNB was not inferior to a 14-day course. Thus, FUBCs may not be necessary for the management of uncomplicated GNB, since it can be adequately treated by a short course of antibiotics [7].

Therefore, we attempted to identify the risk factors for a positive FUBC result in GNB and developed a predictive scoring model to reduce the need for performing unnecessary FUBCs.

Methods

Patients

We retrospectively reviewed all gram-negative episodes of bacteremia in a tertiary care university-affiliated 1,300-bed hospital in South Korea from December 1, 2015 to December 1, 2017. Patients under 18 years of age, those who died within 2 days, and patients with concomitant gram-positive bacteremia or fungemia were excluded from the study (Fig. 1). New episodes of bacteremia identified by FUBC (different species were identified by the FUBC than those identified in the initial blood culture) were also excluded when we compared the FUBC-positive and -negative groups. The study was approved by the institutional review board of Seoul National University Bundang Hospital.

Variables and groups

The variables were as follows: comorbidities, primary sources of infection, antibiotic status at the time of FUBC, identified microorganisms, susceptibility to antibiotics, fever, complete blood count, levels of C-reactive protein (CRP), quick sequential organ failure assessment (qSOFA) score, inotropic requirement, and source control status.

Patients who were subjected to FUBC 2–7 days after the initial blood culture, were assigned to the FUBC group, whereas patients who were not subjected to FUBC were assigned to the No-FUBC group. Cases were assigned to the FUBC-positive group if microorganisms with identical susceptibilities to antibiotics were identified in at least one pair of FUBCs. Cases in which bacteremia had been eliminated were assigned to the FUBC-negative group. GNB was classified into eradicable and non-eradicable sources of infection according to the possibility of removal of the primary source of infection [8–10]; for example, removal of a central venous catheter or other endovascular devices; drainage of a dilated bile duct or hydronephrosis; surgical debridement of the skin, soft tissue infection, or osteomyelitis; drainage or removal of an intra-abdominal abscess; and drainage of empyema or a lung abscess.

An unfavorable treatment response was defined as the presence of at least two of the following variables: fever, aggravated leukocytosis, and no decrease in the level of CRP on the day that the FUBC was performed. Susceptible antibiotics were deemed to have been administered effectively when they were administered at least 1 day before the FUBC according to the results of the antibiotics sensitivity test conducted in compliance with the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Adequate source control was defined as control of an eradicable source of infection at least 1 day before the FUBC was performed [3, 9].

We compared the differences in clinical characteristics between the FUBC and the no-FUBC groups to assess selection bias. Subsequently, we divided the FUBC group into eradicable and non-eradicable sources of infection and performed multivariate logistic regression analyses to identify the independent risk factors for a positive FUBC. We built a predictive scoring model by assigning scores according to the beta-coefficient of the logistic regression analyses and verified it using receiver operating characteristic curve (ROC) analysis.

Statistical analyses

The statistical analyses were performed using IBM SPSS version 25.0. Fisher's exact and Chi-square tests were used to analyze categorical variables, and student's t-tests were used for continuous variables. Multivariate logistic regression analyses were performed using variables with p-values of less than 0.1 in the univariate analyses. A p-value of less than 0.05 was considered statistically significant in the multivariate analyses.

Results

Overall, 1,481 GNB cases were identified during the study period. Of these, FUBCs were performed in 1,276 cases (86.2%), and 122 produced positive results (9.6%) (Fig. 1). Comparisons between the FUBC group and the no-FUBC group are shown in Table 1. Variables such as hematologic malignancy, the presence of an intravascular device, and the presence of extended spectrum beta lactamase (ESBL)-producing microorganisms were significantly higher in the FUBC group. There was no significant difference in the incidence of in-hospital mortality between the two groups.

Table 1
Comparisons of clinical characteristics of gram-negative bacteremia between the follow-up blood culture (FUBC) and no-FUBC groups.

	FUBC-drawn (n = 1276)	No FUBC-drawn (n = 205)	p-value
Age, years (± SD)	68.85 (± 14.27)	69.2 (± 14.13)	0.744
Sex (M)	628 (49.2%)	117 (57.1%)	0.042*
Body weight (kg)	59.90 (± 11.56)	59.24 (± 12.62)	0.533
Comorbidity			
DM	404 (31.7%)	70 (34.1%)	0.519
Liver cirrhosis	95 (7.4%)	17 (8.3%)	0.776
ESRD on HD	2 (1.0%)	35 (2.7%)	0.154
ESRD on PD	6 (0.5%)	0 (0.0%)	1.000
Rheumatic disease	18 (1.4%)	1 (0.5%)	0.500
Hematologic malignancy	136 (10.7%)	7 (3.4%)	0.001*
Solid malignancy	361 (28.4%)	60 (29.4%)	0.802
Solid organ transplantation	34 (2.7%)	5 (2.4%)	1.000
Bone marrow transplantation	28 (2.2%)	1 (0.5%)	0.167
Intravascular device	308 (24.1%)	19 (9.3%)	0.000*
Neutropenia	127 (10.0%)	6 (2.9%)	0.002*
High-dose steroid	24 (1.9%)	1 (0.5%)	0.239
Microorganism			
Escherichia coli	722 (56.6%)	113 (55.1%)	0.705
Klebsiella pneumoniae	250 (19.6%)	45 (22.0%)	0.451
Pseudomonas aeruginosa	62 (4.9%)	7 (3.4%)	0.384

*$p < 0.05$

SD, standard deviation; M, male; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis; ESBL, extended-spectrum beta-lactamase; PBSI, polymicrobial bloodstream infection; SSTI, skin and soft tissue infection; CNS, central nervous system

[a]AmpC-encoded *Enterobacteriaceae* includes *Serratia marcescens*, *Providencia stuartii*, *Proteus vulgaris*, *Citrobacter spp.*, *Enterobacter spp.*, and *Morganella morganii*

	FUBC-drawn (n = 1276)	No FUBC-drawn (n = 205)	p-value
AmpC-encoded *Enterobacteriaceae*[a]	100 (7.8%)	21 (10.2%)	0.237
Acinetobacter baumannii	24 (1.9%)	1 (0.5%)	0.239
ESBL-producing	313 (24.5%)	32 (15.6%)	0.006*
Other gram-negative	110 (8.6%)	17 (8.3%)	0.895
PBSI	50 (3.9%)	8 (3.9%)	1.000
Hospital onset	328 (25.7%)	53 (25.9%)	1.000
Site of infection			
Urinary genital tract	502 (39.3%)	71 (34.6%)	0.217
Liver abscess	56 (4.4%)	7 (3.4%)	0.583
Biliary	303 (23.7%)	86 (42.0%)	0.000*
Intra-abdominal	135 (10.6%)	18 (8.8%)	0.462
Respiratory	56 (4.4%)	5 (2.4%)	0.255
SSTI	13 (1.0%)	1 (0.5%)	0.707
Catheter-related	40 (3.1%)	2 (1.0%)	0.109
Bone and joint infection	12 (0.9%)	1 (0.5%)	1.000
Cardiovascular	3 (0.2%)	0 (0.0%)	1.000
CNS infection	3 (0.2%)	0 (0.0%)	1.000
Primary bacteremia	143 (11.2%)	10 (4.9%)	0.006*
In-hospital mortality	87 (6.8%)	18 (8.8%)	0.379

*$p < 0.05$

SD, standard deviation; M, male; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis; ESBL, extended-spectrum beta-lactamase; PBSI, polymicrobial bloodstream infection; SSTI, skin and soft tissue infection; CNS, central nervous system

[a]AmpC-encoded *Enterobacteriaceae* includes *Serratia marcescens*, *Providencia stuartii*, *Proteus vulgaris*, *Citrobacter spp.*, *Enterobacter spp.*, and *Morganella morganii*

Positive and negative clinical characteristics in the FUBC groups are compared in Table 2, according to the eradicability of the infection source, and the identified independent risk factors are listed in Table 3. In cases where the source of infection was eradicable, the independent risk factors were as follows: the presence of ESBL-producing microorganisms, catheter-related bloodstream infection, unfavorable

treatment responses, a qSOFA score of at least 2 points, the administration of effective antibiotics, and adequate source control. In cases where the source of infection was non-eradicable, the independent risk factors were as follows: end-stage renal disease on hemodialysis, unfavorable treatment responses, and the administration of effective antibiotics. We assigned points to the independent risk factors for positive FUBC, based on the beta-coefficients from the logistic regression analysis (Table 3). In cases of eradicable and non-eradicable sources of infection, the values of the area under the curve of the receiver operating characteristic curve (AUC-ROC) of each scoring model were 0.861 (95% confidence interval (CI) 0.806–0.916) and 0.792 (95% CI, 0.724–0.861), respectively (Table 3, Fig. 2). The sensitivities, specificities, positive predictive values (PPVs), and negative predictive values (NPVs) according to the cut-off values are listed in Table 4.

Table 2
Clinical characteristics of gram-negative bacteremia according to the results of follow-up blood cultures (FUBCs) and the eradicability of the source of infection.

	Eradicable source of infection			Non-eradicable source of infection		
	Positive FUBC (n = 55)	Negative FUBC (n = 411)	p-value	Positive FUBC (n = 66)	Negative FUBC (n = 736)	p-value
Age, years (± SD)	69.18 (± 12.19)	70.15 (± 13.35)	0.610	70.15 (± 14.25)	67.98 (± 14.88)	0.254
Sex (M)	29 (52.7%)	222 (54.0%)	0.886	26 (39.4%)	346 (47.0%)	0.235
Body weight (kg)						
Comorbidity						
DM	19 (34.5%)	121 (29.4%)	0.531	25 (37.9%)	238 (32.3%)	0.358
Liver cirrhosis	6 (10.9%)	31 (7.5%)	0.422	4 (6.1%)	54 (7.3%)	1.000
ESRD on HD	4 (7.3%)	7 (1.7%)	0.031*	6 (9.1%)	18 (2.4%)	0.010*
ESRD on PD	0 (0.0%)	0 (0.0%)	N.A.	2 (3.0%)	4 (.0.5%)	0.081
Rheumatic disease	1 (1.8%)	0 (0.0%)	0.119	2 (3.0%)	15 (2.0%)	0.644
Hematologic malignancy	4 (7.3%)	8 (2.0%)	0.042*	12 (18.2%)	109 (14.9%)	0.474
Solid malignancy	17 (30.9%)	149 (36.4%)	0.457	16 (24.2%)	176 (24.0%)	0.966
Solid organ transplantation	2 (3.6%)	9 (2.2%)	0.627	4 (6.1%)	19 (2.6%)	0.113
Bone marrow transplantation	2 (3.6%)	1 (0.2%)	0.038*	2 (3.0%)	22 (3.0%)	1.000
Intravascular device	75 (18.2%)	26 (47.3%)	0.000*	4 (6.1%)	19 (2.6%)	0.113

*$p < 0.05$

SD, standard deviation; N.A., not available; M, male; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis; ESBL, extended-spectrum beta-lactamase; PBSI, polymicrobial bloodstream infection; SSTI, skin and soft tissue infection; CNS, central nervous system

[a]AmpC-encoded *Enterobacteriaceae* includes *Serratia marcescens*, *Providencia stuartii*, *Proteus vulgaris*, *Citrobacter spp.*, *Enterobacter spp.*, and *Morganella morganii*

	Eradicable source of infection			Non-eradicable source of infection		
Neutropenia	1 (1.8%)	8 (2.0%)	1.000	11 (16.7%)	105 (14.3%)	0.608
High-dose steroid	1 (1.8%)	4 (1.0%)	0.468	4 (6.1%)	15 (2.0%)	0.063
Microorganism						
Escherichia coli	22 (40.0%)	205 (49.9%)	0.197	36 (54.5%)	456 (62.0%)	0.291
Klebsiella pneumoniae	11 (20.0%)	91 (22.1%)	0.735	14 (21.2%)	133 (18.1%)	0.527
Pseudomonas aeruginosa	5 (9.1%)	19 (4.6%)	0.185	5 (7.6%)	33 (4.5%)	0.231
AmpC-encoded *Enterobacteriaceae*[a]	7 (12.7%)	49 (11.9%)	1.000	4 (6.1%)	39 (5.3%)	0.774
Acinetobacter baumannii	1 (1.8%)	6 (1.5%)	0.587	2 (3.0%)	15 (2.0%)	0.644
ESBL-producing	21 (38.2%)	84 (20.4%)	0.003*	39 (59.1%)	169 (23.0%)	0.000*
Other gram-negative	9 (16.4%)	34 (8.3%)	0.052*	5 (7.6%)	59 (8.0%)	0.899
PBSI	5 (9.1%)	32 (7.8%)	0.789	1 (1.5%)	12 (1.6%)	1.000
Hospital onset	22 (40.0%)	66 (16.1%)	0.000*	19 (28.8%)	216 (29.3%)	1.000
Site of infection						
Urinary genital tract	12 (21.8%)	80 (19.5%)	0.718	38 (57.6%)	372 (50.5%)	0.305
Liver abscess	2 (3.6%)	39 (9.5%)	0.205	0 (0.0%)	13 (1.8%)	0.615
Biliary infection	9 (16.4%)	218 (53.0%)	0.000*	1 (1.5%)	73 (9.9%)	0.024*
Intra-abdominal	5 (9.1%)	38 (9.2%)	1.000	6 (9.1%)	85 (11.5%)	0.687

*$p < 0.05$

SD, standard deviation; N.A., not available; M, male; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis; ESBL, extended-spectrum beta-lactamase; PBSI, polymicrobial bloodstream infection; SSTI, skin and soft tissue infection; CNS, central nervous system

[a]AmpC-encoded *Enterobacteriaceae* includes *Serratia marcescens*, *Providencia stuartii*, *Proteus vulgaris*, *Citrobacter spp.*, *Enterobacter spp.*, and *Morganella morganii*

	Eradicable source of infection			Non-eradicable source of infection		
Respiratory	1 (1.8%)	2 (0.5%)	0.315	7 (10.6%)	44 (6.0%)	0.180
SSTI	3 (5.5%)	4 (1.0%)	0.039*	2 (3.0%)	4 (0.5%)	0.081
Catheter-related	18 (32.1%)	22 (5.4%)	0.000*	0 (0.0%)	0 (0.0%)	N.A.
Bone and joint infection	3 (5.5%)	2 (0.5%)	0.013*	1 (1.5%)	6 (0.8%)	0.453
Cardiovascular	2 (3.6%)	1 (0.2%)	0.038*	0 (0.0%)	0 (0.0%)	N.A.
CNS infection	0 (0.0%)	0 (0.0%)	N.A.	0 (0.0%)	2 (0.2%)	1.000
Primary bacteremia	0 (0.0%)	0 (0.0%)	N.A.	11 (16.7%)	131 (17.8%)	0.869
Inotropic requirement	24 (5.8%)	10 (18.2%)	0.003*	9 (13.6%)	53 (7.2%)	0.061
Unfavorable treatment response	30 (55.6%)	130 (32.5%)	0.001*	31 (48.4%)	215 (30.0%)	0.002*
qSOFA score ≥ 2	20 (36.4%)	45 (10.9%)	0.000*	16 (24.2%)	108 (14.7%)	0.039
Effective antibiotics	34 (61.8%)	350 (85.2%)	0.000*	27 (40.9%)	639 (86.8%)	0.000*
Adequate source control before FUBC	13 (23.6%)	322 (78.3%)	0.000*	N.A.	N.A.	N.A.

*$p < 0.05$

SD, standard deviation; N.A., not available; M, male; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, hemodialysis; PD, peritoneal dialysis; ESBL, extended-spectrum beta-lactamase; PBSI, polymicrobial bloodstream infection; SSTI, skin and soft tissue infection; CNS, central nervous system

[a]AmpC-encoded *Enterobacteriaceae* includes *Serratia marcescens*, *Providencia stuartii*, *Proteus vulgaris*, *Citrobacter spp.*, *Enterobacter spp.*, and *Morganella morganii*

Table 3

Independent risk factors and assigned scores used to build the predictive scoring model for positive follow-up blood culture in gram-negative bacteremia, according to eradicable and non-eradicable sources of infection.

Eradicable source of infection				
	Beta-coefficient	Odds ratio (95% CI)	p-value	Assigned score
ESBL-producing microorganism infection	1.001	2.720 (1.179–6.271)	0.019	+ 1
CRBSI	1.374	3.95 (1.522–10.255)	0.005	+ 1
Unfavorable treatment response*	0.802	2.229 (1.262–3.937)	0.006	+ 1
qSOFA score ≥ 2 on the day of FUBC	0.864	2.371 (1.034–5.438)	0.041	+ 1
Effective antibiotics administration before the day of FUBC	-1.007	0.365 (0.164–0.814)	0.014	-1
Adequate source control before the day of FUBC	-1.983	0.138 (0.064–0.294)	0.000	-2
Non-eradicable source of infection				
ESRD on HD	1.406	4.081 (1.331–12.515)	0.014	+ 1
Unfavorable treatment response*	0.802	2.229 (1.262–3.937)	0.006	+ 1
Effective antibiotics administration before the day of FUBC	-2.015	0.133 (0.069–0.258)	0.000	-2

CI, confidence interval; ESBL, extended-spectrum beta-lactamase; CRBSI, catheter-related bloodstream infection; qSOFA, quick sequential organ failure assessment; FUBC, follow-up blood culture; ESRD, end-stage renal disease; HD, hemodialysis.

*Unfavorable treatment response was defined as positive result for at least 2 variables along with the presence of fever, aggravated leukocytosis, and no decrease of C-reactive protein on the day of FUBC.

Table 4
Receiver operating characteristics and predictability of scoring models for positive follow-up blood culture in gram-negative bacteremia, according to the various cut-off values.

	AUC (95% CI)	Cut-off	Sensitivity	Specificity	PPV	NPV
Eradicable source of infection*	0.861 (0.806–0.916)	-2	88.5%	67.0%	27.7%	97.6%
		-1	76.9%	82.1%	38.1%	96.1%
		0	46.2%	95.6%	60.0%	92.6%
		1	17.3%	99.3%	75%	90.63%
		2	3.8%	100%	100%	87.9%
Non-eradicable source of infection	0.792 (0.724–0.861)	-2	83.9%	58.4%	14.4%	97.6%
		-1	58.9%	86.9%	27.3%	96.2%
		0	39.3%	95.5%	42.3%	95.0%
		1	3.6%	100.0%	100.0%	92.5%

AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value

*Gram-negative bacteremia in which the primary source of infection could be removed, e.g., removal of a central venous catheter or any other endovascular device, drainage of a dilated bile duct or hydronephrosis, surgical debridement of skin and soft tissue infection or osteomyelitis, drainage or removal of an intra-abdominal abscess, or drainage of empyema or a lung abscess.

When we applied a cut-off value of 0, the specificities of the eradicable and non-eradicable sources of infection were 95.6% and 95.5%, respectively. The NPVs of the predictive scoring models in the eradicable and non-eradicable source infections were 92.6% and 95.0%, respectively.

Discussion

Our study revealed that FUBCs were performed in most of the patients with GNB, but less than 10% produced positive results. In contrast to gram-positive bacteremia, positive FUBC results were not common in GNB [1, 3].

In eradicable sources of infection, variables such as ESBL-producing organisms, catheter-related bloodstream infections (CRBSIs), unfavorable treatment responses, and qSOFA scores of at least 2 were independent risk factors, but when effective antibiotics were administered and there was adequate source control the day before performing FUBC, the probability of negative conversion of bacteremia in FUBC increased significantly. When appropriate management (e.g., administration of effective antibiotics and source control) was performed, and there was a clear clinical response (qSOFA score < 2), the score predicted by the model did not exceed the cut-off value (zero points), and the probability of negative conversion in FUBC was as high as 92.6%. In *Staphylococcus aureus* infections, delays in the removal of

eradicable sources of infection, the initial administration of inappropriate antibiotics, and delays in the delivery of appropriate antibiotics were important risk factors for persistent bacteremia [9, 11]. Early source control (within 48 h) was also important for eradicating bacteremia in both gram-positive and gram-negative bacteremia [3]. Therefore, as with *S. aureus* bacteremia, in cases of GNB with eradicable sources of infection—regardless of the site of infection, underlying diseases, or causative microorganisms—if there is appropriate management and the clinical response is favorable, FUBC provides little benefit.

In cases in which the source of infection was non-eradicable, hemodialysis and an unfavorable treatment response were independent risk factors. However, if effective antibiotics were administered to the patient, bacteremia was usually eliminated. If effective antibiotics were administered—regardless of the underlying disease, microorganism type, or treatment response—the score did not exceed the cut off-value (zero points), and the probability of negative conversion of bacteremia was 95.0%.

Therefore, performing FUBC to evaluate the response to treatment can be avoided in most uncomplicated cases of GNB. In GNB cases, FUBC could be applied selectively to patients with a high risk of positive FUBCs, unlike in *S. aureus* bacteremia or candidemia.

Our study has some limitations. First, there may have been bias towards the FUBC group, because the study was conducted retrospectively. However, variables such as hematologic malignancy, presence of an intravascular device, and ESBL-producing microorganisms—which were significantly more prevalent in the FUBC group than in the no-FUBC group— were also significant risk factors for positive FUBCs (Table 1). This means that there was a higher probability of persistent bacteremia in the FUBC group than in the no-FUBC group. The NPVs of predictive scoring models in real-world cases of GNB would be higher than those indicated in the present study. Therefore, this selection bias did not alter our conclusion. Second, we did not determine how FUBC affects patient outcomes such as mortality, morbidity, length of stay in hospital, or total cost of medical care. Therefore, our findings alone will not be sufficient to change routine practice. A recent study revealed that when FUBCs were performed in cases of severe gram-negative bloodstream infection, they were associated with improved clinical outcomes [12]. If FUBCs are performed selectively according to the results of our predictive scoring model, clinical outcomes may be improved, and costs may be reduced. However, further investigations such as a prospective randomized control study should be conducted to reveal the exact clinical impact of FUBC in GNB.

Conclusion

In this study, although FUBC was commonly used in cases of GNB, there were few positive results (<10% of cases). We expect that the application of our simple predictive scoring model will reduce the need for performing unnecessary FUBC in uncomplicated cases of GNB.

Abbreviations

Follow-up blood culture(FUBC), Gram-negative bacteremia (GNB), C-reactive protein (CRP), Quick sequential organ failure assessment (qSOFA) score, Extended spectrum beta lactamase (ESBL), Confidence interval (CI), Positive predictive values (PPVs), Negative predictive values (NPVs), Catheter-related bloodstream infection (CRBSI)

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board of Seoul National University Bundang Hospital (B-1805/468-101). and the requirement for informed consent was waived due to the retrospective design of the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the study are available from the corresponding author on reasonable request.

Competing interests

There are no conflicts of interest to declare

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Author contributions

Conceptualization, Methodology, Writing – original draft, Investigation, Data curation, Formal analysis: J.J, K.H.S, Writing – review & editing: K.I.J, C.K.K, N.H.K, P.G.C, J.H.B, Data interpretation, Writing – review & editing: K.H.S, W.B.P, E.S.K, S.W.P, N.J.K, M.D.O, H.B.K. All authors have provided final approval for the final version of the manuscript.

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Figures

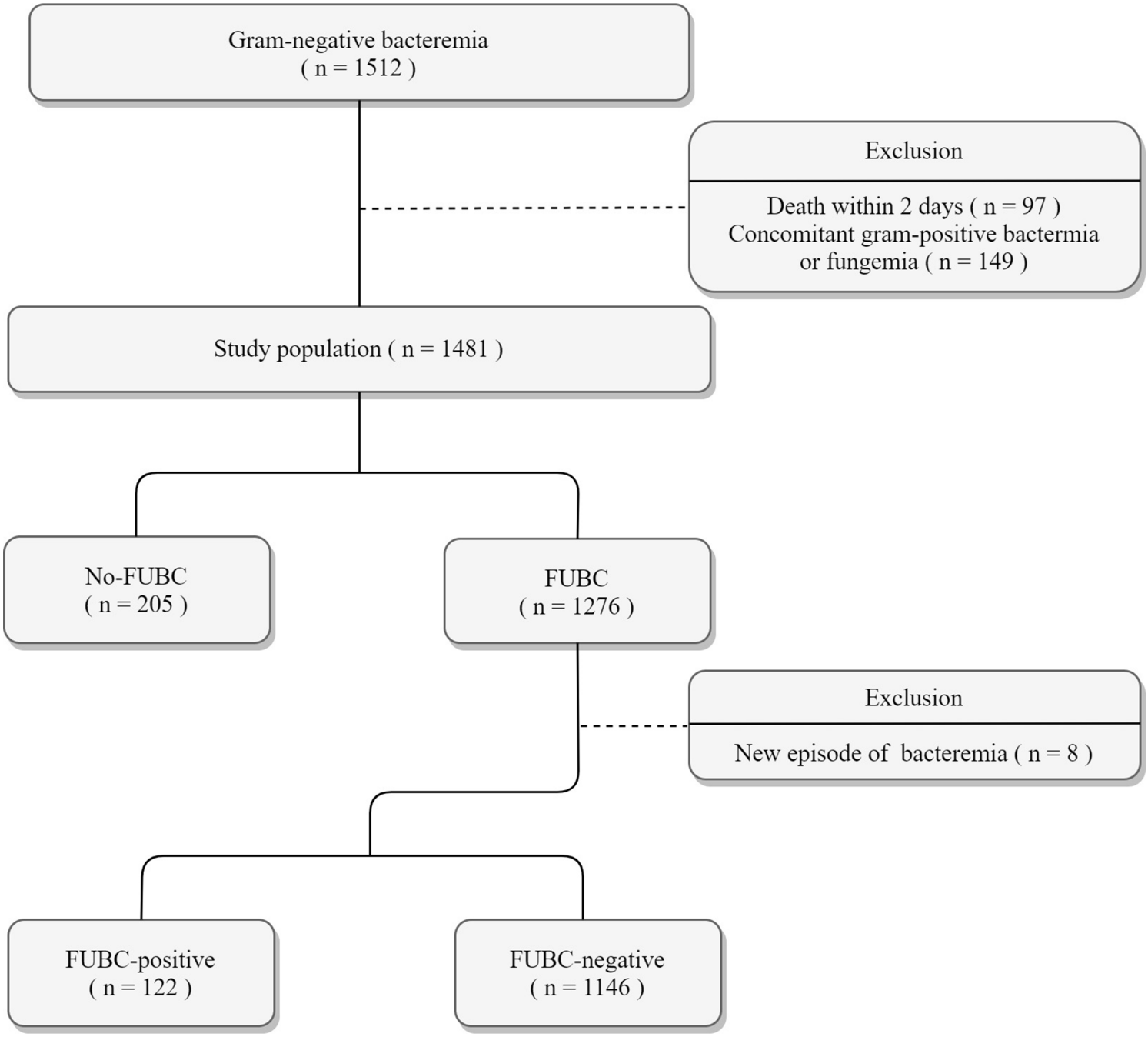

Figure 1

Flow chart of the study. Inclusion and exclusion criteria for the study population. FUBC: follow-up blood culture.

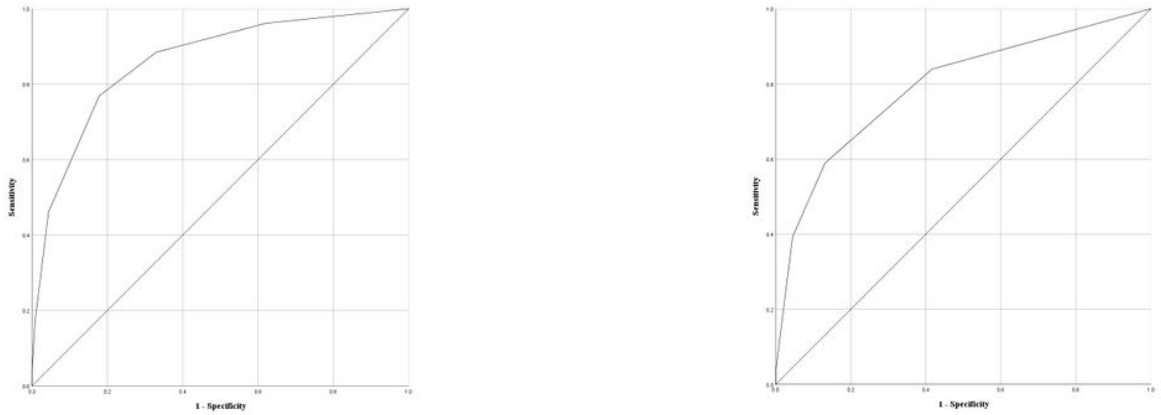

Figure 2

(A) Receiver operating characteristic (ROC) analysis of the predictive scoring model in cases with eradicable sources of infection. The area under the curve (AUC) was 0.861 (95% confidence interval (CI) 0.806–0.916). (B) ROC analysis of the predictive scoring model in cases with non-eradicable sources of infection. The AUC was 0.792 (95% CI, 0.724–0.861).