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KIND (Korea INfectious Diseases) Study Group

Predicting Central Nervous system Complications in *Staphylococcus aureus* Bacteremia using Clinical Scoring System

SNUH

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Abstract

Introduction
Central nervous system (CNS) complications occurring in patients with *Staphylococcus aureus* bacteremia (SAB) are the most severe complications, showing worse morbidity and mortality. In this study, we compared clinical data of SAB patients between cases with CNS complication and without CNS complication, and analyzed the risk factor of CNS complications.

Methods
Clinical data from cases with SAB that occurred during 5 years at 4 hospitals were collected. Presence of CNS complications were confirmed by brain magnetic resonance imaging or computed tomography in cases of infarct, hemorrhage or brain abscess, and by lumbar puncture in cases of meningitis. We further excluded the cases who already had CNS lesions such as traumatic injury, brain tumor, or cerebrovascular accident because it is difficult to ascertain whether a new lesion occurs or not. We also excluded the cases who were died or transfer out within 7 days of bacteremia onset.
Cases who had CNS complications were classified as complication group, whereas cases who did not showed neurologic complications were classified as non-complication group. We compared the clinical profiles between complication group and non-complication group, and analyzed the risk factor of CNS complications by multi-variate logistic regression analysis.

Results
A total of 1085 cases of SAB patients were included. Among these, 43 (4.0%) cases were complication group, while 948 (87.4%) cases were non-complication group. Ninety-four (8.7%) cases were excluded because CNS lesions were already present. In complication group, 23 cases showed multiple embolic infarction, 8 cases showed intracranial hemorrhage, 8 cases showed both infarction and hemorrhage, and 4 cases showed brain abscess or meningitis. Compared to non-complication group, complication group showed higher SOFA score and longer bacteremia duration. Proportion of methicillin susceptible isolates, endovascular infection, and presence of any metastatic infection were higher in complication group (table 1). When selecting by having more than 4 variables among SOFA score ≥ 6 (weight 2), methicillin susceptible isolates, endovascular infection (weight 2), and presence of metastatic infection, it helps to distinguish whether CNS complications are occur (Area under curve of ROC curve= 0.79, p<0.001).

Discussion
CNS complication could be predicted by scoring system using clinical variables, and useful in deciding early CNS evaluation.

Objective

1. We described the clinical characteristics and risk factors of CNS complications in patients with *S. aureus* bacteremia
2. We also suggested the scores to predict whether CNS complication occur.

Methods

Hospital: Four university affiliated hospitals
Inclusion criteria: Staphylococcus aureus bacteremia
Exclusion criteria: Age under 15 years, polymicrobial infection, obvious contamination

Definition of CNS complication;
1) multiple embolic infarct
2) Intra-cranial hemorrhage (Subarachnoid, intracerebral, intra-ventricular…)
3) Brain abscess
4) Cerebritis, meningitis

Group 1) confirmed CNS complications (by CNS imaging)
Group 2) Confirmed no CNS complications (by CNS imaging)
Group 3) No CNS symptoms, but not performed CNS imaging
Group 4) pre-existed CNS lesion (tumor, ICH, SAH, old infarct… before SAB)

Results

Figure 1. Flow-chart of Selection of enrolled patients

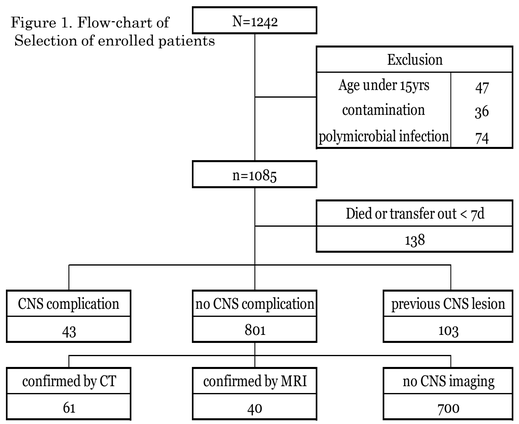

Figure 2.Distribution of SOFA score

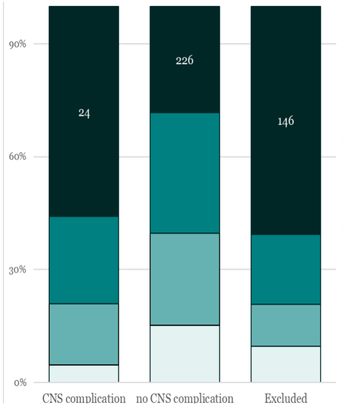

Figure 3.ROC curve of score to predict CNS complications using clinical variables

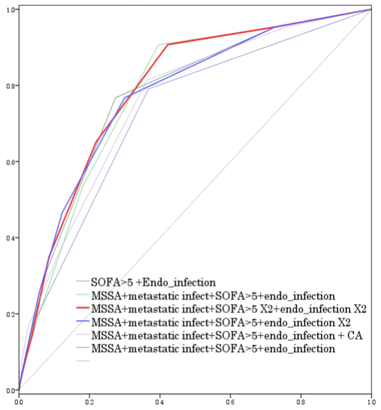

Table 1. Baseline characteristics and risk of CNS complications in *S. aureus* bacteremia patients with or without CNS complications

Variables	Complication Group (n=43)	Non-complication group (n=801)	p-value	Adjusted odds ratio	P-value
Sex (male)	23 (54%)	499 (62%)	0.25		
Age (mean ± S.D)	66 (±17)	64 (±16)	0.38		
Community onset infection	30 (70%)	450 (56%)	0.08	1.28 (0.59-2.82)	0.53
Methicillin susceptible isolates	27 (63%)	380 (47%)	0.05	2.17 (1.06-4.46)	0.03
SOFA score (median (IQR))	6 (3-9)	3.5 (1-6)	0.01		
SOFA >5	24 (55.8%)	226 (28.2%)	<0.001	1.14 (1.06-1.23)	<0.01
Prolonged bacteremia over 4d	24 (55.8%)	280 (35.0%)	0.006	1.62 (0.81-3.21)	0.17
Prolonged bacteremia over 7 d	10 (23%)	134 (17%)	0.27		
Duration of bacteremia (median (IQR))	4 (1-6)	2 (0-5)	0.01		
Endovascular involvement of infection	18 (42%)	106 (13%)	<0.01	2.80 (1.35-3.81)	<0.01
Endocarditis as primary site	8 (19%)	13 (2%)			
Endovascular except endocarditis	9 (21%)	70 (9%)			
Presence of prosthesis	4 (9%)	16 (2%)	<0.01	2.90 (0.79-10.62)	0.109
Presence of any metastatic infection	20 (47%)	155 (19%)	<0.01	2.14 (1.05-4.35)	0.04
Mortality					
30 day-mortality	6 (16%)	76 (10%)	0.27		
90 day-mortality	11 (34%)	121 (19%)	0.03		
In-hospital mortality	9 (24%)	109 (14%)	0.08		

Among the 1242 patients from four hospitals, 1085 patients of *S. aureus* bacteremia were included in the study.

Central nervous (CNS) complications were occurred in 43 patients, whereas 801 patients did not suffered from CNS complications (figure 1).

Distribution of SOFA score was showed in figure 2.

Table 2. Various model of predicting CNS complications using clinical variables

Model	Score (value)	AUC	CNS complication	No CNS complication	Sensitivity	Specificity
SOFA>5 endovascular infection	0	0.727	9 (20.9%)	507 (63.3%)	1	0
	1		26 (60.5%)	256 (32.0%)	0.791	0.633
	2		8 (18.6%)	38 (4.7%)	0.186	0.953
SOFA>5 endovascular infection MSSA metastatic infection	0	0.775	2 (4.7%)	219 (27.3%)	1	0
	1		8 (18.6%)	363 (45.3%)	0.953	0.273
	2		20 (46.5%)	160 (20.2%)	0.767	0.727
	3		11 (25.6%)	52 (6.5%)	0.302	0.926
	4		2 (4.7%)	7 (0.9%)	0.047	0.991
SOFA>5 endovascular infection X 2 MSSA metastatic infection	0	0.775	2 (4.7%)	219 (27.3%)	1	0
	1		8 (18.6%)	342 (42.7%)	0.953	-726
	2		13 (30.2%)	142 (17.7%)	0.767	0.7
	3		9 (20.9%)	52 (6.5%)	0.465	0.878
	4		9 (20.9%)	39 (4.9%)	0.265	0.943
	5		2 (4.7%)	7 (0.9%)	0.047	0.991
SOFA>5 X 2 endovascular infection MSSA metastatic infection	0	0.781	2 (4.7%)	219 (27.3%)	1	0
	1		2 (4.7%)	265 (33.1%)	9.953	0.273
	2		16 (37.2%)	172 (21.5%)	0.907	0.604
	3		15 (34.9%)	103 (12.9%)	0.535	0.819
	4		6 (14.0%)	35 (4.4%)	0.186	0.948
	5		2 (4.7%)	7 (0.9%)	0.047	0.991
SOFA>5 X 2 endovascular infection X 2 MSSA metastatic infection	0	0.79	2 (4.7%)	219 (27.3%)	1	0
	1		2 (4.7%)	244 (30.5%)	0.953	0.273
	2		11 (25.6%)	163 (20.3%)	0.907	0.578
	3		13 (30.2%)	107 (13.4%)	0.651	0.782
	4		9 (20.9%)	39 (4.9%)	0.349	0.915
	5		4 (9.3%)	22 (2.7%)	0.14	0.962
	6		3 (4.7%)	7 (0.9%)	0.047	0.991
SOFA>5 endovascular infection MSSA metastatic infection, Community acquired	0	0.758	2 (4.7%)	195 (24.3%)	1	0
	1		6 (14.0%)	315 (39.3%)	0.953	0.243
	2		19 (44.2%)	196 (24.5%)	0.814	0.637
	3		9 (20.9%)	75 (9.4%)	0.372	0.881
	4		5 (11.6%)	18 (2.2%)	0.163	0.975
	5		2 (4.7%)	2 (0.2%)	0.047	0.998

In univariate analysis, Methicillin susceptible isolates, higher SOFA score, endovascular infection as primary site, presence of prosthesis, and presence of metastatic infection was associated with CNS complications (Table 1).

Calculate predicting scores from various composition of these variables were tried, and among these, using methicillin susceptible isolates, SOFA score 6 or higher (weight 2), endovascular infection (weight 2) as site of infection, and presence of metastatic infection revealed good prediction. (Table 2)

Using Receiver operating Characteristic curve (ROC), model composed by above factors showed highest area under curve (0.79, p<0.001), and using cut-off value 3 or more showed 65.1% of sensitivity, and 78.2% of specificity. If we used the cut-off vale, 2 or more, sensitivity was increased to 90.7%, but specificity decreased to 57.8% (figure 3).

Conclusions

CNS complication could be predicted by scoring system using clinical variables, and useful in deciding early CNS evaluation.

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