Prognostic Value of B-type Natriuretic Peptide With the Sequential Organ Failure Assessment Score in Septic Shock

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Abstract: *Background:* The aim of this study was to evaluate the prognostic value of B-type natriuretic peptide (BNP) in combination with the sequential organ failure assessment (SOFA) score in patients with septic shock at the time of emergency department (ED). *Methods:* Study subjects included all consecutive patients with septic shock who were treated with resuscitation bundle therapy between January 2010 and July 2012. SOFA scores and BNP were measured at ED recognition. The primary outcome was 28-day mortality. The area under the receiver operating characteristic curve was used to compare the predictive ability of SOFA score alone and in combination with BNP. *Results:* A total of 290 patients with septic shock admitted to ED were included. The BNP and SOFA score were higher in nonsurvival group compared with survival group (1,156.0 versus 469.1 pg/mL, $P < 0.01$; 9.9 versus 8.0, $P < 0.01$). In the receiver operating characteristic curves for predicting 28-day mortality, the area under the curves of SOFA score combined with BNP was 0.728 (95% confidence interval [CI]: 0.658–0.798) and SOFA score alone was 0.682 (95% CI: 0.610–0.755). Although the predictive ability of SOFA with BNP was statistically higher than that of SOFA alone ($P = 0.02$), it could not increase prognostic accuracy clinically significantly. SOFA with BNP was an independent predictor of 28-day mortality (odds ratio: 1.40, 95% CI: 1.15–1.71). *Conclusions:* The combination of SOFA with BNP at the time of ED presentation may provide superior prognostic accuracy to the patients with septic shock. However, further studies need to validate the prognostic usefulness of SOFA with BNP.

Key Indexing Terms: Sepsis; Brain natriuretic peptide; Organ dysfunction; Prognosis. **[Am J Med Sci 2015;349(4):287–291.]**

Despite major advances in intensive care, sepsis remains a major source of morbidity and mortality in the United States.[1–3] Mortality in sepsis is predominantly because of multiple organ failure, which is characterized by early myocardial dysfunction.[4] Therefore, evaluating the severity of organ dysfunction and assessing mortality risk in sepsis patients will be helpful in identification of subgroups with high mortality risk, selection of therapeutic interventions and improvement of quality of care.

The sequential organ failure assessment (SOFA) score was created by the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine, with the intent of creating an objective tool to describe individual and aggregate organ failure.[5] It is a simple and objective score that allows for calculation of both the number and the severity of organ dysfunction in 6 organ systems (respiratory, coagulatory, hepatobiliary, cardiovascular, renal and neurologic) (Table 1). The usefulness of the SOFA score has been previously validated in large cohorts of critically ill patients.[6,7] However, its prognostic performance did not be reported consistent results, especially in emergency department (ED) populations.[8–10] In addition, SOFA score required only inotropic agents as a measure of cardiac dysfunction, which is almost appeared in patients with septic shock (Table 1). Thus, it may be needed adjustment of SOFA score using additional marker for cardiac dysfunction.

B-type natriuretic peptide (BNP), secreted in response to ventricular wall tension, has been used for the early diagnosis of heart failure in patients presenting to the ED with dyspnea.[11–13] Recently, elevated BNP levels have been reported in patients with septic shock.[14–16] However, the clinical usefulness of BNP as organ failure marker has not been investigated yet.

The aim of this study was to evaluate the prognostic value of SOFA score alone and in combination with BNP for predicting 28-day mortality in patients with septic shock at the time of ED.

METHODS

Patients

This retrospective cohort single-center study was conducted at 2,800-bed, university-affiliated, tertiary referral center in Seoul, Korea, with the approval of the Ethics Committee. The cohort was composed of 290 consecutive patients with septic shock who are measured BNP at the time of diagnosis in ED and treated with protocol-driven resuscitation bundle therapy including early-goal directed therapy (EGDT) between January 2010 and July 2012.[17] Diagnosis of septic shock was accompanied by refractory hypotension (systolic arterial blood pressure < 90 mm Hg or mean arterial blood pressure < 60 mm Hg) requiring vasopressors, despite adequate fluid therapy.[18] Patients were excluded if they have one of the following: age < 18 years, pregnancy, absolute contraindication for a central venous catheter, transfer from other hospital, acute myocardial infarction, heart failure, trauma, do not resuscitate status, and for patients with multiple admissions, only the first admission was considered. Therapeutic strategy was carried out according to the standard protocol for sepsis, including EGDT, antibiotics, vasopressors, lung-protective ventilation, glucocorticoids and surgical intervention if indicated.[17] The primary outcome of this study was the 28-day mortality.

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TABLE 1. The sequential organ failure assessment score

Score	1	2	3	4
Respiration				
PaO_2/FiO_2	<400	<300	<200 with respiratory support	<100 with respiratory support
Coagulation				
Platelet count (×1,000/μL)	<150	<100	<50	<20
Liver				
Bilirubin (mg/dL)	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular				
Hypotension	MAP < 70 mm Hg	Dopamine ≤5 or dobutamine (any dose)[a]	Dopamine >5 or epinephrine ≤0.1 or norepinephrine ≤0.1	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1
Central nervous system				
GCS	13–14	10–12	6–9	<6
Renal				
Creatinine (mg/dL) or urine output	1.2–1.9	2.0–3.4	3.5–4.9 or <500 mL/d	>5.0 or <200 mL/d

Six organ systems are evaluated on a scale of 1–4 each, according to the criteria indicated.
[a] Adrenergic agents administered for at least 1 hr (doses given are in $\mu g \cdot kg^{-1} \cdot min^{-1}$).
GCS, glasgow coma scale; MAP, mean arterial pressure.

Data Collection

Demographic and clinical data, including age, gender, symptoms, medical history, initial vital signs, blood results, 28-day course and diagnosis on admission, were retrieved from our septic shock registry. SOFA score was calculated in ED at the time of recognition of septic shock. The serum BNP levels were measured from blood samples that were drawn at ED admission. The BNP levels were estimated by using a chemiluminescence immunoassay (ADVIA Centaur; Bayer Diagnostics, Tarrytown, NY) in a central laboratory. The analytical sensitivity of this assay was 2.0 pg/mL. With this assay, a normal level was <100 pg/mL.

Statistical Analysis

Continuous variables are expressed as mean with standard deviation or median and full range if the assumption of a normal distribution was violated. Categorical variables were given in terms of numbers and percentages. The primary analysis compared 28-day survivors with nonsurvivors. All variables were tested for normal distribution using the Kolmogorov-Smirnov test. Student's t test was used to compare the means of normally distributed continuous variables, whereas the Mann-Whitney's U test was used to compare noncontinuous variables. The χ^2 or Fisher's exact test was applied for categorical variables. Univariate and multivariate analyses were performed using logistic regression analysis to evaluate the association of BNP with 28-day mortality. The results of multivariate logistic regression analysis were reported as odds ratios and 95% confidence intervals (CIs). Receiver operating characteristic curves (ROC) were constructed and area under the curves (AUCs) were evaluated.[19] The optimal cutoff values of BNP for predicting 28-day mortality were estimated by ROC. Discrimination capability of AUC between SOFA score alone and in combination with BNP was compared using a nonparametric approach. A 2-sided P value <0.05 was considered statistically significant. All statistical analyses were performed by using SPSS for Windows version 18.0 (SPSS Inc, Chicago, IL).

RESULTS

A total of 290 patients with septic shock in the ED were enrolled in the study. The mean age of the cohort was 63.9 years and 170 patients were male. Overall, 227 patients survived and 63 patients died, yielding a 28-day mortality rate of 21.7%. The incidence of myocardial dysfunction, defined as ejection fraction < 45%, was 23.2%. Table 2 summarizes the demographics and initial clinical characteristics between survivors and nonsurvivors. More nonsurvivors were in group of EGDT failure (71.4% versus 58.1%), mechanical ventilation (71.4% versus 22.0%) and continuous renal replacement therapy (34.9% versus 7.5%). In addition, nonsurvivors had higher respiratory rate (25.5 versus 22.5), initial lactate levels (5.8 versus 3.5 mmol/L), BNP (1,156.0 versus 469.1 pg/mL) and SOFA score (9.9 versus 8.0) than survivors (all $P < 0.05$; Tables 2 and 3). Table 4 shows the relationship between BNP interquartile range and hemodynamic characteristics. In particular, the comparison of mortality according to the quartile level of BNP was as follows: 1st quartile (BNP < 100 pg/mL) 12.2%, 2nd quartile (100 ≤ BNP < 250 pg/mL) 14.8%, 3rd quartile (250 ≤ BNP < 650 pg/mL) 21.0% and 4th quartile (BNP ≥ 650 pg/mL) 39.7% (Figure 1). We allocated 4 points as the new severity score of cardiac dysfunction like other severity of dysfunction in SOFA score: 1 point for 2nd quartile, 2 points for 3rd quartile and 4 points for 4th quartile of BNP. Multivariate analysis showed that SOFA score combined with BNP was independently associated with mortality (1.40 [95% CI: 1.15–1.71], $P < 0.01$; Table 5).

In the ROC curves for predicting 28-day mortality, the AUC of SOFA score combined with BNP was 0.728 (95% CI: 0.658–0.798, $P < 0.01$) and SOFA score alone was 0.682 (95% CI: 0.610–0.755, $P < 0.01$). The predictive ability of SOFA score combined with BNP was significantly improved than that of SOFA score alone ($P = 0.02$; Figure 2).

DISCUSSION

This study evaluated whether SOFA score in combination with BNP can predict the 28-day mortality in patients