Aging Clin Exp Res (2016) 28:917–924
DOI 10.1007/s40520-015-0500-7

ORIGINAL ARTICLE

Are prognostic scores and biomarkers such as procalcitonin the appropriate prognostic precursors for elderly patients with sepsis in the emergency department?

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Received: 12 July 2015 / Accepted: 13 November 2015 / Published online: 7 December 2015

Abstract

Background The mortality of patients with severe sepsis and septic shock is still high, and the prognosis of elderly patients tends to be particularly poor. Therefore, this study sought to conduct a comparative analysis of the abbreviated mortality in emergency department sepsis (abbMEDS) score, sequential organ failure assessment (SOFA) score, infection probability score (IPS), initial procalcitonin (PCT), and cytokine levels to investigate the effectiveness of each index in predicting the prognosis of elderly patients with sepsis in the emergency department (ED).

Methods This was a single-center prospective study, and classified 55 patients (≥65 years of age) with systemic inflammatory response syndrome (SIRS) from January 2013 to December 2013 in the ED. A total of 36 elderly patients were diagnosed with sepsis. The prediction of prognosis using the prognostic scores (abbMEDS, SOFA, IPS) was analyzed. An early blood examination (WBC count, C-reactive protein, PCT, and cytokines) was conducted within the first 2 h of the patient's arrival at the ED.

Results The median (IQR) age of subjects was 76.5 (70.5–81.5). After 28 days, 27 subjects (75 %) had survived, and 9 (25 %) had died. Fifteen (41.7 %) were sent to intensive care units (ICUs). The SOFA score and abbMEDS showed higher median (IQR) values of 9.5 (7.0–11.0) and 13.5 (12.0–15.0), respectively, in the ICU group than in the general ward group ($p < 0.001$). Analysis of the levels of PCT, IL-10, IL-6, and IL-5 had a significantly better ability to predict ICU admission ($p = 0.001$, $p = 0.023$, $p = 0.030$, $p = 0.001$). The prediction of mortality in the first 28 days via SOFA and the abbMEDS resulted in scores of 11.0 (8.0–11.0) and 14.0 (12.5–15.5) ($p = 0.004$, $p = 0.003$), respectively. However, levels of IPS, PCT, and cytokines did not show significant differences.

Conclusions In predicting ICU admission and the death of elderly sepsis patients in ED, SOFA and abbMEDS scores were effective. Of the various biomarkers, PCT, IL-10, IL-6, and IL-5 were effective in predicting ICU admission, but were not effective in predicting the death of elderly sepsis patients.

Keywords Emergencies · Elderly · Sepsis · Procalcitonin · Prognosis

Abbreviations

ED	Emergency department
abbMEDS	Abbreviated mortality in emergency department sepsis
SOFA	Sequential organ failure assessment
ICU	Intensive care unit
IPS	Infection probability score
CRP	C-reactive protein
WBC	White blood cell
PCT	Procalcitonin
SIRS	Systemic inflammatory response syndrome
GCS	Glasgow coma scale

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ROC	Receiver operation characteristic
AUC	Area under the curve
PPV	Positive predictive value
NPV	Negative predictive value

Background

The number of elderly patients has increased throughout the world. According to reports from the national statistics office of the Republic of Korea, the proportion of the population that is 65 or older was approximately 13 % in 2015, and is expected to increase up to 40 % by 2060 [1]. Accordingly, the number of elderly patients hospitalized in the emergency department (ED) is also likely to increase. However, the death rate of patients with severe sepsis and septic shock is still high, and the prognosis of elderly patients tends to be particularly poor [2]. At the time that an elderly patient with sepsis arrives at the ED, the patient's initial symptoms are likely to be ambiguous or minor, but they develop into a serious aggravation of the disease [3, 4]. Therefore, it is critical to focus on the existence of severe sepsis when diagnosing an elderly patient and to start active and appropriate antibiotic treatment in order to improve their prognosis.

Many studies have been conducted in the ED and intensive care units (ICUs) to discover sepsis in advance and to predict the prognosis thereof. The mortality in emergency department sepsis (MEDS) score reflects the death-related prognosis of sepsis patients [5]. Moreover, the abbreviated MEDS (abbMEDS) score, excluding the standards of band neutrophils, is also well known to predict the mortality and ventilator weaning of sepsis patients [6]. The sequential organ failure assessment (SOFA) scoring system was found to be effective in estimating the death rate in research targeting hospitalized patients in ICUs [7]. To predict these infections, Peres introduced the infection probability score (IPS) [8]. Such a scoring system is known to be more accurate than the APACHE II score, and it is more effective in predicting reactions to treatments [9, 10].

In general, in cases when infection is in doubt, a high procalcitonin (PCT) level is likely to yield a positive blood culture [11–13]. However, predicting sepsis using the PCT level in an elderly patient can be less precise. Although PCT can be used to diagnose bacteremia in elderly patients (75 or older) in the ED, the PCT level is not an independent factor when diagnosing local infections [14]. If the prognostic score is determined, the expression of biomarkers, such as cytokines, can predict the death rate or ICU admission of elderly sepsis patients at the time of arrival in the ED, their detection will help the healthcare team arrange the ICU for early intensive care and rapid antibiotic treatment for elderly sepsis patients. However, there has been little investigation of effectiveness of the abbMEDS, SOFA, IPS, and other scoring systems in predicting the prognosis of ICU admission and mortality in elderly sepsis patients. Consequently, this study attempted to conduct a comparative analysis of abbMEDS, SOFA, IPS, initial PCT, and cytokine levels in order to investigate the effectiveness of each index in predicting the prognosis of elderly sepsis patients.

Methods

This was a single-center prospective study, and classified 55 patients (≥65 years of age) with systemic inflammatory response syndrome (SIRS) from January 2013 to December 2013 in the ED of Incheon St. Mary's Hospital. A total of 36 patients were diagnosed with sepsis. The protocol was approved by the Institutional Review Board of Incheon St. Mary's Hospital. As the clinical measurements were part of routine patient management in the ED, informed consent was unnecessary, which was confirmed by the institutional review of board. Patients were excluded from the study if they had any of the following conditions: trauma, myocardial infarction, cerebral infarction, SIRS due to nonbacterial origin, vague diagnosis, evidence of an immunocompromised state (e.g., malignancy), or a history of administration of antibiotics before visiting the ED within the previous 14 days. The diagnosis of sepsis was defined by examinations of emergency physicians as follows: microbiological tests, including the culture of body fluids; radiological analyses, including X-rays, ultrasonography, and computed tomography; and serology. Clinically suspected sepsis was also diagnosed as sepsis. Severe sepsis was diagnosed as sepsis associated with organ dysfunction, hypoperfusion, or hypotension despite adequate fluid therapy, including septic shock.

The demographic data and clinical characteristics of the patients were collected at the time of the initial visit to the ED. Ages, genders, initial vital signs (blood pressure, heart rate, breathing rate, temperature, etc.), the level of consciousness upon arrival at the ED, final diagnosis, and ICU admission and death of patients were investigated. In addition, the worst blood pressure within the first 24 h in the ED was recorded and analyzed. An early blood examination (WBC count, CRP, PCT, and bilirubin) was conducted within the first 2 h of the arrival at the ER. PCT was measured by sandwich immunoassay using a VIDAS BRAHMS PCT kit (bioMerieux, Marcy L'Etoile, France), and cytokines [interleukin (IL)1, IL5, IL6, IL10, IL13, IL17, TNFα, and IFNγ] were simultaneously measured via a multiplex fluorescent bead assay using FlowCytomix (eBioscience, San Diego, CA, USA) and a BD Facs Canto II (BD Bioscience, Sparks, MD, USA). Antibiotic therapy was initiated after blood sampling in the ED.

The abbMEDS score was calculated based on the initial medical records and the following nine independent death-related factors were considered in the calculation: terminal illness, tachypnea or hypoxia, septic shock, platelet count, age, lower respiratory tract infection, nursing home residency, and altered mental status [6]. Terminal illness was defined as metastatic cancer; the term "elderly" represented those aged 65 or older; dyspnea was defined as having a breathing rate of 20 times per minute; and hypoxia was defined as having a CO2 concentration of 32 mmHg or below (less than 90 % oxygen saturation), in which a mask or endotracheal intubation was required to maintain an appropriate oxygen level. A case in which sepsis was accompanied by low blood pressure, even with the infusion of isotonic saline at 20–30 ml/kg, was defined as septic shock. A change in consciousness was defined as a case in which the Glasgow coma scale score (GCS score) was less than 15. The SOFA score is calculated from the scores for six organ systems, using one item each to evaluate the respiratory, cardiovascular, hepatic, coagulation, renal, and neurologic systems. The respective items are the Pao_2/Fio_2, platelet count, bilirubin, hypotension, Glasgow coma scale score, and creatinine. Each score is graded from 0 to 4 according to the degree of dysfunction [7]. In comparison, the IPS including the SOFA score is based on body temperature, heart rate, respiratory rate, C-reactive protein (CRP) level, and white blood cell (WBC) count (Table 1). The SOFA score and IPS were recorded when new patients arrived at the ED, and the final diagnoses were based on clinical and imaging findings and medical records.

Statistical analysis

Statistical analyses were performed using SPSS 12.0 (SPSS Inc., Chicago, USA). To compare the two groups, median and quartile values were measured for cases in which the continuous variables were not normally distributed, and the Mann–Whitney *U* test was conducted. The evaluation of the prediction of prognosis using the prognostic scores (SOFA, abbMEDS), PCT, CRP, and cytokines were analyzed using receiver operation characteristic curves (ROCs). The cutoff value, which was the maximum area under the ROC curve (AUC), was selected, and sensitivity, specificity positive and negative predictive values (PPV and NPV), and accuracies were calculated with a 95 % confidence interval. For cases with discontinuous variables, Pearson's Chi-squared test and Fisher's exact test were conducted at a significance level of $p < 0.05$.

Results

Clinical characteristics of elderly patients

During the research period, the presence of biomarkers, including cytokines, was evaluated in 36 elderly patients (>65 years old) hospitalized with sepsis at the ED. Twenty (55.6 %) were males and 16 (44.4 %) were females. The median (IQR) age of the subjects was 76.5 (70.5–81.5). After 28 days, 27 (75 %) patients had survived and 9 (25 %) had expired. In addition, 15 (41.7 %) and 21 (58.3 %) patients were sent to the ICUs and general units, respectively. Upon the final diagnosis, most of the patients (22 patients, 61.1 %) were diagnosed with respiratory infection, followed by 7 patients (19.4 %) with hepatobiliary infection and 7 patients (19.4 %) with urinary infection. Eight patients (22.2 %) showed positive blood culture results.

For both the sepsis and severe sepsis groups, the age and gender were not found to have significant differences. The blood pressure at the time of arrival and the worst blood pressure recorded during the first 24 h were found to be lower in the severe sepsis group. Moreover, the rate of the final diagnosis did not differ in the two groups, but ICU admission occurred more frequently [9 patients (90.0 %)] in the severe sepsis group. WBC count and CRP did not significantly differ in the two groups (Table 2).

Comparison of the prediction of ICU admission according to prognostic scores and biomarkers

The SOFA score showed a median (IQR) value of 9.5 (7.0–11.0) and 2.0 (1.0–4.0) in ICU group and general ward group, respectively, showing a statistically higher rate in the

Table 1 Infection probability score

IPS points	0	1	2	3	6	8	12
Body temperature (°C)	≤37.5		>37.5				
Heart rate (beats/min)	≤80					81–140	>140
Respiratory rate (breaths/min)	≤25	>25					
White blood cell ($\times 10^9$/L)	5–12	>12		≤5			
C-reactive protein (mg/dL)	≤6				>6		
SOFA score	≤5		>5				

SOFA Sequential organ failure assessment

Table 2 A comparison of the clinical characteristics of elderly patients (>65 years) with sepsis and severe sepsis in the emergency department

	Sepsis group ($n = 26$)	Severe sepsis group ($n = 10$)	P value
Sex (n, %)			
Male	15 (57.7)	5 (50.0)	0.722
Female	11 (42.3)	5 (50.0)	
Age (years)[a]	77.5 (73.3–81.3)	73.0 (69.0–81.5)	0.633
Initial vital signs[a]			
SBP (mmHg)	117.0 (107.0–133.3)	77.0 (73.0–106.5)	0.001
DBP	71.5 (66.8–81.3)	51.0 (43.0–67.5)	0.005
HR (beats/min)	105.5 (85.5–122.0)	103.0 (96.0–112.5)	0.926
BT (°C)	37.7 (36.7–38.4)	37.2 (36.7–38.1)	0.251
Worst blood pressure[a]			
SBP (mmHg)	95.5 (90.0–117.0)	70.0 (65.0–84.0)	<0.001
DBP	60.0 (55.8–71.0)	42.0(39.5–55.0)	<0.001
Alteration of mental state (n, %)	8 (30.8)	7 (70.0)	0.397
Site of infection (n, %)			
Respiratory infection	16 (61.5)	6 (60.0)	0.996
Hepatobiliary infection	5 (19.2)	2 (20.0)	
Urinary infection	5 (19.2)	2 (20.0)	
WBC count ($\times 10^9$/L)	14.6 (9.7–21.9)	10.5 (3.8–21.3)	0.271
CRP (mg/L)	121.7 (34.6–160.8)	144.7 (117.3–173.1)	0.155
Bacteremia (n, %)	7 (26.9)	1 (10.0)	0.397
ICU admission (n, %)	6 (23.1)	9 (90.0)	<0.001
Mortality (n, %)	4 (15.4)	5 (50.0)	0.079

SBP Systolic blood pressure, *DBP* diastolic blood pressure, *HR* heart rate, *BT* body temperature, *WBC* white blood cell, *CRP* C-reactive protein, *ICU* intensive care unit

[a] Median value with interquartile range; statistical analyses were performed via the Mann–Whitney *U* test

ICU group ($p < 0.001$). The abbMEDS score was also measured to be higher in the ICU group (13.5, IQR 12.0–15.0) than in the general ward group (8.0, IQR 6.0–8.0) ($p < 0.001$). On the other hand, there were no significant differences in the IPS score of the two groups ($p = 0.391$) (Table 3). In predicting admission to the ICU through ROC curve analysis, the AUC values of SOFA and the abbMEDS were 0.933 and 0.949, respectively. At a cutoff value of 4, SOFA showed a sensitivity of 93.3 % and a specificity of 76.2 %. At a cutoff value of 8, the abbMEDS showed a sensitivity of 100 % and a specificity of 81.0 % (Table 4).

PCT had a median (IQR) value of 14.5 (0.8–30.9) ng/mL for the prediction of the admission of elderly sepsis patients to the ICU after initial examination at the time of arrival in the ED, while it had a median value of 0.5 (0.2–0.8) ng/mL for general ward admission ($p = 0.001$). WBC count, CRP and ESR were found not to be significant in predicting admission to the ICU ($p = 0.252$, $p = 0.465$, $p = 0.150$). The cytokines IL-10, IL-6, and IL-5 showed significantly higher results than cases of admission in general units, giving a significant result in predicting ICU admission ($p = 0.023$, $p = 0.030$, $p = 0.001$) (Table 3).

In predicting admission to the ICU through ROC curve analysis, the AUC of PCT, IL-5, was found to be 0.810. The cutoff values at 0.8 ng/mL and 24.02 pg/mL were as follows: 80.0 % sensitivity, 81.0 % specificity, 75.0 % PPV, and 85.0 % NPV (Table 4).

Comparison of the prediction of mortality according to the prognostic score and biomarkers

From the prediction of mortality in the first 28 days, SOFA and abbMEDS resulted in scores of 11.0 (8.0–11.0) and 14.0 (12.5–15.5), respectively ($p = 0.004$, $p = 0.003$) (Table 5). The 28-day mortality prediction through ROC curve analysis yielded AUC values of 0.815 and 0.838 for SOFA and abbMEDS, respectively. At a cutoff value of 7, SOFA showed a sensitivity of 66.7 % and a specificity of 85.2 %, while at a cutoff value of 11, abbMEDS showed a sensitivity of 87.5 % and a specificity of 77.8 %. However, neither PCT nor cytokines were shown to have significant differences in predicting mortality. CRP values for patients with death and survival were 170.0 (131.2–172.3) and 118.3 (42.5–160.0), respectively

Table 3 Prognostic scores and laboratory findings of elderly patients (>65 years) in the prediction of ICU and general ward admissions in the emergency department

	ICU admission ($n = 15$)	General ward admission ($n = 21$)	P value
SOFA score	9.5 (7.0–11.0)	2.0 (1.0–4.0)	<0.001
AbbMEDS score	13.5 (12.0–15.0)	8.0 (6.0–8.0)	<0.001
IPS	15.0 (12.0–16.0)	15.0 (11.0–17.0)	0.391
WBC ($\times 10^9$/L)	10.5 (7.6–22.1)	15.0 (12.8–21.1)	0.252
ESR (mm/h)	39.5 (26.0–51.0)	52.0 (30.0–73.0)	0.465
CRP (mg/L)	144.7 (109.0–171.7)	116.6 (37.9–160.0)	0.150
Bilirubin (mg/dl)	1.0 (0.7–1.6)	0.6 (0.6–1.1)	0.202
Procalcitonin (ng/mL)	14.5 (0.8–30.9)	0.5 (0.2–0.8)	0.001
IFNγ (pg/mL)	4.1 (0–42.2)	0.8 (0–43.9)	0.849
IL-17	2.7 (0–14.9)	0 (0–8.6)	0.409
IL-10	38.7 (7.5–298.3)	10.8 (3.8–24.4)	0.023
IL-6	501.5 (164.9–3462.1)	66.5 (28.2–218.5)	0.030
IL-13	24.7 (0–37.8)	0 (0–33.2)	0.340
IL-5	33.5 (25.7–50.1)	3.4 (0–24.0)	0.001
IL-1	38.33 (0–74.2)	0 (0–12.8)	0.180
TNFα	56.5 (5.2–97.4)	15.4 (10.1–25.2)	0.191

Median value with interquartile range; statistical analyses were performed via the Mann–Whitney U test

SOFA Sequential organ failure assessment, *abbMEDS* abbreviated mortality in emergency department sepsis, *IPS* infection probability score, *WBC* white blood cell, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *ICU* intensive care unit, *IFN* interferon, *IL* interleukin, *TNF* tumor necrosis factor

Table 4 Diagnostic values of the prognostic scores and biomarkers in predicting ICU admission of elderly sepsis patients in the ED

	AUC	Cut-off	Sensitivity, 95 % CI	Specificity, 95 % CI	PPV, 95 % CI	NPV, 95 % CI
SOFA score	0.933	4	93.3 (68.1–99.8)	76.2 (52.8–91.8)	73.7 (48.8–90.9)	94.1 (71.3–99.9)
AbbMEDS score	0.949	8	100.0 (76.8–100.0)	81.0 (58.1–94.6)	77.8 (52.4–93.6)	100.0 (80.5–100.0)
Procalcitonin	0.810	0.8	80.0 (51.9–95.7)	81.0 (58.1–94.6)	75.0 (47.6–92.7)	85.0 (62.1–96.8)
IL10	0.724	4.45	93.3 (68.1–99.8)	47.6 (25.7–70.2)	56.0 (34.9–75.6)	90.9 (58.7–99.8)
IL6	0.714	162.25	80.0 (51.9–95.7)	71.4 (47.8–88.7)	66.7 (41.0–86.7)	83.3 (58.6–96.4)
IL5	0.810	24.02	80.0 (51.9–95.7)	81.0 (58.1–94.6)	75.0 (47.6–92.7)	85.0 (62.1–96.8)

SOFA Sequential organ failure assessment, *abbMEDS* abbreviated mortality in emergency department sepsis, *IL* interleukin

($p = 0.052$). In the prediction of death through ROC curve analysis, CRP resulted in an AUC of 0.720, with the following cutoff values: sensitivity of 88.9 %, specificity of 55.6 %, PPV of 40.0 %, and NPV of 93.7 % at 120 mg/L (Table 6).

Discussion

Elderly patients tend to possess complex chronic diseases, show nontypical symptoms, take various drugs, lack the ability to communicate, and exhibit mental changes with fever. Most elderly patients that present to the hospital with sepsis are initially visited in the ED. As long as severe sepsis in elderly patients can be accurately identified in the ED, the prognosis thereof can be improved, and the mortality rate of the disease can be reduced. Therefore, it is critical to perform evaluations of sepsis by applying initial blood tests and clinical symptoms when visiting elderly patients with possible sepsis in the ED. Once severe sepsis in elderly patients can be predicted in advance with an appropriate set of initial blood sampling tests or prognostic tool, both time and cost can be saved in the ED. Several days are required to acquire an effective blood culture result in diagnosing bacteremia and isolating bacteria. Therefore, once the prognostic score and biomarkers, which allow for the immediate prediction of prognosis in the ED, are found, early and effective treatments will become available for critically ill elderly patients with severe sepsis in the ED. In this study, the SOFA and abbMEDS scores predicted the death of elderly sepsis patients in the ED, while the SOFA and abbMEDS scores, together with PCT, IL-10, IL-6, and IL-5 levels in the ED, predicted ICU admission.

Table 5 Prognostic scores and laboratory findings of elderly patients (>65 years) in the prediction of mortality in the emergency department

	Death ($n = 9$)	Survival ($n = 27$)	P value
SOFA score	11.0 (8.0–11.0)	4.0 (1.5–6.5)	0.004
AbbMEDS score	14.0 (12.5–15.5)	8.0 (6.0–11.5)	0.003
IPS	15.0 (15.0–16.0)	15.0 (12.0–17.0)	0.667
WBC ($\times 10^9$/L)	11.1 (8.0–23.2)	14.3 (9.9–20.6)	0.693
ESR (mm/h)	41.0 (20.5–50.5)	49.5 (29.0–70.5)	0.914
CRP (mg/L)	170.0 (131.2–172.3)	118.3 (42.5–160.0)	0.052
Bilirubin (mg/dl)	0.9 (0.6–0.95)	0.9 (0.6–1.4)	0.749
Procalcitonin (ng/mL)	1.5 (0.3–32.4)	0.8 (0.35–8.4)	0.494
IFNγ (pg/mL)	0.0 (0.0–99.7)	6.6 (0.0–43.0)	0.615
IL-17	0.0 (0.0–6.5)	0.0 (0.0–16.9)	1.000
IL-10	9.3 (6.8–137.9)	16.9 (3.8–137.0)	0.641
IL-6	328.1 (85.0–1885.6)	147.9 (28.6–806.8)	1.000
IL-13	0.0 (0.0–40.7)	21.8 (0.0–34.5)	0.693
IL-5	28.7 (15.6–47.9)	9.4 (0–33.5)	0.205
IL-1	12.8 (0–84.8)	3.1 (0–46.0)	0.450
TNFα	27.2 (2.6–90.0)	17.3 (10.1–93.7)	0.971

Median value with interquartile range; statistical analyses were performed via the Mann–Whitney U test

SOFA Sequential organ failure assessment, *abbMEDS* abbreviated mortality in emergency department sepsis, *IPS* infection probability score, *WBC* white blood cell, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *ICU* intensive care unit, *IFN* interferon, *IL* interleukin, *TNF* tumor necrosis factor

Table 6 Diagnostic values of the prognostic scores and biomarkers in predicting the 28-day mortality of elderly sepsis patients in the ED

	AUC	Cut-off	Sensitivity, 95 % CI	Specificity, 95 % CI	PPV, 95 % CI	NPV, 95 % CI
SOFA score	0.815	7	66.7 (29.9–92.5)	85.2 (66.3–95.8)	60.0 (26.2–87.8)	88.5 (69.8–97.6)
Abbreviated-MEDS score	0.838	11	87.5 (47.3–99.7)	77.8 (57.7–91.4)	53.8 (25.1–80.8)	95.5 (77.2–99.9)
CRP	0.720	120	88.9 (51.8–99.7)	55.6 (35.3–74.5)	40.0 (19.1–63.9)	93.7 (69.8–99.8)

SOFA Sequential organ failure assessment, *abbMEDS* abbreviated mortality in emergency department sepsis, *CRP* C-reactive protein

The SOFA score reflects physiological and laboratory findings. Jones showed that the mortality area under the receiver operating characteristic curve (AUC) was 0.75 for SOFA scores calculated in the ED after identifying patients with severe sepsis [7]. This is comparable to the AUC of 0.815 in our study of elderly sepsis patients. The SOFA score is limited because it does not consider age or comorbidity. In comparison, the abbMEDS score is calculated using independent factors related to death: terminal illness, tachypnea or hypoxia, septic shock, platelet count, age, lower respiratory tract infection, nursing home residency, and altered mental status [6]. Shapiro concluded that scoring systems for ICUs, including APACHE, have limitations to their application in the ED, and therefore, MEDS scoring system was established to predict the death rate of sepsis patients in states of emergency [5]. Chen found that the MEDS scores of 276 ED patients with severe sepsis gave an AUC of 0.75 for mortality and patients with a MEDS score $\geq$12 had a significantly higher mortality rate of 48.9 % [15]. In addition, a multicenter prospective cohort study found that ED patients with SIRS had an overall mortality rate of 9 %, with a MEDS score AUC of 0.88 (95 % CI, 0.83–0.92) [16]. AbbMEDS scoring system is the same as the previous MEDS scoring system without the immature neutrophil index, and it is argued that it is helpful in predicting the death rate in the retrospective cohort study of adult ED patients with sepsis admitted to hospital [6]. In our study of elderly sepsis patients in the ED, the abbMEDS gave an AUC of 0.838 for mortality prediction with a cutoff value of 11. We found that the SOFA and abbMEDS scores gave similar AUC values for mortality, although the abbMEDS had a better sensitivity of 87.5 % at a cutoff value of 11 in elderly sepsis patients.

IPS is also known to be more effective than the APACHE II or Karnofsky score in predicting infectious disease, and it is also useful in predicting patients' reactions to treatments [8–10]. However, so far, few studies have attempted to predict the admission of elderly sepsis patients to the ICU or the death rate of such patients in the ED based on the IPS. In this study, the initial SOFA score

was considered to be significant for predicting admission to the ICU or death. However, IPS, which requires much more data, including SOFA, is not helpful in predicting ICU admission and death. The components of the IPS score are as follows: heart rate (0, 8, 12), CRP (0, 6), WBC count (0, 1, 3), temperature (0, 2), SOFA (0, 2), and breathing rate (0, 1). Mainly, the IPS score is decided by the heart rate, CRP, temperature, and WBC count, but the SOFA and breathing rate take up comparatively lower proportions [8]. In this study, the heart rate, CRP, WBC count, and temperatures did not exhibit significant differences among elderly severe sepsis patients, so they were considered to not be highly influential on the overall IPS. In a previous study, the average IPS value for patients in the ICU was 11.4, whereas the median IPS value was found to be higher in this study: 15.0 (12.0–16.0) [10]. This cutoff value is higher than the result of a study of adults, which may result from the smaller number of elderly patients, implying a need for further relevant research.

In a recent prospective geriatric study, we found that the Multidimensional Prognostic Index (MPI) was more effective than the any of the frailty instruments Pilotto et al. used to predict all-cause mortality in hospitalized elderly patients [17]. The MPI is calculated using 63 items in eight domains: activities of daily living, instrumental activities of daily living, mental status (assessed by a short portable questionnaire), mini nutritional assessment, Exton-Smith score, cumulative index rating scale, number of medications, and cohabitation status. A higher MPI is significantly related to higher mortality in hospitalized elderly patients with pneumonia [18]. However, use of the MPI may be limited in the ED where rapid decisions are required. We did not evaluate the MPI and suggest that a future study should examine its use for predicting the mortality of elderly sepsis patients in the ED.

In general, in previous studies of adults in the ED, PCT showed good results for the prediction of bacteremia [11, 12]. PCT is valuable in the diagnosis of sepsis and the assessment of severe sepsis/septic shock in the ED [13, 14, 19, 20]. However, in this study, PCT showed a significant result in predicting the admission of elderly sepsis patients to the ICU, while it turned out to be insignificant in predicting death. One limitation of this study was the small sample size. In addition, medical histories of elderly patients may differ, and unknown diseases may exist because many elderly people tend not to visit hospitals often. Thus, it can be difficult to predict the death of an elderly sepsis patient solely based on a single biomarker. Many studies showed effective CRP and PCT values in diagnosing sepsis [21–24]. In addition, higher CRP was significantly associated with mortality [22]. When distinguishing bacterial infection on SIRS patients in a comparative study on PCT and CRP values, PCT tended to have more effective results in most of the cases [13, 21, 23]. However, in some studies, the CRP value had better results than PCT in diagnosing bacterial infection [24]. In this study, the prediction of the death rate of elderly sepsis patients showed a specificity of 55.6 % and a sensitivity of 88.9 % with a cutoff value of 120 mg/L.

Various existing studies address the presence of cytokines in sepsis patients [25–28]. Of the many different cytokines, IL-6 is especially related to the diagnosis and severity of sepsis [25]. In this study, IL-10, IL-6, and IL-5 were found to be statistically significant in predicting ICU admission, but they were not meaningful in predicting the death rate of elderly sepsis patients. Therefore, the cytokine interaction in elderly sepsis patients may be more complicated, so close attention must be paid to applying a multiple cytokine profile, which has a clinically uncertain effectiveness, to elderly sepsis patients.

The limitations of this study are as follows. First, the study was conducted based on a single organization, within a limited period of time with a small sample size, so close attention is required to generalize the results. Second, although most cases of sepsis developed from respiratory diseases, disease may have had various causes, so there are possible limitations in interpreting the cutoff values of PCT and cytokines regarding the mortality and ICU admission of elderly sepsis patients. This study did not aim to evaluate the prognosis of each primary infection, but it presents a meaningful attempt to evaluate prognosis of elderly sepsis patients in the ED using biomarkers, including the three prognostic scores and levels of various cytokines. Further studies should examine changes in biomarker values and frailty instruments for each infected region in a large sample of elderly sepsis patients.

Conclusion

In predicting the ICU admission and death of elderly sepsis patients in the ED, the SOFA and abbMEDS scores were effective. Of the various biomarkers, PCT, IL-10, IL-6, and IL-5 were effective in predicting ICU admission, but they were not effective in predicting the death of elderly sepsis patients. Thus, caution is advised in evaluating the levels of cytokines, including PCT, in the prediction of the prognosis of elderly sepsis patients in the ED.

Acknowledgments The authors declare that this study did not receive any outside funding or support.

Compliance with ethical standards

Conflict of interest The authors do not have any financial or other relationships that might pose any conflicts of interest.

Statement of human and animal rights All procedures performed in studies involving the patients were in accordance with the ethical standards of the institutional and/or national research. The protocol was approved by the Institutional Review Board of Incheon St. Mary's Hospital.

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