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Original Contribution

High immunoglobulin E values at admission predict mortality in patients with sepsis: a study performed in the ED

Qian Zhang, PHD ^{a,1}, Guijuan Dong, MD ^{b,1}, Xin Zhao, MD ^b, Chun-Sheng Li, MD ^{b,*}^a Department of Cardiology, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China^b Department of Emergency Medicine, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China

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ABSTRACT

Objectives: Gamma immunoglobulin E (IgE) is associated with allergic reactions but has not been described as being activated after sepsis. This study aimed at detecting the prognostic value of plasma IgE level in sepsis progression in the emergency department (ED).

Methods: Plasma IgE and related cytokines levels were measured on enrollment, and the Acute Physiology and Chronic Health Evaluation II score, Sequential Organ Failure Assessment score, and Mortality in Emergency Department Sepsis score were calculated on ED admission. A 28-day follow-up was performed for all patients.

Results: A total of 480 patients were consecutively enrolled in this study. The results revealed that nonsurvivors were in a more severe critical state, with reflected by higher IgE level and higher scoring systems ($P < .001$). Multivariate logistic regression analysis showed that IgE level was independent predictor of severe sepsis (odds ratio, 1.034; 95% confidence interval, 1.023–1.044; $P < .001$) and 28-day mortality (odds ratio, 1.038; 95% confidence interval, 1.027–1.053; $P < .001$). The areas under the receiver operating characteristic curve (AUC) analysis showed that IgE was a useful parameter in prognosis of severe sepsis (AUC was 0.830; cutoff value was 303.08 $\mu\text{g/L}$) and 28-day mortality (AUC was 0.700; cutoff value was 299.96 $\mu\text{g/L}$). Importantly, the AUC of combination of IgE and Mortality in Emergency Department Sepsis score performed for the most significant prognostic ability than each parameter, respectively, in this cohort ($P < .001$).

Conclusions: The results of this study indicate that septic patients with higher IgE level present with higher risk of mortality, and a combination of IgE level with scoring systems significantly increased the predictive accuracy for severe sepsis and 28-day mortality.

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1. Introduction

Sepsis, the systemic inflammatory response syndrome (SIRS) induced by pathogenic microorganism infection, is associated with a high risk of death. Although the treatment of sepsis appears significantly improved over the past 20 years (eg, effective antibiotics, hemofiltration, and immune therapy), the mortality of sepsis still remained high [1,2]. It is known that immune system dysfunction is the main pathophysiological procedure in the development of sepsis.

There is increasing evidence on the relationship between endogenously produced immunoglobulins and prognosis in sepsis. Hyperimmunoglobulin E syndrome is a primary immunodeficiency disorder characterized by recurrent severe pulmonary infections, pneumatoceles, eczema, staphylococcal abscesses, mucocutaneous candidiasis, and elevated serum immunoglobulin E (IgE) concentrations

[3,4]. Although high plasma IgE levels is postulated to be detrimental to patients with sepsis, studies exploring the risk of sepsis in high plasma IgE levels patients are limited by small sample size [5], and the potential involvement of allergy-related or IgE-dependent immune system activation in the response to sepsis syndrome has not been adequately investigated until now. Given the above considerations, the objective of this study is to explore the value of plasma IgE levels on admission in the evaluation of the severity and prognosis of septic patients in the emergency department (ED) and compare with conventional clinical risk parameters of sepsis severity (measured using the Mortality in Emergency Department Sepsis [MEDS] score) in a large sample of septic patients in the ED.

2. Methods

2.1. Study population

This prospective cohort study was conducted in the ED of Beijing Chaoyang Hospital, which is a tertiary university teaching hospital with an average of 240 000 annual ED visits. Patients who were consecutively admitted to the ED with signs of SIRS between February 2013

* Corresponding author at: Emergency Department, Beijing Chaoyang Hospital, Capital Medical University, 8# Worker's Stadium South Road, Chao-yang District, Beijing 100020, China. Tel./fax: +86 10 85231051.

E-mail address: lcscyy@163.com (C.-S. Li).

¹ These authors contributed to the work equally and should be regarded as cofirst authors.

and November 2013 were assessed for possible enrollment according to inclusion and exclusion criteria.

The inclusion criteria were as follows: (a) age 18 years or older; (b) diagnosis of SIRS, sepsis, severe sepsis, or septic shock according to the criteria of the 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference and surviving sepsis campaign guidelines [6,7]; (c) SIRS due to acute pancreatitis or sepsis due to specific infections based on microbiological evidence. The infections were determined to be community-acquired pneumonia, acute pyelonephritis, acute intraabdominal infection, and primary bacteremia. These evaluations were conducted at the same time that blood samples were obtained.

The exclusion criteria were as follows: younger than 18 years, terminal stage of disease (malignant cancer of any type, AIDS, end-stage liver or renal disease), pregnancy, allergic diseases or immune diseases, and treatment with immunosuppressants (eg, organ transplant recipients). This study was approved by the institutional review board of Beijing Chaoyang Hospital and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent forms were obtained from all patients or their legal relatives.

2.2. Data collection

At enrollment, subject data, including name, age, sex, medical history, and vital signs, were recorded. Laboratory examinations and imaging results were recorded at ED admission. A standardized form was used to collect the data. Demographic data, including name, age, sex, and telephone number, were recorded immediately after enrollment. Clinical data, including comorbidities, vital signs, and results of auxiliary examinations, were also recorded.

Three clinical scores were recorded: the Acute Physiology and Chronic Health Evaluation (APACHE) II score [8], Sequential Organ Failure Assessment (SOFA) score [9], and MEDS score were calculated using highest values obtained at ED admission [10]. At the clinical presentation of sepsis, blood cultures and cultures of specimen drawn from the site of infection, hematologic and chemistry data, arterial lactate, and blood gas determinations were done systematically. Microbial infections were characterized based on clinical features, laboratory findings, and imaging tests according to criteria of the International Sepsis Forum Consensus Conference on Definitions of Infection [11]. Infection sites were categorized as pneumonia, peritonitis, urinary tract infection, exacerbation of chronic obstructive pulmonary disease, primary bacteremia (excluding untreated *Staphylococcus epidermidis* bacteremia), miscellaneous sites (mediastinitis, prostatitis, osteomyelitis, and others), or multiple sites. Mainstays of therapy for patients were antibiotics and fluid resuscitation. Other interventions, including vasoactive agents, mechanical ventilation, and transfusion of blood products, were administered if necessary.

2.3. Cytokine assays

Venous blood samples were obtained at ED admission and collected in tubes containing heparin or ethylenediaminetetraacetate and stored at -80°C after collection for analysis within 24 hours. Total plasma IgE concentrations were determined on blinded specimens by an automated microparticle enzyme immunoassay (IMx; Abbott Diagnostics, North Chicago, IL). Within-run and between-run coefficients of variation over the 0.1 to 480 $\mu\text{g/L}$ working range were less than 3% [12]. Plasmas interferon γ (IFN- γ) and interleukin 4 (IL-4) were determined using a commercial enzyme-linked immunosorbent assay kit (Dakewe, Beijing, China) according to manufacturer's instructions. The lower detection limit of the IFN- γ and IL-4 assays was 5 and 2.5 pg/mL, respectively. Plasma procalcitonin (PCT) levels were measured by BioMerieux Mini VIDAS immunoassay analyzer (Block Scientific, New York, NY), the reportable detection range was 0.05 to 200 ng/mL [13].

2.4. Follow-up

For outcome assessment, a follow-up examination was planned at 28 day after study inclusion. Patients who survived until follow-up were counted as survivors, whereas patients who died within the follow-up period were counted as nonsurvivors. Hospital records of all patients were followed for 28 days or until death after enrollment. For patients who were discharged from hospital before 28 days, the follow-up was completed by telephone interview.

2.5. Statistical analysis

Continuous variables were expressed as mean $\pm$ SD or median and interquartile range (IQR) with normal distribution or skewed distribution, respectively. For multigroup comparisons, Kruskal-Wallis 1-way analysis of variance was applied. Two-group comparisons were performed nonparametrically using the Mann-Whitney U test for skewed distributed data. Categorical variables were compared using the χ^2 test. To determine the predictive value of IgE, PCT, leukocyte, percentage of neutrophils, and scoring systems, receiver operating characteristic (ROC) curves were constructed, and the areas under the curve (AUCs) were also calculated. Based on optimal thresholds determined according to ROC curve analysis, prognostic parameters (sensitivity, specificity, and positive and negative predictive values) were also calculated. Correlations between plasma IgE concentrations and laboratory or clinical parameters were investigated by using Spearman test. The distribution of the time-to-event variables was estimated using the Kaplan-Meier method with log-rank testing. Binary logistic regression analysis was used to determine the independent predictors of outcomes. All statistical tests were 2 tailed, and $P < .05$ was considered statistically significant in all tests.

3. Results

3.1. Characteristics of enrolled subjects

A total of 480 patients included in the study protocol met all the specified inclusion criteria. Baseline clinical parameters for survivors and nonsurvivors are shown in Table 1. There were no significant differences between survivors and nonsurvivors with respect to age, sex, onset time, coexisting conditions, site of infection, temperature, and percentage of neutrophils. Median IgE, IL-4, IFN- γ , and PCT concentrations; leukocyte count; respiratory rates; heart rates; and scoring systems were significantly higher in nonsurvivors than survivors at 28-day follow-up.

3.2. Comparison of plasma IgE levels in survivors and nonsurvivors according to 28-day mortality

Nonsurvivors were in a more severe critical state as reflected by significantly higher plasma IgE concentrations compared to survivors at 28-day follow-up in patients (329.1 [243.5–477.2] vs 282.6 [209.1–409.8] $\mu\text{g/L}$; $P = .001$). Similarly, these differences were also significant with respect to the levels of PCT, APACHE II scores, SOFA scores, and MEDS scores between nonsurvivors and survivors (Table 1).

3.3. Predictive value of multiple variables for severe sepsis and 28-day mortality

The AUC of IgE for predicting severe sepsis was 0.830, higher than that of PCT (0.756), leukocyte count (0.566), percentage of neutrophils (0.567), APACHE II (0.715), and MEDS score (0.782) (all $P < .01$), respectively. The AUC of IgE in combination with APACHE II or MEDS score was 0.918 and 0.924, markedly higher than that of APACHE II or MEDS score (all $P < .01$), but there were no differences compared with IgE alone (all $P > .05$). The AUC of IgE in combination with SOFA score was 0.943,

Table 1
Baseline characteristics of the study cohort

Variables	Survivors at 28 d	Nonsurvivors at 28 d	P
No. of patients, n	297	183	
Age (y), median (IQR)	71 (61–77)	72 (64–78)	.112
Sex (male), n (%)	183 (61.6)	110 (60.3)	.743
Onset time (d), median (IQR)	2 (1–5)	3 (1–5)	.280
Coexisting conditions, n (%)			
Hypertension	173 (58.2)	102 (56.0)	.564
Diabetes mellitus	141 (47.6)	84 (45.8)	.631
Coronary vessel disease	123 (41.3)	74 (40.3)	.788
COPD	112 (37.7)	67 (36.6)	.774
Cerebrovascular disease	63 (21.2)	37 (20.5)	.822
Neoplastic disease	26 (8.8)	17 (9.2)	.872
Source of infection, n (%)			
Pneumonia	202 (67.9)	122 (66.7)	.723
Intraabdominal infection	56 (19.0)	36 (19.8)	.787
Pyelonephritis	32 (10.8)	21 (11.3)	.829
Central nervous system infection	5 (1.6)	3 (1.5)	.903
Other infections	2 (0.7)	1 (0.6)	.931
Vital signs			
Temperature (°C)	37.2 (36.5–38.3)	37 (36.2–38.4)	.081
Respiratory rates (beats per minute)	32 (26–34)	32 (28–36)	.003
Heart rates (beats per minute)	109 (96–120)	115 (98.5–129.5)	.005
Mean arterial pressure (mm Hg)	92.05 (19.61)	85.59 (23.15)	<.001
Laboratory findings			
IgE (μg/L)	275.18 (139.42–545.31)	314.86 (176.5–629.72)	<.001
IL-4 (ng/L)	284.6 (157.1–506.5)	310.80 (161.5–546.1)	<.001
IFN-γ (ng/L)	314.37 (179.6–557.2)	282.00 (147.3–508.3)	<.001
PCT (ng/mL)	0.27 (0.05–2.02)	1.61 (0.30–10.34)	<.001
Leukocyte count (×10 ⁹ /L)	11.19 (7.69–15.67)	12.76 (8.90–18.94)	.003
Neutrophils (%)	85.5 (77.9–90.8)	85.8 (79.1–92.2)	.137
Severity of illness			
APACHE II score	14.0 (10.0–19.0)	20.0 (15.0–26.0)	<.001
SOFA score	4.0 (2.0–6.0)	6.0 (4.0–10.0)	<.001
MEDS score	10.0 (7.0–13.0)	14.0 (10.0–19.0)	<.001

Abbreviation: COPD, chronic obstructive pneumonia disease.

obviously higher than SOFA score or IgE alone (all $P < .01$), respectively (Table 2 and Fig. 1A). The AUC of IgE for predicting 28-day mortality was 0.700, significantly greater than that of leukocyte count (0.551) and percentage of neutrophils (0.567) and lower than APACHE II, SOFA, and MEDS scores (all $P < .01$), but there was no difference compared with

PCT (0.673; $P > .05$), and the AUC of IgE in combination with APACHE II or SOFA score was markedly greater than APACHE II, SOFA score, or IgE alone (all $P < .05$), respectively (Table 2 and Fig. 1B).

Using a IgE cutoff of 303.08 and 299.96 μg/L for predicting severe sepsis and 28-day mortality, the sensitivity was 73.9% and 77.5%, and the specificity was 77.9% and 80.6%, respectively (Table 3).

Table 2
Areas under the curve of multiple variables in prediction of severe sepsis and 28-day mortality

	Variable	AUC	95% CI	
			Lower limit	Upper limit
Severe sepsis	IgE	0.830	0.789	0.872
	PCT	0.756	0.720	0.793
	Leukocyte count	0.566	0.519	0.613
	Neutrophils%	0.567	0.521	0.612
	APACHE II	0.715	0.675	0.755
	SOFA	0.841	0.811	0.871
	MEDS	0.782	0.745	0.820
	IgE + APACHE II ^a	0.918	0.898	0.939
	IgE + SOFA ^b	0.943	0.927	0.959
	IgE + MEDS ^a	0.924	0.904	0.944
28-d mortality	IgE	0.700	0.653	0.746
	PCT	0.673	0.627	0.719
	Leukocyte count	0.551	0.494	0.608
	Neutrophils%	0.559	0.505	0.613
	APACHE II	0.789	0.750	0.829
	SOFA score	0.776	0.735	0.818
	MEDS score	0.863	0.857	0.923
	IgE + APACHE II ^c	0.800	0.762	0.838
	IgE + SOFA ^c	0.781	0.740	0.823
	IgE + MEDS ^d	0.890	0.857	0.923

Abbreviation: CI, confidence interval.

^a Compared with APACHE II score or MEDS score, all $P < 0.01$.

^b Compared with IgE or SOFA score, all $P < .01$.

^c Compared with IgE and APACHE II score or SOFA score, all $P < .05$.

^d Compared with IgE, $P < .01$.

3.4. Independent predictors for multiple variables for predicting severe sepsis and 28-day mortality

To test whether plasma IgE levels could predict severe sepsis and 28-day mortality, we initially performed binary logistic regression analysis, incorporating multiple demographic, clinical, and laboratory variables. However, after univariate analysis, only plasma IgE levels, PCT, leukocyte count, APACHE II, SOFA, and MEDS score were identified as the independent predictors of incidence of severe sepsis and 28-day mortality ($P < .05$) (the results are shown in Table 3).

3.5. Relationships of plasma IgE levels with other variables

To determine the correlations of plasma IgE levels with other variables, a Spearman analysis was conducted. The analysis results showed that plasma IgE levels correlated significantly with PCT ($r = 0.512$; $P < .001$), leukocyte count ($r = 0.121$; $P = .002$), percentage of neutrophils ($r = 0.187$; $P < .001$), APACHE II score ($r = 0.294$; $P < .001$), SOFA score ($r = 0.443$; $P < .001$), and MEDS score ($r = 0.389$; $P < .001$), respectively.

To further investigate the trend of plasma IgE levels with scoring systems, we reclassified all septic patients based on values of APACHE II, SOFA, and MEDS scores. Plasma IgE levels within the 4 groups of increasing of the categories of APACHE II, SOFA, and MEDS scores are illustrated in Fig. 2. Median IgE levels were found significantly elevated with increasing of APACHE II score, and there was significant difference between any new 2 groups (all $P < .01$) (Fig. 2A). Likewise, similar data

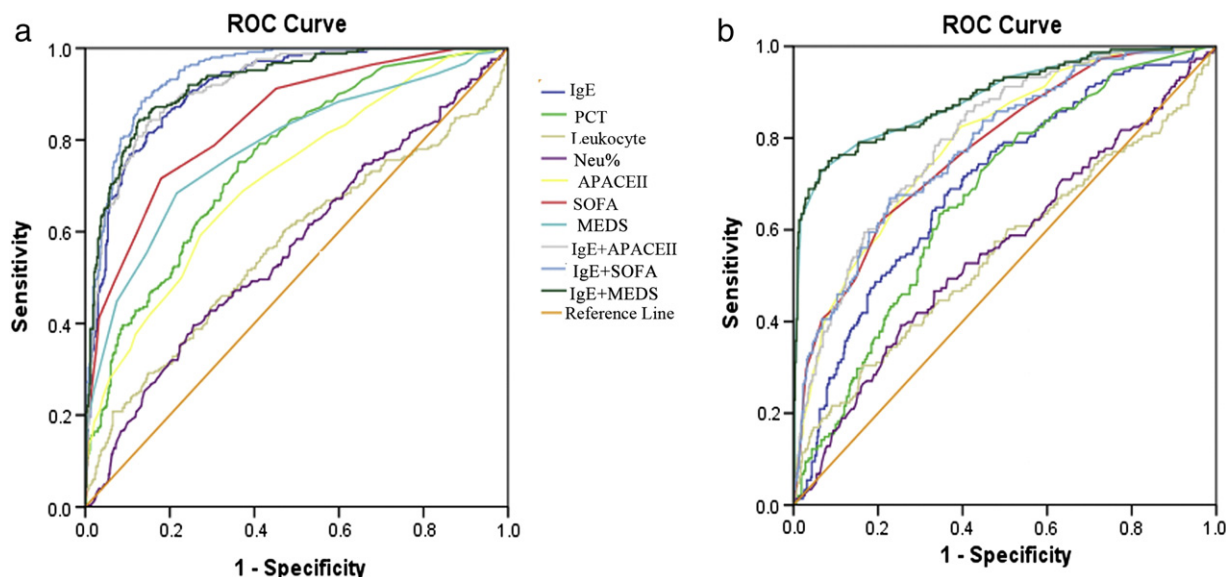


Fig. 1. Receiver operating characteristic curves of IgE, PCT, leukocyte count, percentage of neutrophils, APACHE II, SOFA, and MEDS score for predicting severe sepsis and 28-day mortality in septic patients. Areas under the ROC curves: IgE (blue line), 0.914 and 0.700, all $P < 0.01$; PCT (green line), 0.756 and 0.673, all $P < 0.01$; leukocyte count (brown line), 0.566 and 0.551, $P = .004$ and $P = .055$; percentage of neutrophils (purple line), 0.567 and 0.559, $P = .004$ and $P = .028$; APACHE II score (yellow line), 0.715 and 0.789, all $P < .01$; SOFA score (red line), 0.841 and 0.776, all $P < .01$; MEDS score (blue green line), 0.782 and 0.890, all $P < .01$; IgE in combination with APACHE II score (light purple line), 0.918 and 0.800, all $P < .01$; IgE in combination with SOFA score (light blue line), 0.943 and 0.781, all $P < .01$; IgE in combination with MEDS score (dark green line), 0.924 and 0.890, all $P < .01$, respectively.

were obtained for SOFA score (all $P < .01$) (Fig. 2B). In comparison, median IgE levels were significantly higher in categories of MEDS score (14–19 scores and >19 scores) than in that of MEDS score (<10 scores and 10–13 scores) (all $P < .0001$), but there was no significant difference between in categories of MEDS score (<10 scores) and in that of MEDS score (10–14 scores) ($P = .167$) (Fig. 2C).

3.6. Survival

Using cutoff values determined by ROC curves, Kaplan-Meier survival curves were established. Kaplan-Meier survival analysis showed that septic patients with plasma IgE levels higher than 299.96 $\mu\text{g/L}$ had a lower probability of survival at 28 days (log-rank test, 62.71; $P < .001$) compared to patients with lower IgE levels (Fig. 3).

4. Discussion

To the best of our knowledge, the present study includes the largest cohort to date of septic patients for which the levels of circulating IgE

were measured in the ED environment. Septic syndrome affects a group of patients with different etiologies (from pneumopathy to peritonitis) caused by different germs (gram-positive or gram-negative bacteria or even fungi) and with different medical history (with or without comorbidities) [14]. Moreover, it is now clear that the host immune response after sepsis is variable from one patient to another and also evolves over time, being associated with both an overwhelming cytokine release called cytokine storm and the later development of sepsis-induced immune dysfunctions [15]. In the current study, we observed a significant association between high IgE level and increased risk of death after sepsis. Moreover, maximal difference in plasmatic IgE concentrations between survivors and nonsurvivors at 28-day follow-up was observed as early as the onset of sepsis.

Sepsis is a complex pathophysiological process. It is widely accepted that although there is a predominance of the hyperinflammatory phase after sepsis initiation, sepsis then rapidly develops a state of immunosuppression [16,17]. Because of the application of antibiotics and other aggressive treatments, many patients may survive the initial proinflammatory stage but eventually die later in a state of immunosuppression

Table 3
Multivariable models for predicting severe sepsis and 28-day mortality

	Variable	P	OR	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	PLR	NLR	Accuracy (%)
Severe sepsis	IgE	.000	1.034	303.08 $\mu\text{g/L}$	73.9	77.9	79.1	72.6	3.34	0.34	83.8
	PCT	.029	1.006	0.445 ng/mL	75.2	63.7	54.7	81.5	2.07	0.39	67.9
	Leukocyte	.017	1.046	$18.275 \times 10^9/\text{L}$	29.2	85.1	53.3	67.4	1.96	0.83	64.6
	Neu %	.206	0.985	90.25	39.6	74.4	47.4	67.9	1.55	0.81	61.6
	APACHE II score	.043	0.944	18.5 score	59.2	72.8	55.8	75.4	2.18	0.56	67.8
	SOFA score	.000	1.490	5.5 score	71.6	82.1	69.9	83.3	4.00	0.35	78.2
	MEDS score	.000	1.327	13.5 score	68.4	78.4	64.8	81.0	3.17	0.40	74.7
	Constant	.000	0.005								
28-d mortality	IgE	.000	1.038	299.96 $\mu\text{g/L}$	77.5	80.6	87.1	68.0	3.99	0.28	64.3
	PCT	.027	0.996	0.920 ng/mL	63.5	65.4	33.8	86.6	1.84	0.56	65.0
	Leukocyte	.038	1.013	$18.525 \times 10^9/\text{L}$	30.4	83.8	34.4	81.2	1.88	0.83	72.2
	Neu %	.393	1.010	90.65	39.2	74.6	30.1	81.5	1.54	0.82	66.9
	APACHE II score	.039	1.040	16.5 score	82.4	60.5	36.7	92.5	2.09	0.29	65.3
	SOFA score	.006	1.002	6.5 score	62.2	79.1	45.3	88.3	2.98	0.48	75.4
	MEDS score	.000	1.784	14.5 score	73.0	93.2	75.0	92.5	10.74	0.29	88.8
	Constant	.000	0.000								

Abbreviations: PPV, positive predictive value; NPV, negative predictive value; PLR, positive likelihood ratio; NLR, negative likelihood ratio.

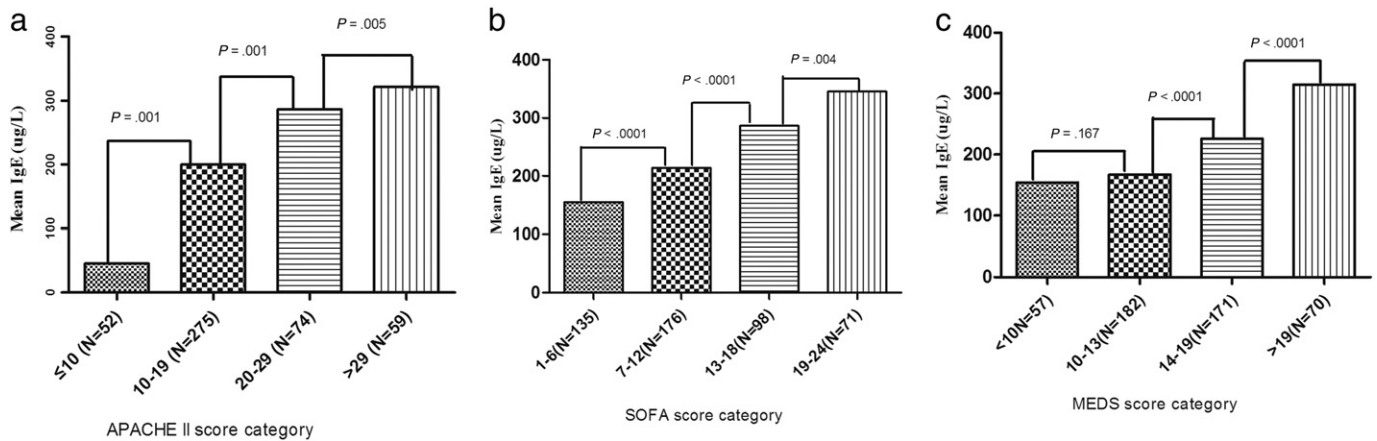


Fig. 2. Comparison of plasma IgE levels based on new groups of values of APACHE II, SOFA, and MEDS scores between any 2 groups. Columns represent mean IgE levels. Numbers of samples are indicated in parentheses.

[18]. Because the ED often serves as the front line for the initial evaluation of sepsis, accurate risk stratification is essential for optimal management of septic patients in the ED. Sepsis is a physiopathological process rather than a specific syndrome, and it is too complex to be described by a single measure. For this reason, neither clinical nor biological markers have been shown to be perfect prognostic tools. Serum levels of IgE in adult septic patients have been evaluated in only 2 other studies. In 1998, DiPiro et al [5] documented increased IgE concentrations and eosinophil counts were found after sepsis and do not appear to be related to the initial injury. Another work by DiPiro et al published in 1992 showed that allergic mechanisms may be involved in the physiologic response to sepsis or that other cells known to be involved in the immune responses to sepsis (macrophages, platelets, and B lymphocytes) may become activated by IgE-dependent mechanisms [12]. Notably, in our study, there were higher negative predictive value for IgE in predicting severe sepsis (72.6%) or 28-day mortality (68.0%), suggesting lower than the corresponding IgE cutoff of 303.08 or 299.96 $\mu\text{g/L}$ might help rule out the possibility for incidence of severe

sepsis or 28-day mortality. In addition, the association between increased IgE levels and higher risk of death was preserved in multivariate analysis including clinical confounders such as SOFA and MEDS scores. This suggests that the predictive value of IgE is independent of patients' initial severity and that IgE level may be informative by itself. Most interestingly, the combination of IgE level and MEDS improved the predictive value compared with each parameter considered alone.

Evidence regarding the role of IgE in sepsis comes mainly as follows: (a) IgE may be involved in the activation of monocytes, macrophages, platelets, eosinophils, and/or B lymphocytes through low-affinity IgE receptors, and this effect may accentuate cell activation in sepsis. (b) IgE may simply be a marker for cytokine regulation/dysregulation that occurs after traumatic injury and sepsis. Allergic reactions and/or cellular activation may be detrimental to the patient if inflammation is enhanced. The findings of high IgE level along with prior reported findings of increased IL-4 and IL-10 plasma concentrations supports the hypothesis that Th2 cytokines are activated in response to sepsis after infection [19]. (c) The possibility exists that allergic mechanisms may be involved in the physiologic response to sepsis. Activated basophils and mast cells not only may release preformed and newly generated mediators of allergy but also may be a source of tumor necrosis factor α , an important primary mediator of the sepsis syndrome. Activation of any of these cells may initiate inflammatory processes that contribute to the development of organ dysfunction.

Our study has some limitations. First, despite containing a relatively large sample size, this study was a single-center study, and the results cannot be extendible to other EDs before a prospective multicenter study. Second, interobserver variability in the process of data collection was not examined, and this may result in the misclassification bias. Although we have no ability to determine how interobserver variability may have affected our results, we attempted to minimize the effects by performing close oversight of the process of data collection. Third, it was difficult to obtain pathogen samples in an ED setting, so the association IgE with pathogen was not unknown. Finally, within only 1-sample window, we just compare the alteration of plasma IgE level at the early stage of sepsis, but keeping track of the immune function and plasma IgE level in later period and comprising the septic patients with other critically ill individuals are also important, which we will view as important areas of future studies. For these reasons, further studies were to develop to investigate the performance of IgE in aforementioned aspects in the future.

In conclusion, by detecting the alteration of plasma IgE level and related cytokines in patients with different levels of illness severity, our results strongly support the hypothesis that septic patients with high IgE level present with higher risk of mortality, and a combination IgE level with scoring systems significantly increased the predictive accuracy for severe sepsis and 28-day mortality. In addition, the inflammatory

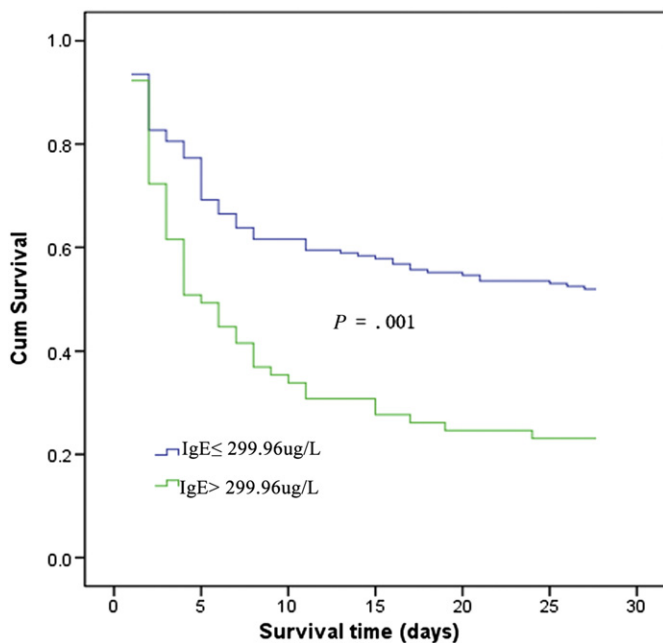


Fig. 3. Survival curves. Kaplan-Meier survival curves showed that septic patients with plasma IgE levels higher than 299.96 $\mu\text{g/L}$ had a lower probability of survival at 28 days (log-rank test, 62.71; $P < .001$) compared to patients with lower levels.

response especially the adaptive immune response is still associated with aggravated sepsis. Thus, we hope that our study provides complementary information to increase understanding of lymphocytic alterations in sepsis, and assessment of plasma IgE might be of help for septic patient stratification. Further studies are needed to confirm these findings in a large cohort of sepsis patients and to investigate the mechanism of immunosuppression in sepsis.

Conflicts of interest

All authors declare that there are no actual or potential conflicts of interest, including any financial, personal, or other relationships.

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