STAPLAg: a convenient early warning score for use in infected patients in the intensive care unit

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Abstract
Sepsis is a life-threatening disease in the intensive care unit (ICU). The current diagnostic criteria for sequential organ failure assessment (SOFA) scores do not reflect the current understanding of sepsis. We developed a novel and convenient score to aid early prognosis.

Retrospective multivariable regression analysis of 185 infected emergency ICU (EICU) patients was conducted to identify independent variables associated with death, to develop the new “STAPLAg” score; STAPLAg was then validated in an internal cohort (n = 106) and an external cohort (n = 79) and its predictive efficacy was compared with that of the initial SOFA score.

Age, and initial serum albumin, sodium, PLR, troponin, and lactate tests in the emergency department were independent predictors of death in infected EICU patients, and were used to establish the STAPLAg score (area under the curve [AUC] 0.865). The initial SOFA score on admission was predictive of death (AUC 0.782). Applying the above categories to the derivation cohort yielded mortality risks of 7.7% for grade I, 56.3% for grade II, and 75.0% for grade III. Internal (AUC 0.884) and external (AUC 0.918) cohort validation indicated that the score had good predictive power.

The STAPLAg score can be determined early in infected EICU patients, and exhibited better prognostic capacity than the initial SOFA score on admission in both internal and external cohorts. STAPLAg constitutes a new resource for use in the clinical diagnosis of sepsis and can also predict mortality in infected EICU patients.

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Abbreviations: ALB = albumin, AUC = area under the curve, CRP = C-reactive protein, CRP/ALB = C-reactive protein/albumin ratio, DBP = diastolic blood pressure, DM = diabetes mellitus, EICU = emergency intensive care unit, Glu = blood glucose, GPS = Glasgow Prognostic Score, Hb = hemoglobin, HLP = hyperlipoidemia. HTN = hypertension, ICU = intensive care unit, K = serum kallium, Lac = serum lactate concentration, LMR = lymphocyte-monocyte ratio, Na = serum sodium, NLR = neutrophil-lymphocyte ratio, PCT = procalcitonin, PLR = platelet-lymphocyte ratio, PLT = blood platelets, SBP = systolic blood pressure, Scr = serum creatinine, SOFA = sequential organ failure assessment, SpO₂ = fingertip percutaneous oxygen saturation, TNI = troponin, WBC = white blood cell count.

Keywords: EICU infection, sepsis, SOFA score, STAPLAg score

1. Introduction
Sepsis remains an ongoing challenge in intensive care medicine and is the leading cause of death in the intensive care unit (ICU).[1] Critically ill elderly patients in ICUs are at a particularly high risk of death associated with sepsis.[2] When sepsis occurs the body exhibits serious abnormalities in circulation and cellular and metabolic functions, and the mortality rate is as high as 25% to 30%. In cases of septic shock the mortality rate can reach 40% to 50%.[3] It is therefore an important public health issue.[4]

The latest international consensus[5] defines sepsis as “life-threatening organ dysfunction caused by a dysregulated host response to infection.” An unsteady host response at the time of infection is far more lethal than direct infection and needs to be identified as soon as possible. Early identification and proper treatment of sepsis are critical for improving the prognosis.[6]

Given the complexity of the pathophysiological mechanisms of sepsis and the diversity of clinical manifestations, its early identification is very difficult. Among patients with suspected infection, in those with a Sequential Organ Failure Assessment (SOFA) score ≥2 points the overall hospital mortality rate is close to 10%.[7] so in 2016 the Society of Critical Care Medicine and the European Society of Critical Care Medicine advocated the use of SOFA scores as sepsis diagnostic criteria.[8] Although the current working group of Surviving Sepsis Campaign temporarily...
uses the SOFA score as a diagnostic criterion for sepsis, the SOFA scoring system has limitations in terms of variables and mortality discrimination. Its content does not fully reflect the hosts overall response to infection-associated imbalance and cannot reflect the influences of advanced age, immune status, tissue oxygen supply, oxygen imbalance, or metabolic disorders on prognosis.

In 2011, Boomer et al[10] reported that splenic CD4+ CD8+ T cell levels decreased and HLA-DR declined with decreased levels of interleukin-6, tumor necrosis factor (TNF)-α, interleukin-10, and TNF-γ from lipopolysaccharide-induced spleen cells in patients with sepsis compared with other critically ill patients without sepsis. They surmised that this confirmed that patients with sepsis are more severely impaired in immune function than critically ill patients without sepsis. Owing to inherent limitations, the SOFA score does not reflect recent progress in sepsis research or our current understanding of the condition. Factors such as age, immune imbalance, imbalance between oxygen supply and oxygen consumption, and the influence of metabolic disorders on mortality in patients with sepsis are not reflected in SOFA scores. As well as being cumbersome in practice, the SOFA score does not perform well with regard to predicting hospital mortality in patients with suspected infections, who reportedly constitute up to 74% of patients in the ICU and 79% of non-ICU patients.[8]

Given the limitations of the SOFA score, we sought to identify some clinically simple indicators related to the imbalance in bodily responses of infected emergency ICU (EICU) patients that are early prognostic predictors, develop a novel and easy-to-use scoring system, and compare it with the SOFA score in 2 patient cohorts.

2. Methods

2.1. Patients

This non-interventional study was conducted in accordance with the ethical principles and standards of the Second Declaration of Helsinki and its subsequent amendments. The study had no influence on treatment or prognoses, nor did it result in any personal information being compromised. The study was approved by the Ethics Association of Renji Hospital affiliated with the Jiaotong University School of Medicine, and informed consent was obtained from all participants. The emergency intensive care unit (EICU) of Renji Hospital affiliated with the Shanghai Jiaotong University School of Medicine has 15 beds and is managed by 5 residents, 3 attending physicians, and 2 chief physicians, whose ratio of nurses to patients is close to 2:1.

2.2. Derivation cohort

Data were retrospectively collected from 185 consecutive patients treated for infection in the EICU of Renji Hospital affiliated with the Shanghai Jiaotong University School of Medicine from March 1, 2015 to February 28, 2017.

2.3. Internal validation cohort

Data were prospectively collected from 106 consecutive patients treated for infection in the EICU of Renji Hospital affiliated with the Shanghai Jiaotong University School of Medicine from March 1, 2017 to February 28, 2018.

2.4. External validation cohort

Data were prospectively collected from 78 consecutive patients treated for infection in the EICU at the People’s Hospital of Shanghai Jiaotong University School of Medicine from February 23, 2017 to December 26, 2017.

2.5. Inclusion and exclusion criteria

The inclusion criteria were age >18 years, infection at the emergency visit, and being admitted to the EICU. Exclusion criteria were the presence of autoimmune disease or advanced malignancy, acute coronary syndrome or acute cerebrovascular accident, and chronic respiratory failure, cirrhosis, or renal insufficiency. Some of these patients had sepsis or were in septic shock. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) in 2016 were used in this research.[9]

2.6. Data collection

The hospitals digital medical records system was used to determine the general demographic characteristics of the patients, their first laboratory test indicators, and clinical data. All blood biochemical tests were performed using the same brand of equipment. Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio (PLR), lymphocyte/monocyte ratio, C-reactive protein (CRP)/albumin (ALB) ratio, and Glasgow Prognostic Score[9] were calculated and recorded. The Glasgow Prognostic Score was calculated as follows: ALB <35 g/L and CRP >10 mg/L, 2 points; ALB >35 g/L and CRP <10 mg/L, or ALB <35 g/L and CRP >10 mg/L, 1 point; ALB >35 g/L and CRP <10 mg/L, 0 points.

2.7. Statistical analysis

The data were analyzed using SAS 9.4 software (SAS, Cary, NC, USA). The measurement data were first tested for normality. Data that were normally distributed were expressed as mean ± standard deviation, and group means were compared via t tests. Data that were not normally distributed were expressed in terms of quartile ranges (Q1–Q3) and compared via nonparametric tests. Comparisons between 2 groups were based on the Chi-Squared test. If the theoretical frequency was exceeded, the Fisher exact probability method was used. Multivariate analysis was performed using a logistic regression model. P < .05 was considered statistically significant. The resolution of each score was evaluated by calculating the area under the receiver-operating characteristic (ROC) curve (AUROC) and corrected via the Hosmer-Lemeshow goodness-of-fit C test. P > .05 was considered to indicate a good correction effect, and ROC curves were compared using the Hanley-McNeil method. Single-factor comparison was performed using datasets from surviving and nonsurviving patients. The principle of variable screening was backward. Logistic regression analysis was performed. The α-input was 0.05 and the α-output was 0.10. The variables selected were determined via the maximum Youden index method. In the “internal verification queue,” the regression of the STAPLAG score in the internal dataset was evaluated using binary regression, and the resolution was evaluated using the ROC curve and the Hosmer-Lemeshow goodness-of-fit C test. The “external verification queue” was used to establish a STAPLAG score with the derivation queue.
3. Results

The demographic characteristics of the derivation cohort patients and their clinical data are shown in Table 1. Survivors and nonsurvivors differed significantly with regard to age, blood ALB, fingertip percutaneous oxygen saturation (SpO2), serum troponin, CRP, serum lactate concentration, neutrophil/lymphocyte ratio, PLR, GPS, and CRP/ALB ratio.

A multivariate logistic regression model was then constructed using the 12 variables in Table 1 that yielded \( P < .1 \) to identify factors that were independently associated with mortality. Six clinical variables independently associated with EICU infection resulting in death were identified; ALB, age, serum troponin, serum sodium, serum lactate, and PLR (Table 2). To reduce clinical practical complexity, cut-off values were determined via the maximum Youden index method and a dichotomy process was performed (Table 3). Based on this analysis, a new scoring system dubbed the STAPLAG score was developed, derived from the words Sodium, Troponin I, Albumin, Platelet/lymphocyte ratio, Lactate concentration, and Age.

In ROC analysis, the STAPLAG score area under the curve (AUC) in the derivation cohort, which was statistically significant, was 0.865 (95% confidence interval [CI] 0.797–0.934; \( P < .001 \)). The AUC was greater than 0.782 for the first SOFA on admission (95% CI 0.691–0.873; \( P < .001 \)), and a Z-test of the AUCs of the 2 results derived from the derivation queue. The internal validation cohort included 106 patients, of whom 76 (71.7%) were male and 30 (28.3%) were female. The mean age of patients admitted to the EICU was 69 years (59–79 years). The first SOFA score on admission was 1.00 (0.00–3.00). In the EICU, 25 (23.6%) patients died within 28 days of being hospitalized. There were no significant differences in the clinical characteristics of the derivation cohort and the internal cohort. Prospective validation (n=106; mortality 23.6%) exhibited better predictive power (AUC 0.884; 95% CI 0.817–0.951) than the first SOFA score on admission (AUC 0.628; 95% CI 0.502–0.754) (Table 4 and Fig. 1b). The above risk categories were applied to the internal

**Table 1**

| Variable          | Survivors (n=158) | Non-survivors (n=27) | \( x^2 \) or \( t \) | \( P \) |
|-------------------|-------------------|----------------------|----------------------|-------|
| SEX               |                   |                      |                      |       |
| 1 M               | 86 (54.43%)       | 18 (66.67%)          | 1.403                | .236  |
| 2 F               | 72 (45.57%)       | 9 (33.33%)           |                      |       |
| Hb (g/L)          | 130.66±23.11      | 124.37±21.04         | 1.360                | .174  |
| SBP (mmHg)        | 122.00±11.08      | 123.36±16.21         | 0.630                | .852  |
| DBP (mmHg)        | 72.18±13.03       | 70.93±14.55          | 0.460                | .649  |
| ALB (g/L)         | 3.14±5.85         | 26.78±4.77           | 3.660                | .000  |
| AGE               | 63 (48–76)        | 74 (62–82)           | 0.007                |       |
| PLT (10^9/L)      | 103 (134–238)     | 193.5 (123–268)      | 0.326                | .745  |
| WBC (10^9/L)      | 10.29 (7.08–14.11)| 12.24 (7.65–23)      | 0.716                | .474  |
| TNI (ng/ml)       | 0.02 (0.01–0.05)  | 0.07 (0.03–0.34)     | 4.620                | .000  |
| Na (mmol/L)       | 134 (130–138.5)   | 129 (128–135)        | –1.823               | .068  |
| K (mmol/L)        | 3.7 (3.3–4.1)     | 3.9 (3.3–4.1)        | 0.685                | .493  |
| Scr (µmol/L)      | 72 (56–94)        | 64 (60–151)          | 1.908                | .057  |
| PCT (ng/ml)       | 0.6 (0.12–2.45)   | 3.82 (0.25–15.43)    | 1.523                | .128  |
| CRP (mg/L)        | 93.55 (15.63–164.21)| 176.35 (68.94–204.56)| 2.977                | .003  |
| GLU (mmol/L)      | 7.83 (6.09–10.42) | 8.06 (6.2–14.15)     | 0.670                | .503  |
| SPO2 (%)          | 99 (98–100)       | 97 (90–90)           | –2.483               | .013  |
| Lac (mmol/L)      | 1.3 (0.9–1.7)     | 2 (1.3–3.2)          | 3.949                | .000  |
| NLR               | 8.56 (4.64–15.67) | 13.45 (7.57–28.8)    | 2.145                | .032  |
| PLR               | 192.97 (136–304.55)| 266.03 (214.2–516.47)| 2.580                | .010  |
| LMR               | 1.88 (1.14–3.12)  | 1.44 (0.63–3.78)     | 1.461                | .144  |
| CRP/ALB           | 2.4 (0.86–4.42)   | 4.94 (1.63–8.09)     | 2.600                | .009  |
| GPS               | 1.87±0.34         | 1.48±0.70            | 2.872                | .009  |

Variables are presented as mean followed by the standard deviation in parentheses in cases of normally distributed data, and as medians followed by the first to the third quartile range in parentheses in cases of non-normally distributed data.

* Number of cases. The comparison between the 2 groups was based on a Chi-Squared test.

The Glasgow Prognostic Score was calculated as follows: ALB < 35 g/L and CRP > 10 mg/L, 2 points; ALB > 35 g/L and CRP < 10 mg/L, 1 point; ALB > 35 g/L and CRP < 10 mg/L, 0 points.\( ^{33} \)

\( P < .05 \) was considered statistically significant.

ALB = albumin, CRP/ALB = C-reactive protein/albumin ratio, CPT = C-reactive protein, DBP = diastolic blood pressure, Glu = blood glucose, GPS = Glasgow Prognostic Score, Hb = hemoglobin, K = serum potassium, Lac = serum lactate concentration, LMR = lymphocyte-monocyte ratio, Na = serum sodium, NLR = neutrophil/lymphocyte ratio, PCT = procalcitonin, PLR = platelet-lymphocyte ratio, PLT = blood platelet, SBP = systolic blood pressure, Scr = serum creatinine, SpO2 = fingertip percutaneous oxygen saturation, TNI = troponin, WBC = white blood cell count.

Two separate validation queues were then used to validate the results derived from the derivation queue. The internal validation cohort included 106 patients, of whom 76 (71.7%) were male and 30 (28.3%) were female. The mean age of patients admitted to the EICU was 69 years (59–79 years). The first SOFA score on admission was 1.00 (0.00–3.00). In the EICU, 25 (23.6%) patients died within 28 days of being hospitalized. There were no significant differences in the clinical characteristics of the derivation cohort and the internal cohort. Prospective validation (n=106; mortality 23.6%) exhibited better predictive power (AUC 0.884; 95% CI 0.817–0.951) than the first SOFA score on admission (AUC 0.628; 95% CI 0.502–0.754) (Table 4 and Fig. 1b). The above risk categories were applied to the internal
### Table 3

| Variable       | Points |
|----------------|--------|
| ALB (g/L)      |        |
| >29.9          | 0      |
| <29.9          | 1      |
| AGE            |        |
| >69            | 1      |
| <69            | 0      |
| TNI (ng/ml)    |        |
| >0.05          | 1      |
| <0.05          | 0      |
| Na (mmol/L)    |        |
| >129           | 0      |
| <129           | 1      |
| Lac (mmol/L)   |        |
| >2             | 1      |
| <2             | 0      |
| PLR            |        |
| >214.98        | 1      |
| <214.98        | 0      |
| Total score    | 6      |
| Risk class     |        |
| Class I 0–2   | 3 (3.41)|
| Class II 3–4  | 12 (25.00)|
| Class III 5–6 | 9 (75.00)|

ALB = albumin, Lac = serum lactate concentration, Na = serum sodium, PLR = platelet-lymphocyte ratio, TNI = troponin.

### Table 4

| Assessment of prediction scores. | Total | Survivors | Non-survivors | AUC | 95% | P | Hosmer-Lemeshow statistic x² | P** |
|----------------------------------|-------|-----------|---------------|-----|-----|---|-----------------------------|-----|
| Derivation cohort (n)            | 185   | 158       | 27            |     |     |   |                            |     |
| SOFA-score                       | 1 (3) | 1 (3)     | 5 (4)         | 0.782| 0.691–0.873| .000| 7.471                      | .399|
| STAPLAg-score                    | 2 (2) | 2 (2)     | 4 (2)         | 0.865| 0.797–0.934| .000| 1.360                      | -   |
| Internal validation cohort (n)   | 106   | 81        | 25            |     |     |   |                            |     |
| SOFA-score                       | 1 (3) | 1 (3)     | 2 (3)         | 0.628| 0.502–0.754| .046| 5.699                      | .001|
| STAPLAg-score                    | 2 (2) | 2 (1)     | 3 (1)         | 0.884| 0.817–0.951| .000| 2.580                      | -   |
| External validation cohort (n)   | 76    | 59        | 17            |     |     |   |                            |     |
| SOFA-score                       | 3.5 (6)| 3 (6)  | 6 (9)         | 0.736| 0.610–0.863| .000| 16.722                     | .008|
| STAPLAg-score                    | 2 (2) | 1.5 (1) | 4 (1)         | 0.918| 0.855–0.981| .000| 0.597                      | -   |

P**: Pairwise comparison to STAPLE score (difference between areas; P value).

**4. Discussion**

Interestingly, the 6 clinical indicators ultimately included in the STAPLAg scoring system are all related to the host’s dysregulation of infection, which is consistent with recent advances in the nature of sepsis. In the present study, first-time admission SOFA assessment was used as a reference to identify factors that are more suitable for the early diagnosis of sepsis. The STAPLAg score was also proactively validated in 2 separate internal and external cohorts.

Delayed diagnosis can lead to delayed administration of antibiotics. There is evidence that a 1-hour delay in the administration of antibiotics can lead to a significant increase in sepsis-associated mortality.[11] Therefore, the development of an optimal diagnostic tool for the early detection of sepsis is highly desirable. The STAPLAg scoring system expressly achieves this goal.

#### 4.1. Serum sodium

Hyponatremia is the most common electrolyte disorder encountered in the clinic. The incidence of hyponatremia in ICU patients is at least 30%, which is similar to the rate of mortality associated with sepsis.[12] Systemic inflammatory responses and immune damage caused by microcirculatory disorders and tissue cell damage render patients prone to hyponatremia. It has also been reported that the release of interleukins in patients with infectious diseases triggers anti-SIADH (syndrome of inappropriate antidiuretic hormone secretion), which leads to hyponatremia.[13] In the present study serum sodium reduction independently predicted the death of infected ICU patients, and the risk of death increased by 71.6% when serum sodium was <129mmol/L.

#### 4.2. Troponin

Myocardial dysfunction is a common complication of sepsis but is not well defined. It may be associated with elevated levels of catecholamines and cytokines in circulation, and their presence significantly worsens the outcome of sepsis.[14,15] In patients with sepsis, cardiac troponin release is reportedly associated with adverse outcomes, including higher mortality and longer stays in the ICU.[16] Mehta et al[17] reported that troponin I is an independent predictor of death associated with a lower left ventricular ejection fraction (P < .001). These results are consistent with the present study, in which initial serum troponin >0.05 ng/ml was associated with a 3.6-fold increase in mortality.

#### 4.3. Serum ALB

Serum ALB is an important component of the glycocalyx on the surface of vascular endothelial cells and has an integral role in...
microvascular perfusion and permeability.\textsuperscript{18} Recent studies have shown that there are immune imbalances and complex pathophysiological states such as synthetic and catabolic disorders in patients with sepsis. Gentile et al.\textsuperscript{19} proposed a new type of “sustained inflammation-immunosuppressive-catabolic syndrome” based on sepsis. Serum ALB <30g/L was considered one of the diagnostic criteria in sepsis patients who have obvious synthetic and catabolic disorders.

In a recent study of 3894 adult patients with acute infections, hypoproteinemia at admission was an independent predictor of 30-day all-cause mortality.\textsuperscript{20} In another study, short-term continuous changes in serum ALB in patients with sepsis had a strong effect on prognosis. A change in serum ALB 1-day or 3-day minimum was more strongly associated with prognosis than 7-day and 14-day minimum.\textsuperscript{21}

In the current study, patients with serum ALB levels <29.9g/L had a 75.2% increase in mortality.

4.4. PLR

Platelets, as well as participating in the coagulation process, also fulfill immune functions, and thus play an important role in the development of sepsis.\textsuperscript{22} Lymphocytes are typically markedly reduced in number in patients with sepsis.\textsuperscript{23} Accordingly, studies have found that PLR is simpler, more convenient, and more informative than evaluating the prognosis of patients using platelets or lymphocytes alone.\textsuperscript{24} Studies have shown that PLR can be used as an indicator to predict mortality in patients with sepsis.\textsuperscript{25}

In the present study, elevated PLR independently predicted death in patients with EICU infection. If the PLR was above 214.98, the risk of death was increased by 176%.

4.5. Lactate concentration

High levels of lactate concentration can reportedly downregulate the rate-limiting glycolytic enzymes hexokinase and phosphofructokinase in various tissues and immune cells, thereby affecting aerobic glycolysis metabolism and inhibiting the activation of immune cells and leading to the immune imbalance associated with sepsis.\textsuperscript{26}

Elevated lactate concentration levels, which are widely used for early diagnosis, management, and risk stratification in patients with septic shock, is associated with high mortality.\textsuperscript{27} Studies indicate that a high concentration of serum lactate concentration may predict mortality.\textsuperscript{28} Previous studies have shown that when serum lactate concentration is >2mmol/L, the sepsis-mortality of refractory hypotension is significantly higher.\textsuperscript{15} In the current...
study, lactate concentration exhibited prognostic value in infected patients. When serum lactate concentration was >2 mmol/L, the risk of death increased by 288%.

### 4.6. Age

Aging is a unique process that permanently alters the systems immunity by interfering with homeostasis. A process known as “inflammatory aging” weakens the abilities of interleukin-6, TNF-α, and CRP to fight infection, and can trigger more serious complications. Thus, the immune system is significantly reduced as aging ensues, and this has been called “immune aging.” In countries with advanced medical services and modern ICUs, approximately 60% of sepsis patients and 75% of patients who die from sepsis are over 65 years of age. The present study was concordant with these observations, in that the risk of mortality was 1.7 times higher in infected patients aged >69 years.

The results of the current study indicate that the new STAPLAg score reflects the pathophysiological mechanism of sepsis, and its components reflect the hosts infection-induced internal environment imbalance, oxygen supply and imbalance, immune imbalance, myocardial dysfunction indicators, and related influential factors. The STAPLAg score was more effective than the first SOFA score on admission for predicting the prognosis of infected EICU patients in the early stage, with AUROC 0.865 (95% CI 0.797–0.934) vs 0.782 (95% CI 0.691–0.873). Both internal and external derivation cohorts were validated, with respective AUROCs of 0.884 (95% CI 0.817–0.951) vs 0.628 (95% CI 0.502–0.754), and 0.918 (95% CI 0.855–0.981) vs 0.736 (95% CI 0.610–0.863).

Infected EICU patients with grade I (0–2 points) had a mortality rate of 7.7%, grade II (3–4 points) patients had a mortality rate of 56.3%, and grade III (5–6 points) patients had a mortality rate of 75.0%. Each component parameter of the STAPLAg score can be obtained quickly, in the early stage of a physiological emergency. The STAPLAg scoring system is also more convenient than the SOFA system. If a prospective multicenter study with a large sample can further verify its clinical value, it is hoped that the STAPLAg score will be applied for the early diagnosis of sepsis. If this occurs, the STAPLAg score may provide a new perspective on the diagnosis of sepsis that differs from that of the SOFA score, and may contribute to earlier identification and more timely intervention of sepsis.

Although the STAPLAg score demonstrated stronger predictive power than the first SOFA score on admission and provides a unique perspective on the clinical diagnostic criteria of sepsis, in clinical practice it is more suitable to use both the STAPLAg score and the SOFA score in combination.

The current study had several limitations. It was a single-center retrospective study involving infected EICU patients. Although strict internal and external cohort validation was performed, caution should be observed when extrapolating the results to other medical institutions. Another limitation is that although EICU clinicians strictly adhered to the required guidelines,
because of the 3-year study period and inevitable differences in patient enrollment times, the treatments they received may have been affected by subjective differences, and such differences may have affected patient outcomes. Lastly, the prediction model utilized dichotomy assignment. While this may have partially reduced predictive performance, the aim was to reduce the complexity of the score and improve the efficiency of implementation.

5. Conclusions

In the current study, a new and convenient predictive scoring system that can be applied early in infected EICU patients was developed and prospectively validated. The STAPLAG score exhibited greater prognostic capacity than the SOFA score on admission in both internal and external cohorts. It is conducive to the early diagnosis and treatment of sepsis, and embodies a new perspective on the clinical diagnosis of sepsis. The STAPLAG score can also predict mortality in infected EICU patients.

Author contributions

Keji Zhang, Dan Lv, and Yuan Gao conceived the study, designed the trial, and obtained research funding. Yuan Huang and Yuxiao Deng supervised the conduct of the trial and data collection. Xinhui Xu managed the data, including quality control. Dan Lv provided statistical advice on study design and collection. Keji Zhang drafted the manuscript, and all authors analyzed the data; Changqing Zhu chaired the data oversight committee. Keji Zhang drafted the manuscript, and all authors contributed substantially to its revision. Dan Lv takes responsibility for the paper as a whole.

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