

# The evaluation of acute physiology and chronic health evaluation II score, poisoning severity score, sequential organ failure assessment score combine with lactate to assess the prognosis of the patients with acute organophosphate pesticide poisoning

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## Abstract

The aim of this study was to assess the ability of acute physiology and chronic health evaluation II (APACHE II) score, poisoning severity score (PSS) as well as sequential organ failure assessment (SOFA) score combining with lactate (Lac) to predict mortality in the Emergency Department (ED) patients who were poisoned with organophosphate.

A retrospective review of 59 stands-compliant patients was carried out. Receiver operating characteristic (ROC) curves were constructed based on the APACHE II score, PSS, SOFA score with or without Lac, respectively, and the areas under the ROC curve (AUCs) were determined to assess predictive value. According to SOFA–Lac (a combination of SOFA and Lac) classification standard, acute organophosphate pesticide poisoning (AOPP) patients were divided into low-risk and high-risk groups. Then mortality rates were compared between risk levels.

Between survivors and non-survivors, there were significant differences in the APACHE II score, PSS, SOFA score, and Lac (all  $P < .05$ ). The AUCs of the APACHE II score, PSS, and SOFA score were 0.876, 0.811, and 0.837, respectively. However, after combining with Lac, the AUCs were 0.922, 0.878, and 0.956, respectively. According to SOFA–Lac, the mortality of high-risk group was significantly higher than low-risk group ( $P < .05$ ) and the patients of the non-survival group were all at high risk.

These data suggest the APACHE II score, PSS, SOFA score can all predict the prognosis of AOPP patients. For its simplicity and objectivity, the SOFA score is a superior predictor. Lac significantly improved the predictive abilities of the 3 scoring systems, especially for the SOFA score. The SOFA–Lac system effectively distinguished the high-risk group from the low-risk group. Therefore, the SOFA–Lac system is significantly better at predicting mortality in AOPP patients.

**Abbreviations:** AChE = acetylcholinesterase, AOPP = acute organophosphate pesticide poisoning, APACHE II = acute physiology and chronic health evaluation II, AUCs = areas under the ROC curve, ED = Emergency Department, GCS = Glasgow Coma Scale, Lac = lactate, OP = organophosphate, PAM = pyraloxime methiodide, PSS = poisoning severity score, ROC = receiver operating characteristic, SOFA = sequential organ failure assessment, WBC = white blood cell.

**Keywords:** acute organophosphate pesticide poisoning, acute physiology and chronic health evaluation II, lactate, poisoning severity score, sequential organ failure assessment

## 1. Introduction

Acute organophosphate pesticide poisoning (AOPP) continues to be a significant global health problem in developing countries, especially in Asian countries such as China. As the high mortality

rates following AOPP, early recognition is life-saving in severe cases. Therefore, there is an increasing number of scoring systems which have been used in clinical in order to evaluate the severity and prognosis of AOPP patients effectively.

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Drs SY and YG have contributed equally to this work and should be regarded as co-first authors.

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Acute physiology and chronic health evaluation II (APACHE II) score, as a commonly used clinical scoring method, may be applied to evaluate the severity and prognosis of acute critical diseases, which was proposed by Knaus etc.<sup>[1]</sup> in 1985. Poisoning severity score (PSS), a disease severity classification system of poisoning, is positively correlated with disease severity for patients with AOPP, which was first proposed by the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) in 1990.<sup>[2]</sup> Additionally, score of sequential organ failure assessment (SOFA) which was put forward by the Europe intensive care unit, is used for assessment of organ damage, predicting mortality in critical patients and, having the advantages of objective, reliable, simple, and easy to get.<sup>[3]</sup> Three rating tools are used widely to evaluate the prognosis of severe patients. There are several researches which have confirmed them to be used for assessing the severity of AOPP patients. However, the diagnostic efficacy is inconsistent.<sup>[4–6]</sup>

Recently, the arterial lactate (Lac) level has been reported as a good biomarker for evaluating status of tissue microcirculation.<sup>[7]</sup> AOPP can cause accumulation of a large number of acetylcholine leading to a series of muscarine, nicotine, and central nervous system symptoms. In this case, the microcirculation status of patients will change.

However, there were few studies reported about the prognostic value of Lac in AOPP patients. To the best of our knowledge, there are no reports which had evaluated the prognosis of AOPP patients using Lac in combination with these 3 rating tools. Therefore, we conducted this study to choose a more effective scoring tool for patients with AOPP.

## 2. Materials and methods

### 2.1. Basic materials

This retrospective study analyzed 59 subjects admitted to the emergency department (ED) of Beijing Chao-yang hospital, Beijing, for AOPP between February 2007 and May 2016. The 59 AOPP patients all met our criteria for selection, so no case was excluded in this study. The subjects were selected according to the following criteria.

1. We included subjects who had been previously exposed to organophosphate (OP) who had the typical clinical presentation.
2. We excluded subjects who had unclear exposed history or who had severe chronic disease. We also excluded subjects who had either refused treatment or had incomplete data.

### 2.2. Methods

1. We collected the outcome event of either getting better or death within 30 days.
2. We collected the clinical data as follows: the basic information; the amount and ingestion time of OP; the vital signs; the routine blood test; the arterial blood gas test; the biochemical indicators test; the serum acetylcholinesterase activity (AChE); the treatment and dose of pyraloxime methiodide (PAM) and atropine; the complications; the usage of mechanical ventilation or not, and the Glasgow Coma Scale (GCS).
3. Lac was measured at the time of admission by the blood gas analyzer (NOVA Biomedical Instruments, Waltham, MA).
4. Based on the above clinical data, we calculated and analyzed the APACHE II score, PSS, and SOFA score.

### 2.3. Statistical analysis

All statistical analyses were performed by SPSS software version 16.0 (SPSS, Chicago, Illinois). Data were expressed as medians and quartiles. Normally distributed data were compared using the independent-samples *t* test. Data with a skewed distribution were analyzed by the Mann–Whitney *U* test. The chi-square test was used for comparison of categorical variables. Receiver operating characteristic (ROC) curves were constructed to assess the predictive value of each indicator. For comparison of the areas under the ROC curve (AUCs), we used the *Z* test:  $Z = (A_1 - A_2) / \sqrt{SE_1^2 + SE_2^2}$ ,  $Z_{0.05} = .96$ ,  $Z_{0.01} = 2.58$ ,  $Z > Z_{0.05}$  represent  $P < .05$ . Based on the ROC curves, we calculated the positive and negative predictive values, the positive and negative likelihood ratios and the thresholds, which determined our risk classes. A 2-tailed  $P < .05$  was considered statistically significant.

## 3. Results

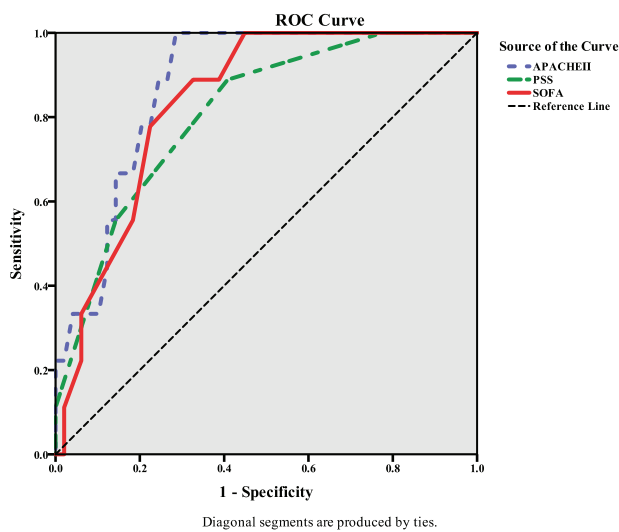
### 3.1. Baseline information

A total of 59 patients with clinically diagnosed AOPP were enrolled in our study. Based on the clinical outcomes the enrolled subjects were assigned into Survival group (N=50) and Non-survival group (N=9). The baseline characteristics of the 2 groups were listed in Table 1. Compared with Survival group, Lac, pH value, white blood cell (WBC), blood glucose levels, the treatment and dose of PAM, the treatment and dose of atropine, APACHE II score, PSS, and SOFA score were significantly higher in Non-survival group ( $P < .05$ ).

**Table 1**  
Basic clinical characteristics of 2 groups.

Parameters	Survivors (N=50)	Non-survivors (N=9)	P values
Age, y	56 (39–70)	57 (34–70)	.799
Men	28 (56.0%)	4 (44.4%)	.782
Amount, mL	200 (115–275)	100 (50–150)	.093
Ingestion time, h	2.0 (2.0–5.5)	2.0 (1.0–3.3)	.828
HR, bpm	93 (79–110)	115 (89–123)	.079
MV	15 (30%)	9 (100%)	<.0001
MAP, mmHg	91 (79–110)	86 (60–114)	.653
pH	7.38 (7.28–7.43)	7.16 (6.98–7.35)	.002
Lac, mmol/L	1.40 (0.93–2.18)	2.75 (0.85–7.3)	.023
WBC ( $\times 10^9/L$ )	14.19 (9.04–18.90)	22.37 (17.05–26.47)	.007
HCT (%)	44.3 (37.1–48.8)	41.1 (41.1–41.1)	.513
Creatinine, mg/dL	66.5 (52.3–81.5)	120.0 (98.0–140.0)	.084
Albumin, mg/dL	39.7 (36.7–43.8)	41.6 (30.6–47.8)	.553
Glucose, mg/dL	8.2 (5.8–10.2)	10.3 (6.2–17.9)	.004
CRP, mg/dL	49.0 (10.3–58.0)	5.0 (5.0–5.0)	.180
AChE, iu/L	622.0 (227.5–1591.0)	260.0 (110.5–674.0)	.139
PAM, g	5.0 (3.0–8.3)	18.0 (14.5–22.5)	<.0001
Atropine, mg	52.0 (30.0–92.5)	380.0 (330.0–436.5)	<.0001
GCS	15 (11–15)	6 (4–8)	<.0001
APACHE II score	10 (6–16)	24 (18–30)	<.0001
PSS	2 (1–3)	4 (3–4)	.0008
SOFA score	2 (1–5)	8 (6–11)	.0004

AChE=acetylcholinesterase, Amount=amount of organophosphate, APACHE II=acute physiology and chronic health evaluation II, CRP=C-reactive protein, GCS=Glasgow Coma Scale, HCT=hematocrit, HR=heart rate, Lac=lactate, MAP=mean arterial pressure, MV=usage of mechanical ventilation, PAM=pyraloxime methiodide, PSS=poisoning severity score, SOFA=sequential organ failure assessment, WBC=white blood cell count.



**Figure 1.** The ROC curves of 3 score systems in predicting mortality. ROC= receiver operating characteristic.

**3.2. Performance of APACHE II score, PSS, and SOFA score in prediction of mortality**

The ROC curves and the AUCs for 3 scoring systems in predicting mortality of AOPP patients were shown in Fig. 1. The AUCs of the APACHE II score, PSS, and SOFA score were 0.876 (95% CI 0.784–0.969), 0.811 (95% CI 0.671–0.951), and 0.837 (95% CI 0.726–0.947), respectively. However, there was no significant difference between each other ( $P > .05$ ). Based on the ROC curves, the cut-off values and the predictive power of the mortality according to 3 scoring systems as well as lactate were listed in Table 2.

**3.3. Performance of 3 scoring systems combining with Lac in prediction of mortality**

The ROC curves of 3 scoring systems combining with Lac were shown in Fig. 2. After combining with Lac, the AUCs of 3 scoring systems were all larger. The AUC of APACHE II score was from 0.876 to 0.922; The AUC of PSS was from 0.811 to 0.878; and importantly, the AUC of SOFA score was from 0.837 to 0.956. However, there was no significant difference between each other ( $P > .05$ ).

**3.4. Performance of SOFA and Lac in risk classification for AOPP patients**

According to the cut-off values, SOFA score levels were divided into low-risk group ( $<4.5$ ) and high-risk group ( $\geq 4.5$ ), whereas Lac levels were divided into low-risk group ( $<2.55$  mmol/L) and

high-risk group ( $\geq 2.55$  mmol/L). SOFA–Lac were divided into low-risk group (SOFA  $<4.5$  and Lac  $<2.55$  mmol/L) and high-risk group (SOFA  $\geq 4.5$  or Lac  $\geq 2.55$  mmol/L). According to the above classification standard, we calculated the mortality at different risk levels. As shown in Fig. 3, the mortality of high-risk group was significantly higher than low-risk group which was 0 ( $P < .05$ ).

**3.5. Distribution of risk levels of SOFA and Lac in AOPP patients with different prognosis**

According to the above classification standard, the proportion of high risk patients was much higher in the Non-survival group than in Survival group. According to the SOFA–Lac classification standard, the patients of the Non-survival group were all at high risk. (As shown in Fig. 4).

**4. Discussion**

AOPP is an important medical care issue facing developing countries. Up to 200,000 people die from the disease worldwide a year, which accounted for 49.1% of all kinds of domestic emergency poisoning.<sup>[6]</sup> Therefore, we should assess the critical degree of AOPP patients as soon as possible. It will be beneficial for emergency physicians to improve the effect of treatment.

**4.1. The relationship between the severity of AOPP and clinical features**

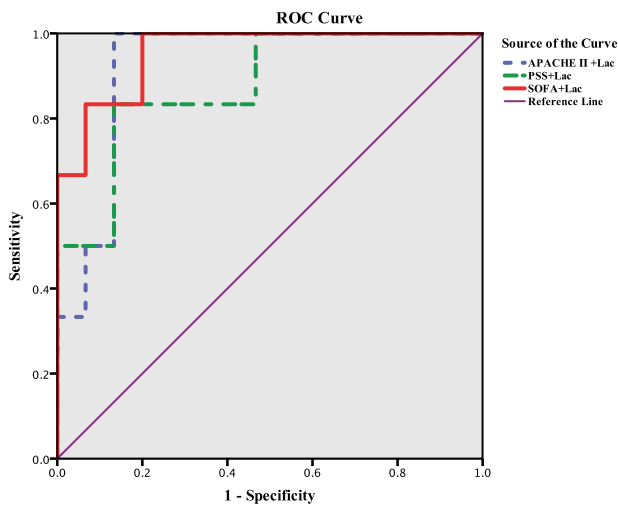
**4.1.1. The relationship between the severity of AOPP and AChE.** OP inhibits AChE, thereby eliciting cholinergic signs and symptoms. In the current study, there were 2 kinds of different conclusions about AChE. Some studies suggest that AChE could reflect the severity of the AOPP patients. However, some research demonstrated that AChE did not associate with the severity of disease.<sup>[8,9]</sup> In our studies, compared with Survival group, there was no significant difference about AChE in Non-survival group at the time of hospitalization. Although some patients had lower level of AChE (32, 90 iu/L), they did not die eventually. We considered the possible reasons were as follows: the lower of AChE, the more sufficient attention it aroused; the earlier respiratory failure detected, the faster mechanical ventilation given; or it related to different kinds of OP.<sup>[9]</sup> Therefore, it was not enough to assess the prognosis of AOPP patients simply relying on AChE at hospitalization.

**4.1.2. The relationship between the severity of AOPP and WBC.** In the AOPP patients, compared with Survival group, WBC increased significantly in Non-Survival group. Its pathological mechanism may be associated with the continued stress on the body. As a kind of strong stress, OP compounds could stimulate the body to produce a series of stress reaction, promoting the increase of WBC. The serious degree of poisoning and the complex pathological changes often caused infection and

**Table 2**  
The predictive value of the 3 scoring systems and the lactate.

	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR-
APACHE II	13.5	100	71	39	100	3.5	0.0
PSS	2.5	89	60	29	97	2.2	0.2
SOFA	4.5	89	68	33	97	2.8	0.2
Lac, mmol/L	2.6	67	93	79	88	10.0	0.4

APACHE II = acute physiology and chronic health evaluation II, Lac = lactate, LR+ = positive likelihood ratio, LR- = negative likelihood ratio, NPV = negative predictive value, PPV = positive predictive value, PSS = poisoning severity score, SOFA = sequential organ failure assessment.



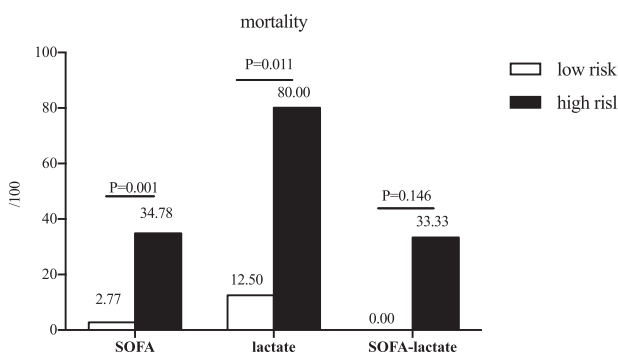
**Figure 2.** The ROC curves of 3 scoring systems combining with Lac in predicting mortality. ROC=receiver operating characteristic.

complications. They influenced each other and ultimately to significantly increase of the number of WBC. Therefore, assessing the WBC could estimate the stress state of AOPP patients and predict their severity.

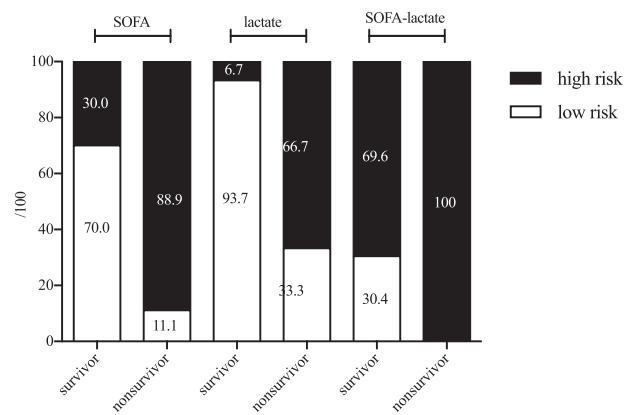
**4.2. The relationship between the severity of AOPP and 3 kinds of scoring systems**

**4.2.1. The relationship between the severity of AOPP and APACHE II score.** APACHE II score contains not only 12 routine physiological measurements but also previous health status (recent surgery, history of severe organ insufficiency, immunocompromised state), and baseline demographics such as age, to be a sensitive index for assessing severity and prognosis in critically ill patients.<sup>[10]</sup> Similar to previous studies, we observed that in Non-survival group with AOPP patients the APACHE II score was significantly higher than survival group. The AUC of APACHE II score was 0.876 and the diagnosis point of death prediction was 13.5, which were similar to the literature.<sup>[4]</sup> The sensitivity, specificity of APACHE II score was higher than other scoring system, whereas because of its complication, it may not be the best choice for ED.

**4.2.2. The relationship between the severity of AOPP and PSS.** PSS was put forward by EAPCCT in 1990 and finalized in 1994.<sup>[11]</sup> The scoring tool made standards of grading for the signs and symptoms of each system. Based on the most severe clinical



**Figure 3.** The mortality of different risk groups.



**Figure 4.** Distribution of risk levels of SOFA and Lac in AOPP patients with different prognosis. AOPP=acute organophosphate pesticide poisoning, SOFA=sequential organ failure assessment.

features, PSS grades severity as (0) none, (1) minor, (2) moderate, (3) severe, and (4) fatal poisoning. Because PSS did not take into account the types and quantities of poisons, it was suitable for all kinds of poisons. Because of its simplicity and intuition, PSS had been widely accepted and adopted. Previous studies showed that PSS could be used to evaluate the severity and prognosis of AOPP patients at hospitalization.<sup>[12]</sup> Our research showed that PSS was significantly higher in Non-survival group than Survival group in AOPP patients. Its diagnosis point of death prediction was 2.5 whereas the predictive ability of death was lower than the APACHE II score or SOFA score.

**4.2.3. The relationship between the severity of AOPP and SOFA score.**

SOFA score was used to assess the extent of organ function which was induced by sepsis originally. In recent years, some research had used it to evaluate the prognosis of patients with acute poisoning.<sup>[13,14]</sup> Most of AOPP patients had different degrees of multiple organ damage which fit into SOFA score. In our study, we found that SOFA score was significantly higher in Non-survival group than Survival group in AOPP patients. Although the AUC of SOFA score in predicting mortality was slightly lower than the APACHE II score, there was no significant difference. Importantly, for its simplicity and objectivity, SOFA score could save more time for physicians to evaluate the condition and to take effective treatment.

**4.3. The severity evaluation of Lac combined with 3 kinds of scoring tools in AOPP patients**

Lac has been used to assess the perfusion status and elevated Lac was shown to be independently associated with mortality in critically ill patients. In our study, we found that Lac was significantly higher in Non-survival group than Survival group in AOPP patients. This may be associated with AChE inhibition by OP, resulting in the accumulation of acetylcholine, the spasm of tracheal smooth muscle, the increase of airway secretions, pulmonary edema, and even respiratory failure. From our study, we found that Lac significantly improved the predictive abilities of the three scoring systems, especially for the SOFA score.

**4.4. Combination of SOFA and Lac has a better predictive ability**

In our study, the AUC of SOFA-Lac in predicting mortality was larger than SOFA alone. In attempt to use it in clinical work more

conveniently, we created SOFA–Lac classification standards. We found that high-risk group had a significantly higher mortality than low risk group, and the mortality of low-risk group was 0. Meanwhile, all the patients of Non-survivors belonged to high risk group. All in all, this risk classification standard effectively distinguished the high-risk group from the low-risk group.

#### 4.5. Limitations of the study

Our study has some limitations. First, this was a single-center study. As a large tertiary teaching hospital, we received numerous severe AOPP patients transferred from smaller hospitals and had the high mortality in our study, which may limit the generalizability to some extent. Multi-center studies may decrease this influence. Second, since the study was retrospective, all data could not be retrieved. The identification of OP compound ingested by patients was based on the container brought by patients' relatives. The amount and ingestion time of OP was mainly based on the description of their relatives, and only a small part based on blood or urine assays. Prospective studies may decrease this influence. Third, our study was a small sample size. The cutoff value of APACHE II was 13.5, with a sensitivity of 100% and a negative predictive value of 0, which may be related to the small size. In the future, a larger sample size is needed to validate the SOFA–Lac system is significantly better at predicting mortality in AOPP patients.

#### 5. Conclusion

The APACHE II score, PSS, SOFA score could all predict the prognosis of patients with AOPP. For its simplicity and objectivity, the SOFA score was a superior predictor of mortality. Lac significantly improved the predictive abilities of the 3 scoring systems, especially for the SOFA score. The SOFA–Lac system effectively distinguished the high-risk group from the low-risk group, and therefore it was significantly better at predicting mortality in AOPP patients.

#### Author contributions

**Conceptualization:** Xue Mei.

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**Resources:** Junshuai Song.

**Supervision:** Xue Mei.

**Writing – original draft:** Shaoxin Yuan.

**Writing – review and editing:** Yusong Gao, Wenqing Ji.

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