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Original Article

Plasma D-D and CRP as predictive indicators for mortality in elderly patients with severe pneumonia

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Abstract: Objective: To evaluate the predictive value of plasma D-D (D-dimer) and CRP (C-reactive protein) levels for mortality risk among elderly patients with severe pneumonia. Methods: Clinical data of 119 patients treated between February 2022 and February 2024 were collected and retrospectively analyzed. Based on survival outcomes, the patients were categorized into a survival group (72 patients) and a death group (47 patients). The D-D and CRP levels were compared between the two groups, and their potential as prognostic markers for mortality risk in elderly patients with severe pneumonia were also assessed. Results: The levels of D-D and CRP in the death group were significantly higher than those in the survival group (all $P<0.05$). D-D had an AUC (area under the curve) of 0.601, with a specificity of 63.83% and a sensitivity of 55.56%. CRP had an AUC of 0.624, with a specificity of 48.94% and a sensitivity of 72.22%. Both biomarkers showed good predictive value. Multivariate Cox regression analysis further confirmed that elevated D-D and CRP levels were independent prognostic factors influencing patient prognosis ($P<0.05$). Conclusions: Elevated levels of D-D and CRP are associated with poorer prognosis and increased mortality risk in elderly patients with severe pneumonia. These findings highlight the potential of these two biomarkers as valuable biomarkers for guiding clinical decision-making and management strategies in this patient population.

Keywords: CRP, D-D, pneumonia, predictive biomarkers

Introduction

Severe pneumonia is a major cause of morbidity and mortality, particularly in the elderly population, who are more vulnerable due to weakened immune systems and the prevalence of comorbidities [1-3]. Despite advancements in medical treatments, the mortality rate in elderly patients remains alarmingly high, necessitating early and reliable predictive indicators for mortality [4]. Among the biomarkers of clinical interest, plasma D-Dimer (D-D) and C-reactive protein (CRP) have gained attention as potential prognostic indicators [5, 6]. This study aimed to evaluate the predictive value of plasma D-D and CRP levels in assessing mortality risk in elderly patients with severe pneumonia.

D-D is a fibrin degradation product, and its level reflects the activity of coagulation and fibrinolytic systems [7, 8]. In patients with severe pneumonia, the processes of inflammation and thrombosis are often disordered, resulting in elevated D-D levels [9]. Some studies have revealed that higher D-D levels are associated with more severe inflammation and thrombosis, thereby increasing the risk of mortality [10]. Thus, plasma D-D can be used as a valuable predictive indicator for prognostic assessment in elderly patients with severe pneumonia.

CRP, a widely recognized marker of acute inflammation, exhibits elevated levels during infection and inflammation [11]. In elderly patients with severe pneumonia, significant inflammatory responses are common, making CRP a clinically important indicator [12]. Research suggests a strong correlation between plasma CRP levels and disease severity as well as patient prognosis in cases of severe pneumonia [13]. Elevated CRP levels often indicate a more severe inflammatory response and systemic injury, contributing to a higher risk of mortality [14]. Accordingly, plasma CRP serves as

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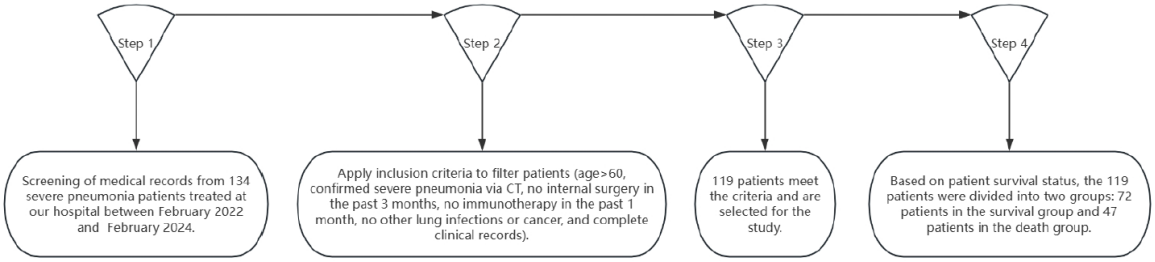

Figure 1. Flow chart of case selection.

another potential predictor of prognosis in elderly patients with severe pneumonia.

While numerous studies have explored the role of D-Dimer and CRP as prognostic markers in conditions such as sepsis and cardiovascular diseases, there is a notable gap in understanding their combined predictive value in elderly patients with severe pneumonia. Existing research largely focuses on younger populations, or evaluates these biomarkers individually, neglecting their potential synergy in predicting outcomes. Furthermore, existing studies often overlook the specific challenges and unique characteristics of elderly patients, such as the influence of comorbidities and age-related physiological changes on biomarker interactions and disease progression.

The primary aim of this research is to evaluate the predictive value of plasma D-D and CRP levels for mortality in elderly patients with severe pneumonia. By examining the correlation between these biomarkers and patient outcomes, this study seeks to determine whether they can serve as reliable early indicators of mortality risk. Hence, the present study aimed to enhance understanding of the predictive capability of D-D and CRP, providing insights to guide treatment and management strategies for this vulnerable population. If proven effective, their integration into clinical practice could improve risk stratification, enable more personalized treatment plans, and ultimately, lead to better patient outcomes.

Materials and methods

Research design

Sample screening: Ethical approval for this retrospective study was obtained from the Ethics Committee at Affiliated Zhejiang Hospital. A total of 134 patients diagnosed with severe pneumonia and treated at Affiliated Zhejiang Hospital between February 2022 and February 2024 were included in this study.

The diagnostic criteria for severe pneumonia, as defined in the study, are as follows [15]:

Major criteria: 1. Requirement for invasive mechanical ventilation. 2. Septic shock necessitating the use of vasopressors.

Minor criteria (at least meeting the 3 of the following): 1. Respiratory rate ≥30 breaths/min. 2. PaO_2/FiO_2 ratio ≤250. 3. Multilobar infiltrates (involving more than one lung lobe). 4. Confusion or disorientation. 5. Uremia (blood urea nitrogen level ≥20 mg/dL). 6. Leukopenia (white blood cell count <4,000 cells/μL) due to infection. 7. Thrombocytopenia (platelet count <100,000/μL). 8. Hypothermia (core temperature <36°C). 9. Hypotension necessitating aggressive fluid resuscitation.

Inclusion and exclusion criteria: Inclusion criteria: Age over 60 years; Diagnosis of severe pneumonia, confirmed by CT examination; No history of immunotherapy within the past month; No concurrent lung infectious diseases. Exclusion criteria: History of internal surgery within the past 3 months; Presence of other malignant tumors; Incomplete or missing clinical data.

Finally, 119 patients met the criteria and were selected for the study (**Figure 1**). The patients were categorized into two groups based on survival outcomes: a survival Group (n=72) and a death Group (n=47).

Data collection: Clinical case data were collected, including APACHE II (acute physiology and chronic health evaluation scoring system), age, sex, respiratory rate, smoking history, number

Table 1. Basic information of included patients

Parameters	n=119
APACHE II	20.87±6.63
Sex (male/female)	86/33 (72.27/27.73)
Age	84.99±9.59
Respiratory rate (times/min)	18.75±4.44
Hypertension	49 (41.18)
Diabetes	32 (26.89)
Smoking history	26 (21.85)
Coronary heart disease	48 (40.34)
D-D (mg/L)	2.30±2.90
CRP (mg/L)	82.86±60.96
Number of affected organs ≥3	106 (89.08)

Note: APACHE II, acute physiology and chronic health evaluation scoring system; D-D, D-dimer; CRP, C-reactive protein.

of affected organs, and other comorbidities. Plasma D-D and CRP levels for each patient were also collected.

Outcome measures

Clinical case data and plasma D-D and CRP levels were compared between the two groups. The potential of plasma D-D and CRP levels as predictive indicators for mortality was evaluated in elderly patients with severe pneumonia. The factors influencing the prognosis of elderly patients with severe pneumonia were analyzed.

Statistical analysis

Data processing and visualization were conducted using GraphPad Prism 8 and SPSS 20.0 statistical software. The categorical data were expressed as numbers and percentage (%) and compared using Chi-square test (χ^2). The quantitative data were described as means ± standard deviations and compared between the two groups using independent sample t-tests. ROC (receiver operating characteristic) analysis was utilized to evaluate the performance of plasma D-D and CRP as predictive indicators for mortality. Cox regression analysis was used to identify significant risk factors for patient prognosis. P<0.05 indicated statistical significance.

Results

Basic information of patients

Clinical data including APACHE II, sex, age, respiratory rate, hypertension, diabetes, smoking history, coronary heart disease, D-D levels, CRP levels, and the number of affected organs were collected and summarized, as shown in **Table 1**.

Comparison of clinical data between the survival group and death group

The two groups showed no significant differences in terms of sex, age, respiratory rate, hypertension, diabetes, smoking history, and coronary heart disease (all P>0.05). In contrast, significant differences were observed between the two groups in the proportion of patients with three or more affected organs (both P<0.05) (**Table 2**).

Comparison of D-D and CRP levels between the survival group and death group

As shown in **Figure 2**, plasma D-D and CRP levels were compared between the two groups. The results showed that both D-D and CRP levels were significantly higher in the death group compared to the survival group (both P<0.05).

Predictive value of D-D and CRP for patient prognosis

To evaluate the predictive value of D-D and CRP for mortality in elderly patients with severe pneumonia, ROC curves were plotted for the patients (**Figures 3**, **4**). CRP demonstrated an area under the ROC curve (AUC) of 0.624, with a specificity of 48.94%, sensitivity of 72.22%, and a cut-off value of 101.870 mg/L. D-D also showed good predictive value, with an AUC of 0.601, specificity of 63.83%, sensitivity of 55.56%, and a cut-off value of 1.110 μg/mL. Moreover, the combined detection of D-D and CRP showed the best predictive performance, with an AUC of 0.632 (**Table 3**).

Analysis of factors affecting the prognosis in elderly patients with severe pneumonia

To facilitate subsequent Cox regression analysis, we organized the population distribution of various parameters between the two groups, as detailed in **Table 4**. Univariate Cox regression analysis identified D-D and CRP levels as significant factors affecting the prognosis of

Table 2. Comparison of clinical data between the survival group and death group

Parameters	Survival group (n=72)		Death group (n=47)		χ^2/t	P
	Number of cases	Percentage	Number of cases	Percentage		
APACHE II	19.68±5.01		22.70±8.27		2.481	0.015
Sex (male/female)	51/21	70.83/29.17	35/12	74.47/25.53	0.188	0.665
Age	84.96±9.85		85.04±9.29		0.047	0.963
Respiratory rate (times/min)	18.45±3.86		19.19±5.22		0.886	0.378
Hypertension	29	40.28	20	42.55	0.061	0.805
Diabetes	18	25.00	14	29.79	0.332	0.565
Smoking history	15	20.83	11	23.40	0.110	0.740
Coronary heart disease	29	40.28	19	40.43	<0.001	0.987
Number of affected organs ≥3	59	81.94	47	100.00	9.527	0.002

Note: APACHE II, acute physiology and chronic health evaluation scoring system.

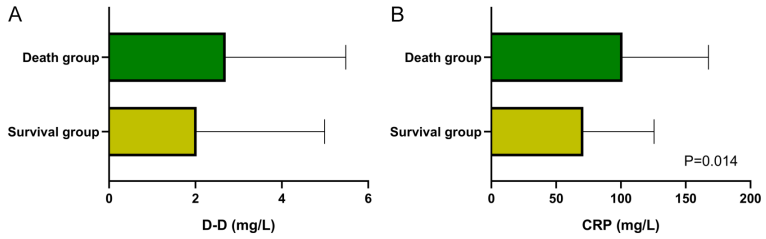

Figure 2. Comparison of D-D (A) and CRP (B) levels between the survival group and death group. Note: D-D, D-dimer; CRP, C-reactive protein.

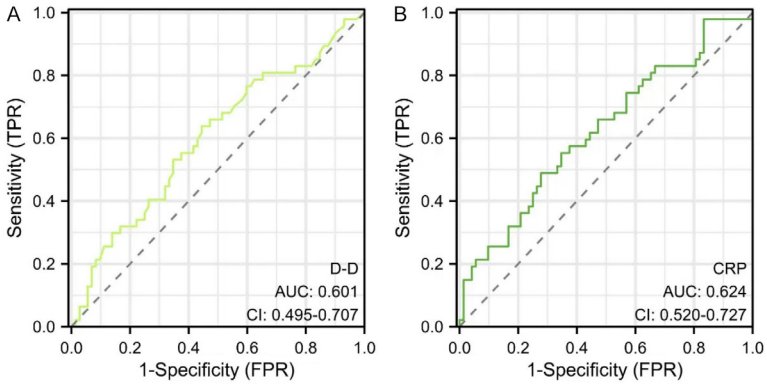

Figure 3. ROC curves for D-D (A) and CRP (B) in predicting mortality in elderly patients with severe pneumonia. Note: D-D, D-dimer; ROC, receiver operating characteristic; CRP, C-reactive protein.

patients (P<0.05), as shown in **Table 5**. Subsequently, multivariate Cox regression further confirmed that D-D and CRP were independent prognostic factors affecting the prognosis of patients (P<0.05), as shown in **Table 6**.

Comparison of oxygenation index between the survival group and death group

The oxygenation index of patients at the time of admission and on the 7th day after admission was recorded. See **Table 7** for details. Compared to admission, the oxygenation index of patients in the survival group significantly increased on the 7th day after admission, while it significantly decreased in the death group (P<0.05).

Discussion

The clinical manifestations of severe pneumonia in elderly patients include symptoms such as dyspnea, high fever, and cough, which can progress to respiratory failure and multiple organ dysfunction in severe cases [16-22]. High D-D levels may be associated with vascular endothelial injury and increased inflammatory response, leading to thrombosis and microcirculation disturbance [23-26]. Therefore, high D-D levels may reflect a more severe disease state and poor prognosis. Similarly, high CRP levels may reflect severe inflammatory response and tissue damage [27-29]. The degree of inflammatory response is closely related to the severity of the disease and prognosis. Therefore, a high CRP level may indicate a poorer prognosis and adverse survival outcomes.

Our findings revealed that plasma D-D and CRP levels were significantly higher in the death group compared to the survival group, under-

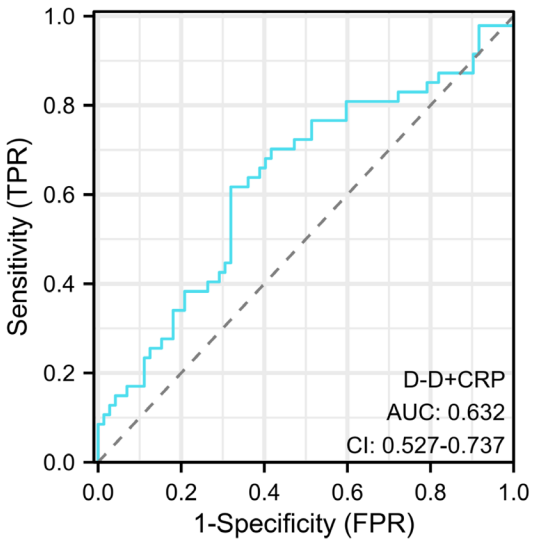

Figure 4. ROC curve for D-D combined with CRP in predicting mortality in elderly patients with severe pneumonia. Note: D-D, D-dimer; ROC, receiver operating characteristic; CRP, C-reactive protein.

scoring their association with poor prognosis and increased mortality in severe pneumonia cases. In addition, ROC analysis further verified the predictive value of plasma D-D and CRP for mortality in elderly patients with severe pneumonia. The AUC of D-D and CRP were 0.601 and 0.624, respectively, indicating their accuracy in predicting the prognosis of patients with severe pneumonia. With specificities of 55.56% and 72.22%, and sensitivities of 63.83% and 48.94% respectively, this indicates that D-D and CRP are accurate and reliable in identifying patients with a poor prognosis. In summary, D-D and CRP have good predictive value in patients with severe pneumonia and can serve as reference indicators for evaluating prognosis and guiding treatment decisions.

A study by Liu et al. [30] investigated the predictive value of indicators such as CRP and D-D for the severity of community-acquired pneumonia in elderly patients with AUCs for CRP and D-D of 0.791 and 0.727, respectively. Their findings proved that CRP and D-D had certain predictive value in assessing the severity of pneumonia, aligning with our findings. Liu's study primarily focused on predicting the severity of community-acquired pneumonia in the elderly, while our research emphasized the prognosis prediction in patients with severe pneumonia. Our study revealed that D-D and CRP had accuracy and reliability in predicting prognosis of patients with severe pneumonia.

Similarly, the study by Ma et al. [31] demonstrated the value of combined indicator detection, such as CRP, for differentiating between viral and bacterial pneumonia infections. Their study revealed significantly elevated serum levels of PCT, CRP, and FIB in both viral and bacterial infections, with these markers serving as independent predictors of bacterial pneumonia. This highlights the diagnostic value of combining multiple indicators like CRP for the early differential diagnosis of pneumonia, providing insights into infection type and guiding appropriate treatment strategies.

Finally, we also analyzed the oxygenation index between the two groups. The oxygenation index showed a significant improvement in the survival group, indicating better pulmonary function and improved oxygenation status. The oxygenation index decreased significantly in the death group, suggesting impaired gas exchange and a worsening condition. These findings suggest that the observed changes in the oxygenation index highlight its potential role in predicting outcomes in patients with severe illness.

Although D-D and CRP have demonstrated good predictive value as indicators of mortality risk in elderly patients with severe pneumonia, several limitations exist in this study. First, this study was based on a relatively small sample size, so larger-scale studies are needed to verify the reliability and reproducibility of these results. Second, the study focused solely on D-D and CRP, without considering other potential predictors that could also influence prognosis. Therefore, future research should consider incorporating other relevant indicators into the analysis to further improve the accuracy and comprehensiveness of the predictive model.

Conclusions

Elevated levels of D-D and CRP are associated with poorer prognosis and worse survival outcomes in elderly patients with severe pneumonia. These findings underscore the potential of D-D and CRP as predictive indicators for assessing mortality risk in this patient population. These findings have important clinical

Table 3. Predictive value of D-D and CRP for mortality

	Area under the curve (AUC)	Confidence interval (CI)	Cut-off	Sensitivity	Specificity	Youden index
D-D	0.601	0.495-0.707	1.110	63.83%	55.56%	19.39%
CRP	0.624	0.520-0.727	101.870	48.94%	72.22%	21.16%
D-D+CRP	0.632	0.527-0.737	0.390	61.70%	68.06%	29.76%

Note: D-D, D-dimer; AUC, area under the curve; CRP, C-reactive protein.

Table 4. Distribution of population

Parameters	Survival group (n=72)		Death group (n=47)	
	Number of cases	Percentage	Number of cases	Percentage
Sex				
Male	51	70.83	35	74.47
Female	21	29.17	12	25.53
Hypertension				
Yes	29	40.28	20	42.55
No	43	59.72	27	57.45
Diabetes				
Yes	18	25.00	14	29.79
No	54	75.00	33	70.21
Smoking history				
Yes	15	20.83	11	23.40
No	57	79.17	36	76.60
Coronary heart disease				
Yes	29	40.28	19	40.43
No	43	59.72	28	59.57
Number of affected organs				
≥3	59	81.94	47	100.00
<3	13	18.06	0	0.00
D-D (mg/L)				
<1.110	38	52.78	16	34.04
≥1.110	34	47.22	31	65.96
CRP (mg/L)				
<115.99	56	77.78	29	61.70
≥115.99	16	22.22	18	38.30
APACHE II				
<21	40	55.56	21	44.68
≥21	32	44.44	26	55.32
Age				
<85	28	38.89	18	38.30
≥85	44	61.11	29	61.70
Respiratory rate (times/min)				
<19	49	68.06	31	65.96
≥19	23	31.94	16	34.04

Note: APACHE II, acute physiology and chronic health evaluation scoring system; D-D, D-dimer; CRP, C-reactive protein.

implications, offering valuable insights for guiding treatment and management decisions for elderly patients with severe pneumonia.

Disclosure of conflict of interest

None.

Table 5. Univariate Cox regression analysis

	B	SE	Wald	Sig.	Exp (B)	95.0% CI for Exp (B)
Sex	0.077	0.335	0.053	0.817	1.080	0.561-(-)
Hypertension	0.123	0.295	0.173	0.678	1.131	0.634-2.016
Diabetes	0.273	0.319	0.732	0.392	1.314	0.703-2.456
Smoking history	0.181	0.345	0.277	0.599	1.199	0.610-2.356
Coronary heart disease	0.049	0.297	0.028	0.868	1.051	0.587-1.881
Number of affected organs	3.231	1.852	3.045	0.081	25.309	0.672-953.619
D-D	0.646	0.308	4.39	0.036	1.908	1.043-3.491
CRP	0.614	0.300	4.182	0.041	1.849	1.026-3.331
APACHE II	0.291	0.293	0.985	0.321	1.338	0.753-2.378
Age	0.018	0.300	0.004	0.953	1.018	0.565-1.833
Respiratory rate	-0.096	0.308	0.097	0.755	0.909	0.497-1.661

Note: APACHE II, acute physiology and chronic health evaluation scoring system; D-D, D-dimer; CRP, C-reactive protein.

Table 6. Multivariate Cox regression analysis

	B	SE	Wald	Sig.	Exp (B)	95.0% CI for Exp (B)
D-D	0.713	0.310	5.281	0.022	2.040	1.111-3.748
CRP	0.692	0.303	5.233	0.022	1.998	1.104-3.616

Note: D-D, D-dimer; CRP, C-reactive protein.

Table 7. Oxygenation index

	At the time of admission	On the 7th day after admission	t	P
Survival group (n=72)	287.74±12.97	310.70±12.27	10.99	<0.001
Death group (n=47)	274.59±11.72	213.48±15.59	21.48	<0.001
t	5.626	38.060		
P	<0.001	<0.001		

Abbreviations

APACHE II, acute physiology and chronic health evaluation scoring system; D-D, D-dimer; AUC, area under the curve; ROC, receiver operating characteristic; CRP, C-reactive protein.

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