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Evaluation value of serum SP-D, CCL25 and pulmonary vascular resistance index on the degree of lung injury and prognosis of traumatic wet lung

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Abstract: Objective To explore the relationship between serum surfactant protein D (SP-D), C-C motif chemokine ligand 25 (CCL25) and pulmonary vascular resistance index (PVRI) with the degree of lung injury and prognosis in severe chest trauma patients complicated with traumatic wet lung (TWL), and to analyze their clinical evaluation values. **Methods** A total of 160 patients with severe chest trauma and TWL admitted to Hebei Medical University Third Hospital from January 2020 to February 2024 were enrolled. Based on the severity of lung injury, they were divided into mild-to-moderate group (n=68) and severe group (n=92). Three indexes (PVRI, serum SP-D, CCL25) and lung injury score (LIS) were compared between different lung injury degree groups,and the correlation of these three indexes with LIS scores and their impact on the prognosis of patients with TWL were analyzed. The predictive values of these three indicators on the degree of lung injury and prognosis of patients with TWL were evaluated. **Results** The mild-to-moderate group had significantly lower PVRI, serum SP-D, CCL25, and LIS scores compared to the severe group (P<0.01). Correlation analysis revealed positive associations between PVRI, SP-D, CCL25, and LIS (r=0.707, 0.776, 0.779, P<0.05). The combined assessment of PVRI,SP-D, and CCL25 for severe lung injury yielded an area under the receiver operating characteristic (ROC) curve (AUC) of 0.920 (95%*CI*: 0.866-0.957) ,with a sensitivity of 85.87% and specificity of 85.29%. Among the 160 patients,114 survived and 46 died with in 30 days. The survival group exhibited lower APACHE Ⅱ scores, PVRI, SP-D, and CCL25 levels than the non-survival group (P<0.05) . Logistic regression identified APACHE Ⅱ score,PVRI, SP-D, and CCL25 as independent risk factors for mortality (P<0.05). The combined assessment of PVRI, SP-D, and CCL25 for prognosis had an AUC of 0.939 (95%*CI*: 0.890-0.970), with a sensitivity of 91.30% and specificity of 84.21%. **Conclusion** PVRI, serum SP-D, and CCL25 are significantly associated with the severity of lung injury in severe chest trauma complicated with TWL and hold high predictive values for both lung injury severity and prognosis.

Keywords: Severe chest trauma; Traumatic wet lung; Lung injury; Surfactant protein D; C-C motif chemokine ligand 25; Pulmonary vascular resistance index

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Traumatic wet lung (TWL) is a common complication of chest trauma. In patients with severe chest trauma, intrapulmonary fluid and secretions increase and accumulate in the bronchi and alveoli, leading to symptoms such as chest pain, cough, and progressive dyspnea. It can easily progress to acute respiratory distress syndrome and further cause secondary hemorrhagic shock and major organ damage [1-2]. TWL progresses rapidly. In the past, clinical diagnosis of TWL mainly relied on CT or X-ray examinations, but the imaging results were not completely consistent with the clinical severity [3-4]. C-C motif chemokine ligand 25 (CCL25) is a chemokine that has a chemotactic effect on thymocytes and dendritic cells. It can activate Toll-like receptor 4 on the surface of lung epithelial cells, disrupt the balance and homeostasis of the immune system, and promote the development of acute lung injury in intensive care patients [5-6]. Surfactant protein D (SP-D) is mainly secreted by type II alveolar epithelial cells and can participate in regulating immune-inflammatory responses and maintaining upper airway defense functions [7]. However, there are few studies at home and abroad on SP-D in evaluating the degree of lung injury. Clinical studies have shown that pulmonary vascular resistance index (PVRI) can reflect pulmonary vascular dysfunction, and the increase of PVRI is related to the prognosis of patients with acute lung injury[8]. At present, there is a lack of clinical studies on PVRI and serological indicators in evaluating the prognosis of severe chest trauma complicated with TWL. This study intends to explore the relationship between serum SP-D, CCL25, PVRI and the degree of lung injury and prognosis in severe chest trauma complicated with TWL, and analyze their clinical evaluation value.

1 Materials and methods

1.1 General information

A total of 160 patients with severe chest trauma complicated by TWL admitted to the Hebei Medical

University The Third Hospital from January 2020 to February 2024 were selected for this study. The study was approved by the hospital Ethics Committee (Approval No.: W2023-016-1), and signed informed consent was obtained from patients and their families. Among the 160 patients, 89 were male and 71 were female; aged 36–71 years, with an average of (53.83±8.36) years. Body mass index (BMI) were ranged from 21 to 27 kg/m², with an average of (24.27±1.21) kg/m². Causes of chest trauma: 100 cases of traffic injuries, 33 cases of blunt instrument injuries, and 27 cases of fall from height injuries. Injury sites: 120 cases of unilateral injury and 40 cases of bilateral injury.

Inclusion criteria: Severe chest trauma with admission within 6 hours after injury; meeting the diagnostic criteria for TWL [9] and confirmed by X-ray, CT, or other examinations; no coagulation dysfunction; no history of immuno suppressant use recently. **Exclusion criteria:** Pre-existing pulmonary infection or organic lesions before injury; TWL caused by other reasons; complicated with malignant tumors; accompanied by multiple injuries such as thoracoabdominal combined injury, abdominal trauma, and limb fractures; pregnant women; mental disorders.

1.2 Detection of serum SP-D and CCL25

All subjects were collected 3 mL of peripheral venous blood after admission. The serum was separated by centrifugation, and the levels of serum SP-D and CCL25 were determined by enzyme-linked immunosorbent assay.

1.3 PVRI detection and calculation

All subjects underwent pulmonary vascular hemodynamic management within 2 hours after admission, for 7 consecutive days or until 12 hours after the patient no longer required assisted ventilation. Cardiac index, mean pulmonary arterial pressure, and pulmonary artery wedge pressure were monitored. PVRI was calculated as (mean pulmonary arterial pressure-pulmonary artery wedge pressure) / cardiac index [10].

1.4 Assessment of lung injury severity

The lung injury score (LIS) system [11] was used to evaluate the severity of lung injury. The worst parameters within 24 hours on the evaluation day were taken as the scoring variables. The LIS score was calculated as (chest X-ray score + hypoxemia score + positive end-expiratory pressure score + lung compliance score)/4. According to the scores, patients with LIS score > 0.1 and < 2.5 were classified as mild-to-moderate lung injury, and those with LIS score ≥ 2.5 as severe lung injury. The 160 patients were divided into mild-to-moderate group (68 cases) and severe group (92 cases).

1.5 Follow-up and prognosis evaluation

All patients were followed up during hospitalization, with the primary endpoint of all-cause mortality. Based on prognosis of the patients, patients were divided into two groups: Survivor group: Patients met the criteria for stable condition (no need for mechanical ventilation and stable vital signs for ≥72 hours) or were discharged smoothly; Non-survivor group: Patients died of TWL-related complications during hospitalization. For patients who were discharged against medical advice or transferred, their 30-day survival status was confirmed by telephone follow-up.

1.6 Observation indicators

Comparison of PVRI, serum SP-D, CCL25, and LIS scores among different degrees of lung injury; analysis of the correlation between PVRI, serum SP-D, CCL25 and LIS scores; evaluation of the value of PVRI, serum SP-D, and CCL25 in assessing lung injury severity; comparison of clinical data [including cause of chest trauma, injury site, Acute Physiology and Chronic Health Evaluation II (APACHEII) score, PVRI, serum SP-D, CCL25, etc.] between patients with different prognoses; analysis of factors influencing prognosis in patients with severe chest trauma complicated by TWL; and evaluation of the prognostic value of PVRI, serum SP-D, and CCL25 in these patients.

1.7 Statistical methods

Data were analyzed using SPSS 27.0. Measurement data were tested for normality (Shapiro-Wilk test) and homogeneity of variance (Levene's test). Normally distributed data with homogeneous variance were expressed as $\bar{x}\pm s$, and differences were compared using the t-test. Count data were expressed as case (%), and differences were analyzed using the χ^2 test. Pearson correlation coefficient was used for correlation analysis. Multivariate logistic regression analysis was performed to identify factors influencing prognosis. Receiver operating characteristic (ROC) curves were used to evaluate the value of PVRI, serum SP-D, and CCL25 in assessing lung injury severity and prognosis. The significance level was set at α=0.05.

2 Results

2.1 Comparison of PVRI, serum SP-D, CCL25 and LIS scores among different lung injury severity groups with TWL

The PVRI, serum SP-D, CCL25 and LIS scores in the mild-to-moderate group were significantly lower than those in the severe group (P<0.05). **[Table 1]**

2.2 Correlation analysis between PVRI, serum SP-D, CCL25 and LIS score

Pearson correlation coefficient analysis showed that PVRI, serum SP-D, and CCL25 were all positively correlated with LIS score (r=0.707, 0.776, 0.779; P<0.05).

2.3 Evaluation value of PVRI, serum SP-D and CCL25 for assessing lung injury severity

Taking the lung injury severity of patients with severe thoracic trauma complicated with TWL as the state variable, patients in the severe group as positive samples, and patients in the mild-to-moderate group as negative samples, ROC curves were plotted with PVRI, serum SP-D, and CCL25 as test variables. The results showed that the AUC of combined assessment of PVRI, serum SP-D, and CCL25 for severe lung injury was 0.920 (95%*CI*: 0.866–0.957), with a sensitivity of 85.87% and specificity of 85.29% (P<0.05). **[Table 2 & Figure 1]**

2.4 Comparison of clinical data between patients with different prognoses

Among the 160 patients, 114 survived and 46 died, who were assigned to the survival group and death group, respectively. There were no statistically significant differences in gender, age, BMI, underlying diseases (diabetes, hyperlipidemia, hypertension, coronary heart disease), causes of chest trauma, or injured sites between the two groups (P > 0.05). The APACHE II score, PVRI, serum SP-D, and CCL25 in the survival group were lower than those in the death group (P < 0.05). **[Table 3]**

2.5 Influencing factors for prognosis of patients with severe chest trauma complicated with TWL

Taking the prognosis of patients with severe chest trauma complicated with TWL as the dependent variable (death=1, survival=0), and APACHE II score, PVRI, serum SP-D, and CCL25 as independent variables (all continuous variables, original values included), logistic regression analysis was performed. The results showed that APACHE II score, PVRI, serum SP-D, and CCL25 were independent influencing factors for death in patients with severe chest trauma complicated with TWL (P < 0.05). **[Table 4]**

2.6 Prognostic value of PVRI, serum SP-D, and CCL25 in patients with severe chest trauma complicated with TWL

Taking the prognosis of patients with severe chest trauma complicated with TWL as state variable, patients in the death group as positive samples, and patients in the survival group as negative samples, with PVRI, serum SP-D, and CCL25 as test variables, ROC curves were plotted. The results showed that the area under the curve (AUC) of the combined assessment of PVRI, serum SP-D, and CCL25 for patient prognosis was 0.939 (95%*CI*: 0.890–0.970), with a sensitivity of 91.30% and specificity of 84.21% (P< 0.05). **[Table 5 & Figure 2]**

Tab.1 Comparison of PVRI, serum SP-D, CCL25 and LIS scores at different levels of lung injury ($\bar{x}$±s)

Group	Number of cases	PVRI [(kPa·s)/L]	SP-D (μg/L)	CCL25 (ng/L)	LIS score (points)
Mild-to-moderate	68	27.18±3.57	123.05±27.56	197.66±54.71	2.11±0.15
Severe	92	30.25±3.63	164.57±42.74	236.28±61.49	3.16±0.23
***t* value**		5.325	7.004	4.113	32.825
***P* value**		<0.001	<0.001	<0.001	<0.001

Tab.2 Value of PVRI, serum SP-D, and CCL25 in assessing the degree of lung injury in patients

Index	AUC	95%CI	Optimal cut-off value	Sensitivity (%)	Specificity (%)	*P* value
PVRI	0.758	0.684–0.822	26.80 (kPa·s)/L	65.22	80.88	<0.001
SP-D	0.748	0.674–0.813	149.09 μg/L	60.87	83.82	<0.001
CCL25	0.775	0.702–0.837	176.33 ng/L	81.52	67.65	<0.001
Combination	0.920	0.866–0.957	-	85.87	85.29	<0.001

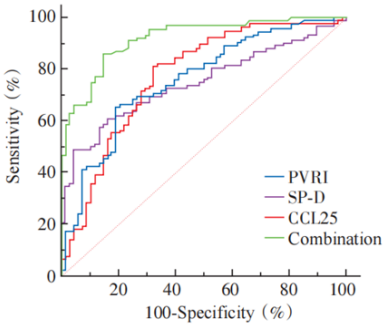

Fig.1 ROC curves of PVRI, serum SP-D, and CCL25 to assess the degree of lung injury in patients

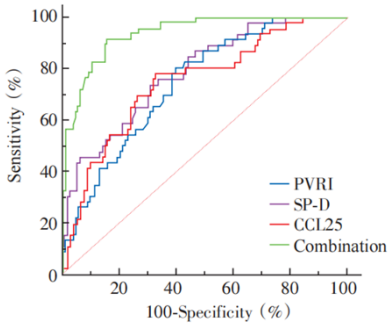

Fig.2 ROC curves of PVRI, serum SP-D, and CCL25 to assess patient prognosis

Tab.3 Comparison of clinical data between patients with different prognoses

Item	Survival group (*n*=114)	Death group (*n*=46)	χ^2/t value	*P* value
Gender [*n*(%)]				
Male	64 (56.14)	25 (54.35)	0.043	0.836
Female	50 (43.86)	21 (45.65)		
Age (years, $\bar{x}$±S)	53.64±8.11	54.30±7.89	0.469	0.639
BMI (kg/m², $\bar{x}$±S)	23.22±1.06	23.41±1.13	1.007	0.316
Diabetes [*n*(%)]	31 (27.19)	10 (21.74)	0.512	0.474
Hyperlipidemia [*n*(%)]	18 (15.79)	9 (19.57)	0.333	0.564
Hypertension [*n*(%)]	34 (29.82)	12 (26.09)	0.224	0.636
Coronary heart disease [*n*(%)]	13 (11.40)	7 (15.22)	0.436	0.509
Cause of chest trauma [*n*(%)]				
Traffic injury	73 (64.04)	27 (58.70)		
Blunt injury	22 (19.30)	11 (23.91)	0.498	0.780
Fall from height	19 (16.67)	8 (17.39)		
Injured site [*n*(%)]				
Unilateral	88 (77.19)	32 (69.57)	1.017	0.313
Bilateral	26 (22.81)	14 (30.43)		
APACHE II score (points, $\bar{x}$±S)	18.96±5.02	24.51±4.88	6.380	<0.001
PVRI [(kPa·s)/L, $\bar{x}$±S]	27.91±3.71	31.53±3.29	5.764	<0.001
SP-D (μg/L, $\bar{x}$±S)	134.60±30.57	177.46±41.15	7.234	<0.001
CCL25 (ng/L, $\bar{x}$±S)	206.85±55.23	252.14±61.18	4.550	<0.001
Smoking [*n*(%)]	23 (20.18)	11 (23.91)	0.274	0.601
Alcohol consumption [n(%)]	27 (23.68)	12 (26.09)	0.103	0.749

Tab.4 Analysis of factors influencing the prognosis of patients with severe thoracic trauma combined with TWL

Index	*β*	Wald χ^2	*S.E.*	*P* value	*OR*	95%CI	
						Lower bound	Higher bound
APACHE II score	0.098	9.912	0.031	<0.05	1.103	1.031	1.179
PVRI	0.095	11.521	0.028	<0.05	1.100	1.012	1.195
SP-D	0.101	8.837	0.034	<0.05	1.106	1.026	1.193
CCL25	0.059	9.604	0.019	<0.05	1.061	1.019	1.104

Tab.5 Prognostic value of PVRI, serum SP-D, and CCL25 in patients with severe chest trauma complicated with TWL

Index	AUC	95%*CI*	Cut-off value	Sensitivity (%)	Specificity (%)	*P* value
PVRI	0.745	0.670–0.811	29.11 (kPa·s)/L	80.43	60.53	<0.001
SP-D	0.787	0.716–0.848	152.94 μg/L	73.91	69.30	<0.001
CCL25	0.751	0.677–0.816	207.10 ng/L	78.26	67.54	<0.001
Combination	0.939	0.890–0.970	-	91.30	84.21	<0.001

3 Discussion

SP-D is a hydrophilic protein mainly secreted by type II alveolar epithelial cells. It exerts innate immune functions in lung injury and can serve as an inflammatory marker for acute lung injury [12]. Li *et al.* [13] reported that SP-D can be used as a biomarker for pulmonary fibrosis, while Agustama *et al.* [14] demonstrated a correlation between serum SP-D levels and the severity of acute respiratory distress syndrome. In this study, serum SP-D levels in the mild-to-moderate group were lower than those in the severe group, and SP-D was positively correlated with LIS scores. It was identified as an independent risk factor for mortality in patients with severe thoracic trauma complicated with TWL. ROC curve analysis further indicated that SP-D has a certain value in evaluating the degree of lung injury in such patients. These findings suggest that SP-D is involved in lung injury processes in patients with severe thoracic trauma complicated with TWL and may serve as a biological indicator for prognostic assessment. Locally expressed SP-D in the lungs promotes pathogen clearance by recognizing carbohydrate structures on viral and bacterial surfaces and regulates pulmonary inflammatory responses. However, in patients with severe thoracic trauma complicated with TWL, neutrophil infiltration in lung tissues increases the permeability of pulmonary microvascular endothelial barriers, leading to elevated SP-D concentrations in the peripheral circulation, which is associated with lung injury [15-16].

CCL25 is expressed in tissues such as intestinal epithelium and thymus, and its transcription and expression are upregulated by nuclear factor κB in macrophages [17]. Through the CCL25/C-C chemokine receptor 9 (CCR9) axis, CCL25 mediates leukocyte chemotaxis, regulates the migratory activity of CCR9-positive lymphocytes, and exacerbates immune-inflammatory tissue damage [18-19]. In this study, serum CCL25 levels were elevated in the severe group and positively correlated with LIS scores, suggesting that CCL25 may reflect the degree of lung injury. Mechanistically, CCL25 activates Toll-like receptor 4 on lung epithelial cells, triggering the nuclear factor κB pathway to upregulate pro-inflammatory factors such as interleukin-6 and tumor necrosis factor-α, thereby promoting lung tissue damage. This forms a positive feedback loop with the nuclear factor κB pathway, exacerbating lung injury in TWL patients [20-21]. Additionally, CCL25 promotes phosphorylation of P38 in alveolar macrophages, enhances neutrophil phagocytosis, and further aggravates lung injury in TWL patients [22]. Ruan et al. [23] previously identified CCL25 as an independent risk factor for secondary acute lung injury in sepsis patients. Consistent with this, our study found CCL25 to be an independent risk factor for mortality in patients with severe thoracic trauma complicated with TWL, indicating its utility in prognostic evaluation, likely through leukocyte chemotaxis and promotion of pulmonary inflammation.

PVRI is a quantitative index reflecting pulmonary artery intimal thickness and elasticity, which quantifies blood resistance in the pulmonary vascular system [24-25]. Jiang *et al.* [26] observed significantly elevated PVRI in children with severe idiopathic pulmonary hypertension experiencing syncope, while Cao *et al.* [27] reported that effective treatment reduces PVRI and improves cardiopulmonary function in patients with severe sepsis complicated by stress cardiomyopathy. In the present study, PVRI was higher in the severe group than in the mild-to-moderate group and positively correlated with LIS scores, indicating that higher PVRI is associated with more severe lung injury in patients with severe thoracic trauma complicated with TWL. Further analysis revealed significantly elevated PVRI in the death group, identifying it as an independent risk factor for mortality. This may be attributed to increased pulmonary vascular resistance and right heart pressure, which induce systemic circulatory dysfunction and insufficient tissue/organ perfusion, thereby worsening prognosis [28]. These results suggest that clinical management of severe thoracic trauma complicated with TWL should focus not only on respiratory mechanics but also on hemodynamic effects. ROC curve analysis demonstrated that PVRI, serum SP-D, and CCL25 individually have prognostic value, while their combination yielded an AUC of 0.939 (95%*CI*: 0.890–0.970) with higher sensitivity and specificity, indicating superior accuracy in prognostic assessment.

In conclusion, PVRI, serum SP-D, and CCL25 are significantly associated with the severity of lung injury in patients with severe thoracic trauma complicated with TWL. Their combined detection provides valuable insights for evaluating lung injury severity and prognosis, offering guidance for clinical diagnosis and treatment. Limitations of this study include the lack of exploration into the consistency between PVRI, serum SP-D, CCL25, and imaging modalities such as CT or X-ray, which warrants further investigation.

Conflict of interest None

Reference

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·论 著·

血清SP-D、CCL25及肺血管阻力指数对创伤性湿肺肺损伤程度及预后的评估价值

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摘要：目的 探讨血清表面活性蛋白D(SP-D)、C-C基序趋化因子配体25(CCL25)及肺血管阻力指数(PVRI)与严重胸外伤合并创伤性湿肺(TWL)患者肺损伤程度及预后的关系，并分析其临床评估价值。**方法** 选取2020年1月至2024年2月河北医科大学第三医院收治的160例严重胸外伤合并TWL患者，根据肺损伤程度分为轻中度组(n=68)、重度组(n=92)。比较不同肺损伤程度组患者PVRI、血清SP-D、CCL25三项指标以及肺损伤评分(LIS)，分析该三项指标与LIS评分的相关性及对TWL患者预后的影响；并分析该三项指标对TWL患者肺损伤程度、预后的评估价值。**结果** 轻中度组PVRI、血清SP-D、CCL25及LIS评分均低于重度组(P<0.01)；相关性分析显示，PVRI、血清SP-D、CCL25与LIS评分分别呈正相关(r=0.707、0.776、0.779，P<0.05)；PVRI、血清SP-D、CCL25联合评估患者重度肺损伤的受试者工作特征(ROC)曲线下面积(AUC)为0.920(95%*CI*：0.866～0.957)，敏感度为85.87%，特异度为85.29%。160例患者中30 d内存活114例，病亡46例；存活组APACHEⅡ评分、PVRI、血清SP-D、CCL25均低于病亡组(P<0.01)；Logistic回归性分析结果显示，APACHEⅡ评分、PVRI、血清SP-D、CCL25均为严重胸外伤合并TWL患者病亡的独立影响因素(P<0.05)；该三项指标联合评估患者预后的AUC为0.939(95%*CI*：0.890～0.970)，敏感度为91.30%，特异度为84.21%。**结论** PVRI、血清SP-D、CCL25与严重胸外伤合并TWL患者肺损伤程度显著相关，三者联合对患者肺损伤程度及预后具有较高的评估效能。

关键词： 严重胸外伤；创伤性湿肺；肺损伤；表面活性蛋白D；C-C基序趋化因子配体25；肺血管阻力指数
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Evaluation value of serum SP-D, CCL25 and pulmonary vascular resistance index on the degree of lung injury and prognosis in traumatic wet lung

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Abstract: Objective To explore the relationship between serum surfactant protein D(SP-D), C-C motif chemokine ligand 25(CCL25) and pulmonary vascular resistance index (PVRI) with the degree of lung injury and prognosis in severe chest trauma patients complicated with traumatic wet lung (TWL), and to analyze their clinical evaluation values. **Methods** A total of 160 patients with severe chest trauma and TWL admitted to Hebei Medical University Third Hospital from January 2020 to February 2024 were enrolled. Based on the severity of lung injury, they were divided into mild-to-moderate group(n=68) and severe group(n=92). Three indexes (PVRI, serum SP-D, CCL25) and lung injury score(LIS) were compared between different lung injury degree groups, and the correlation of these three indexes with LIS scores and their impact on the prognosis of patients with TWL were analyzed. The predictive values of these three indicators on the degree of lung injury and prognosis of patients with TWL were evaluated. **Results** The mild-to-moderate group had significantly lower PVRI, serum SP-D, CCL25, and LIS scores compared to the severe group (P<0.01). Correlation analysis revealed positive associations between PVRI, SP-D, CCL25, and LIS (r=0.707, 0.776,

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0.779, P<0.05). The combined assessment of PVRI, SP-D, and CCL25 for severe lung injury yielded an area under the receiver operating characteristic (ROC) curve (AUC) of 0.920 (95%CI: 0.866-0.957), with a sensitivity of 85.87% and a specificity of 85.29%. Among the 160 patients, 114 survived and 46 died within 30 days. The survival group exhibited lower APACHE Ⅱ scores, PVRI, SP-D, and CCL25 levels than the non-survival group (P<0.05). Logistic regression identified APACHE Ⅱ score, PVRI, SP-D, and CCL25 as independent risk factors for mortality (P<0.05). The combined assessment of PVRI, SP-D, and CCL25 for prognosis had an AUC of 0.939 (95%CI: 0.890-0.970), with a sensitivity of 91.30% and specificity of 84.21%. **Conclusion** PVRI, serum SP-D, and CCL25 are significantly associated with the severity of lung injury in severe chest trauma complicated with TWL and hold high predictive values for both lung injury severity and prognosis.

Keywords: Severe chest trauma; Traumatic wet lung; Lung injury; Surfactant protein D; C-C motif chemokine ligand 25; Pulmonary vascular resistance index

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创伤性湿肺(traumatic wet lung,TWL)是胸外伤常见合并症,严重胸外伤患者肺内液体、分泌物增多,积蓄在支气管、肺泡中,导致胸痛、咳嗽、进行性呼吸困难等症状,易进展为急性呼吸窘迫综合征(acute respiratory distress syndrome, ARDS),还可继发失血性休克、主要脏器损伤等[1-2]。TWL病情进展迅速,既往临床主要通过CT或X线检查诊断TWL病情改变,但其影像学结果与临床严重程度不完全相同[3-4]。C-C基序趋化因子配体25(CCL25)属趋化因子,对胸腺细胞、树突状细胞等具有趋化作用,能激活肺上皮细胞表面Toll样受体4,破坏免疫系统的平衡稳态,对重症监护患者急性肺损伤的发生有预测价值[5-6]。表面活性蛋白D(SP-D)主要由Ⅱ型肺泡上皮细胞分泌,可参与调节免疫炎症反应,维持上气道防御功能[7]。临床研究表明,肺血管阻力指数(PVRI)可反映肺血管功能障碍,PVRI提升与急性肺损伤患者预后相关[8]。本研究探讨血清SP-D、CCL25及PVRI与严重胸外伤合并TWL患者肺损伤程度及预后的关系,分析其临床评估价值。

1 资料与方法

1.1 一般资料 选取2020年1月至2024年2月河北医科大学第三医院收治的160例严重胸外伤合并TWL患者为研究对象,经医院伦理委员会批准(伦理受理号:W2023-016-1),征得患者和家属签字同意。160例患者中男89例,女71例;年龄36~71(53.83±8.36)岁;身体质量指数(BMI)21~27(24.27±1.21)kg/m^2;胸外伤原因:交通伤100例,钝器伤33例,高处坠落伤27例;受伤侧别:单侧120例,双侧40例。纳入标准:严重胸外伤,胸外伤6 h内入院;符合TWL诊断标准[9],并经X线、CT等检查确诊;无凝血功能障碍;近期无免疫抑制剂用药史。排除标准:受伤前已存在肺部感染或肺部器质性病变;其他原因所致TWL;合并恶性肿瘤;伴胸腹联合伤、腹部外伤、四肢骨折等多发伤;妊娠期女性;精神异常者。

1.2 血清SP-D、CCL25检测 受检者均于入院后采集3 mL外周静脉血,离心分离血清,采用酶联免疫吸附法测定血清SP-D、CCL25水平。

1.3 PVRI监测和计算 受检者均于入院后2 h内进行肺血管血流动力学管理,连续7 d或至患者无需辅助呼吸后12 h。监测心排血指数、肺动脉平均压、肺动脉楔压,计算PVRI=(肺动脉平均压-肺动脉楔压)/心排血指数[10]。

1.4 肺损伤程度判断 采用肺损伤评分(LIS)系统[11]判断肺损伤程度,均以评价当日24 h内最差参数为评分变量值,计算LIS评分=(胸部X线片评分+低氧血症评分+呼吸末正压评分+肺顺应性评分)/4。根据分值,0.1分<LIS评分<2.5分为轻中度肺损伤,LIS评分≥2.5分为重度肺损伤,将160例患者分为轻中度组(68例)、重度组(92例)。

1.5 随访与预后评估 患者住院期间均接受全程随访,主要观察终点为全因死亡。根据预后情况分为两组,存活组:患者达到病情稳定标准(无需机械通气且生命体征平稳≥72 h)或顺利出院;病亡组:患者住院期间因TWL相关并发症死亡。对自动出院或转院患者,通过电话随访确认其30 d生存状态。

1.6 观察指标 比较不同肺损伤程度组患者PVRI、血清SP-D、CCL25水平及LIS评分;分析PVRI、血清SP-D、CCL25与LIS评分的相关性;分析PVRI、血清SP-D、CCL25对患者肺损伤程度的评估价值;比较不同预后患者临床资料,包括胸外伤原因、受伤侧别、急性生理与慢性健康评分(APACHEⅡ)、PVRI、血清SP-D、CCL25等;分析严重胸外伤合并TWL患者预后的影响因素;分析PVRI、血清SP-D、CCL25对严重胸外伤合并TWL患者预后的评估价值。

1.7　统计学方法　采用SPSS 27.0对数据进行分析。计量资料使用Shapiro-Wilk正态检验和Levene方差齐性检验，确认呈方差齐性、近似服从正态分布，以$\bar{x}\pm s$表示，比较行t检验，方差不齐时行校正t检验；计数资料以例(%)表示，比较行χ^2检验；以Pearson相关法进行相关性分析；多因素logistic回归分析严重胸外伤合并TWL患者预后的影响因素；受试者工作特征曲线(ROC)分析PVRI、血清SP-D、CCL25对严重胸外伤合并TWL患者肺损伤程度、预后的评估价值。检验水准α=0.05。

2　结　果

2.1　不同肺损伤程度TWL患者PVRI、血清SP-D、CCL25及LIS评分比较　轻中度组PVRI、血清SP-D、CCL25及LIS评分均低于重度组($P<0.01$)。见表1。

2.2　PVRI、血清SP-D、CCL25与LIS评分的相关性分析　Pearson相关系数法分析显示，PVRI、血清SP-D、CCL25与LIS评分均呈正相关(r=0.707、0.776、0.779，$P<0.05$)。

2.3　PVRI、血清SP-D、CCL25对TWL患者肺损伤程度的评估价值　以严重胸外伤合并TWL患者肺损伤程度为状态变量，重度组患者为阳性样本，轻中度组患者为阴性样本，以PVRI、血清SP-D、CCL25为检验变量，绘制ROC曲线，结果显示PVRI、血清SP-D、CCL25联合评估患者重度肺损伤的ROC曲线下面积(AUC)为0.920(95% *CI*: 0.866～0.957)，敏感度为85.87%，特异度为85.29%。见表2、图1。

表1　不同肺损伤程度组PVRI、血清SP-D、CCL25及LIS评分比较　($\bar{x}\pm s$)

Tab.1　Comparison of PVRI, serum SP-D, CCL25 and LIS scores at different levels of lung injury groups　($\bar{x}\pm s$)

组别	例数	PVRI[(kPa·s)/L]	SP-D (μg/L)	CCL25 (ng/L)	LIS评分 (分)
轻中度组	68	27.18±3.57	123.05±27.56	197.66±54.71	2.11±0.15
重度组	92	30.25±3.63	164.57±42.74	236.28±61.49	3.16±0.23
t值		5.325	7.004	4.113	32.825
P值		<0.001	<0.001	<0.001	<0.001

表2　PVRI、血清SP-D、CCL25对TWL患者肺损伤程度的评估价值

Tab.2　Value of PVRI, serum SP-D, and CCL25 in assessing the degree of lung injury in TWL patients

指标	AUC	95%*CI*	最佳截断值	敏感度(%)	特异度(%)
PVRI	0.758	0.684～0.822	26.80 (kPa·s)/L	65.22	80.88
SP-D	0.748	0.674～0.813	149.09 μg/L	60.87	83.82
CCL25	0.775	0.702～0.837	176.33 ng/L	81.52	67.65
联合	0.920	0.866～0.957	–	85.87	85.29

2.4　不同预后患者临床资料比较　160例患者中存活114例，病亡46例，分别计入存活组、病亡组。两组性别、年龄、BMI、基础病(糖尿病、高脂血症、高血压、冠心病)、胸外伤原因、受伤侧别比较差异均无统计学意义($P>0.05$)，存活组APACHEⅡ评分、PVRI、血清SP-D、CCL25均低于病亡组($P<0.01$)。见表3。

2.5　严重胸外伤合并TWL患者预后的影响因素　以严重胸外伤合并TWL患者预后作为因变量(病亡=1，

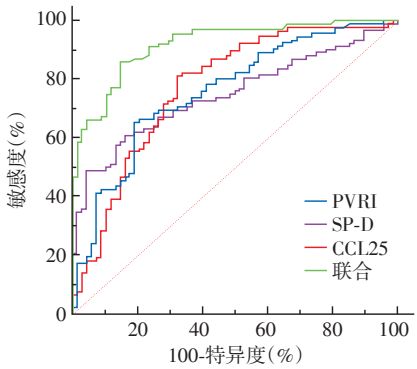

图1　PVRI、血清SP-D、CCL25评估TWL患者肺损伤程度的ROC曲线

Fig.1　ROC curves of PVRI, serum SP-D, and CCL25 in assessing the degree of lung injury in TWL patients

表3　不同预后患者临床资料比较

Tab.3　Comparison of clinical data of patients with different prognoses

项目	存活组(n=114)	病亡组(n=46)	χ^2/t值	P值
性别[例(%)]				
男	64(56.14)	25(54.35)	0.043	0.836
女	50(43.86)	21(45.65)		
年龄(岁，$\bar{x}\pm s$)	53.64±8.11	54.30±7.89	0.469	0.639
BMI(kg/m^2，$\bar{x}\pm s$)	23.22±1.06	23.41±1.13	1.007	0.316
糖尿病[例(%)]	31(27.19)	10(21.74)	0.512	0.474
高脂血症[例(%)]	18(15.79)	9(19.57)	0.333	0.564
高血压[例(%)]	34(29.82)	12(26.09)	0.224	0.636
冠心病[例(%)]	13(11.40)	7(15.22)	0.436	0.509
胸外伤原因[例(%)]				
交通伤	73(64.04)	27(58.70)		
钝器伤	22(19.30)	11(23.91)	0.498	0.780
高处坠落伤	19(16.67)	8(17.39)		
受伤侧别[例(%)]				
单侧	88(77.19)	32(69.57)	1.017	0.313
双侧	26(22.81)	14(30.43)		
APACHEⅡ评分(分，$\bar{x}\pm s$)	18.96±5.02	24.51±4.88	6.380	<0.001
PVRI[(kPa·s)/L，$\bar{x}\pm s$]	27.91±3.71	31.53±3.29	5.764	<0.001
SP-D(μg/L，$\bar{x}\pm s$)	134.60±30.57	177.46±41.15	6.389	<0.001
CCL25(ng/L，$\bar{x}\pm s$)	206.85±55.23	252.14±61.18	4.550	<0.001
吸烟[例(%)]	23(20.18)	11(23.91)	0.274	0.601
饮酒[例(%)]	27(23.68)	12(26.09)	0.103	0.749

存活=0），将 APACHEⅡ评分、PVRI、血清 SP-D、CCL25 作为自变量（均为连续变量，原值代入），进行 logistic 回归分析，结果显示 APACHEⅡ评分、PVRI、血清 SP-D、CCL25 均为严重胸外伤合并 TWL 患者病亡的独立影响因素（$P<0.05$）。见表 4。

2.6　PVRI、血清 SP-D、CCL25 对严重胸外伤合并 TWL 患者预后的评估价值　以严重胸外伤合并 TWL 患者预后为状态变量，病亡组患者为阳性样本，存活组患者为阴性样本，以 PVRI、血清 SP-D、CCL25 为检验变量，绘制 ROC 曲线，结果显示 PVRI、血清 SP-D、CCL25 联合评估患者预后的 AUC 为 0.939（95%*CI*：0.890～0.970），敏感度为 91.30%，特异度为 84.21%。见表 5、图 2。

表 4　严重胸外伤合并 TWL 患者预后的影响因素分析

Tab.4　Analysis of influencing factors of prognoses in patients with severe thoracic trauma combined with TWL

因素	β	Waldχ^2	*SE*	*P* 值	*OR* 值	95%*CI*	
						下限	上限
APACHEⅡ评分	0.098	9.912	0.031	<0.05	1.103	1.031	1.179
PVRI	0.095	11.521	0.028	<0.05	1.100	1.012	1.195
SP-D	0.101	8.837	0.034	<0.05	1.106	1.026	1.193
CCL25	0.059	9.604	0.019	<0.05	1.061	1.019	1.104

表 5　PVRI、血清 SP-D、CCL25 对严重胸外伤合并 TWL 患者预后的评估价值

Tab.5　Prognostic value of PVRI, serum SP-D, and CCL25 in the assessment of patients with severe thoracic trauma combined with TWL

指标	AUC	95%*CI*	截断值	敏感度（%）	特异度（%）
PVRI	0.745	0.670～0.811	29.11（kPa·s）/L	80.43	60.53
SP-D	0.787	0.716～0.848	152.94 μg/L	73.91	69.30
CCL25	0.751	0.677～0.816	207.10 ng/L	78.26	67.54
联合	0.939	0.890～0.970	–	91.30	84.21

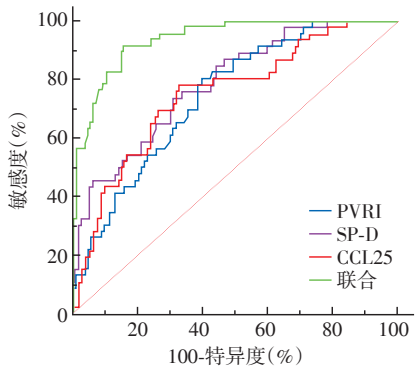

图 2　PVRI、血清 SP-D、CCL25 评估患者预后的 ROC 曲线

Fig.2　ROC curves of PVRI, serum SP-D, and CCL25 to assess prognosis of patient

3　讨　论

SP-D 是一种亲水性蛋白，主要由Ⅱ型肺泡上皮细胞分泌，在肺损伤中具有天然免疫功能，可作为急性肺损伤炎症标志物[12]。李智等[13]报道指出，SP-D 可作为肺纤维化的生物标志物；Agustama 等[14]研究显示，血清 SP-D 水平与 ARDS 严重程度有一定相关性。本研究结果显示，轻中度组血清 SP-D 低于重度组，与 LIS 评分均呈正相关，是严重胸外伤合并 TWL 患者病亡的独立影响因素，经 ROC 曲线分析，SP-D 对严重胸外伤合并 TWL 患者肺损伤程度有一定评估价值。提示 SP-D 参与严重胸外伤合并 TWL 患者肺损伤改变，可作为评估患者预后的生物指标。表达于肺局部的 SP-D 可通过识别病毒、细菌表面的糖类结构促进病原体清除，调节肺部炎性反应；而随着严重胸外伤合并 TWL 患者肺组织中性粒细胞浸润，增加了肺微血管内皮屏障的通透性，因此外周循环中 SP-D 浓度升高，与严重胸外伤合并 TWL 肺损伤情况有关[15-16]。

CCL25 表达于小肠上皮、胸腺等组织，受巨噬细胞中核因子κB 影响，其转录、表达增加[17]。CCL25 可通过 CCL25/CC 族趋化因子受体 9（CCR9）生物轴参与白细胞趋化，调节 CCR9 阳性淋巴细胞的趋化运动，加重组织免疫炎症性损伤[18-19]。本研究中，重度组患者血清 CCL25 水平升高，与 LIS 评分呈正相关，提示 CCL25 可一定程度反映患者肺损伤程度。CCL25 一方面能活化肺上皮细胞表面 Toll 样受体 4，激活核因子κB 通路，上调白介素-6、肿瘤坏死因子α等促炎因子水平，促进肺组织损伤，且与核因子κB 通路互相影响、相互促进，形成恶性循环，参与严重胸外伤合并 TWL 患者肺损伤进展[20-21]。另一方面，CCL25 可促进肺泡巨噬细胞中 P38 的磷酸化，增强中性粒细胞吞噬作用，加重 TWL 患者肺损伤程度[22]。阮本良等[23]研究表明，CCL25 是影响脓毒症患者继发急性肺损伤的独立危险因素。本研究观察到 CCL25 是严重胸外伤合并 TWL 患者病亡的独立影响因素，提示血清 CCL25 有利于评估患者预后，可能与上述白细胞趋化、促进肺组织炎症反应有关。

PVRI 是评定非动脉内膜厚度、弹性的量化指标，可反映肺血管系统中的血液阻力[24-25]。姜小坤等[26]研究显示，重度特发性肺动脉高压发生晕厥患儿的 PVRI 明显升高。曹莉等[27]研究表明，重症脓毒症合并应激性心肌病患者经有效治疗后 PVRI 明显降低，心肺功能改善。本研究结果显示，重度组 PVRI 高于轻中度组，与 LIS 评分呈正相关，可见随着 PVRI 升

高，严重胸外伤合并TWL患者肺损伤严重度升高。进一步分析显示，病亡组PVRI显著升高，为严重胸外伤合并TWL患者病亡的独立影响因素。其原因是PVRI升高表明肺血管阻力较大，右心压力较高，引发体循环障碍、组织器官灌注不足，影响患者预后[28]。提示对于严重胸外伤合并TWL患者临床不仅需关注呼吸力学，也应增加对血流动力学效应的关注。ROC曲线显示，PVRI、血清SP-D、CCL25均对严重胸外伤合并TWL预后有一定评估作用，联合检测的AUC为0.939（95%CI：0.890～0.970），敏感度、特异度更高，表明PVRI、血清SP-D、CCL25联合检测更利于准确评估严重胸外伤合并TWL患者的预后。

综上所述，PVRI、血清SP-D、CCL25与严重胸外伤合并TWL肺损伤程度显著相关，联合检测对患者肺损伤程度及预后具有评估价值，对临床诊断与治疗有一定指导意义。本研究仍存在一定局限性，未探讨PVRI、血清SP-D、CCL25与CT、X线等评估方式的一致性，有待后期进一步研究。

利益冲突 无

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