

## • 肺动脉高压专题研究 •

## 肝素酶与危重症相关肺动脉高压患者预后及病情严重程度的关系

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**【摘要】 目的** 探讨肝素酶与危重症相关肺动脉高压(CIR-PH)患者预后及病情严重程度的关系。**方法** 回顾性选取2021年4月—2022年6月兰州大学第一医院重症医学科收治的108例CIR-PH患者为研究对象,根据预后情况将其分为死亡组( $n=28$ )和生存组( $n=80$ )。比较两组一般资料〔包括年龄、性别、BMI、肺动脉高压(PH)临床分类、肝素酶、NT-proBNP及急性生理学和慢性健康状况评价系统II(APACHE II)评分〕、右心导管检查结果〔包括平均肺动脉压(mPAP)、肺毛细血管楔压(PCWP)、肺血管阻力(PVR)、平均右心房压(mRAP)和心排血量(CO)〕及超声心动图检查结果〔包括右心室直径(RVD)、右心房直径(RAD)、肺动脉宽度(PAW)、肺动脉流速(PAV)、肺动脉压(PAP)、三尖瓣反流速度(TRV)〕。CIR-PH患者预后的影响因素分析采用单因素、多因素Cox比例风险回归分析,采用ROC曲线分析肝素酶、NT-proBNP对CIR-PH患者死亡的预测价值,肝素酶与CIR-PH病情相关指标的(NT-proBNP、APACHE II评分、mPAP、PCWP、PVR、CO)相关性分析采用Pearson相关分析。**结果** 死亡组年龄、RVD、RAD大于生存组,肝素酶、NT-proBNP、APACHE II评分、mPAP、PCWP、PVR、mRAP、PAP高于生存组,CO低于生存组,TRV快于生存组( $P<0.05$ )。单因素Cox比例风险回归分析结果显示,年龄、肝素酶、NT-proBNP、APACHE II评分、mPAP、PCWP、PVR、mRAP、CO、RVD、RAD、PAP、TRV可能是CIR-PH患者死亡的影响因素( $P<0.05$ )。多因素Cox比例风险回归分析结果显示,肝素酶、NT-proBNP、mPAP、mRAP是CIR-PH患者死亡的独立影响因素( $P<0.05$ )。ROC曲线分析结果显示,肝素酶预测CIR-PH患者死亡的AUC为0.784〔95%CI(0.688~0.879)〕,最佳截断值为10.4  $\mu\text{g/L}$ ,灵敏度为0.500,特异度为0.875;NT-proBNP预测CIR-PH患者死亡的AUC为0.761〔95%CI(0.662~0.860)〕,最佳截断值为3 775 ng/L,灵敏度为0.357,特异度为0.950。Pearson相关分析结果显示,肝素酶与CIR-PH患者NT-proBNP( $r=0.639$ )、APACHE II评分( $r=0.763$ )、mPAP( $r=0.876$ )、PCWP( $r=0.858$ )、PVR( $r=0.846$ )呈正相关,与CO( $r=-0.702$ )呈负相关( $P<0.001$ )。**结论** 肝素酶是CIR-PH患者死亡的独立影响因素,其对CIR-PH患者死亡有一定预测价值,且其与CIR-PH患者病情严重程度密切相关。

**【关键词】** 肺动脉高压;危重症;肝素裂合酶;肝素酶;预后**【中图分类号】** R 541.5 **【文献标识码】** A DOI: 10.12114/j.issn.1008-5971.2024.00.067

## Relationship between Heparanase and Prognosis and Disease Severity in Patients with Critical Illness-Related Pulmonary Hypertension

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**【Abstract】 Objective** To investigate the relationship between heparanase and prognosis and disease severity in patients with critical illness-related pulmonary hypertension (CIR-PH). **Methods** A total of 108 patients with CIR-PH admitted to Department of Emergency Critical Care Medicine, the First Hospital of Lanzhou University from April 2021 to June 2022 were retrospectively selected as the research objects. According to the prognosis, they were divided into death group ( $n=28$ ) and survival group ( $n=80$ ). The general data [including age, gender, BMI, clinical classification of pulmonary hypertension (PH), heparanase, NT-proBNP and acute physiology and chronic health evaluation II (APACHE II) score], right heart catheterization results [including mean pulmonary artery pressure (mPAP), pulmonary capillary wedge pressure (PCWP), pulmonary vascular

resistance (PVR), mean right atrial pressure (mRAP), cardiac output (CO)] and echocardiography results [including right ventricular diameter (RVD), right atrial diameter (RAD), pulmonary artery width (PAW), pulmonary artery velocity (PAV), pulmonary artery pressure (PAP), tricuspid regurgitation velocity (TRV)] were compared between the two groups. Univariate and multivariate Cox proportional hazard regression analysis were used to analyze the influencing factors of prognosis in CIR-PH patients. ROC curve was used to analyze the predictive value of heparinase and NT-proBNP for death in patients with CIR-PH. Pearson correlation analysis was used to analyze the correlation between heparinase and CIR-PH disease-related indicators (NT-proBNP, APACHE II score, mPAP, PCWP, PVR and CO). **Results** The age, RVD and RAD in the death group were larger than those in the survival group, heparinase, NT-proBNP, APACHE II score, mPAP, PCWP, PVR, mRAP and PAP were higher than those in the survival group, CO was lower than that in the survival group, and TRV was faster than that in the survival group ( $P < 0.05$ ). Univariate Cox proportional hazard regression analysis showed that age, heparinase, NT-proBNP, APACHE II score, mPAP, PCWP, PVR, mRAP, CO, RVD, RAD, PAP, TRV may be the influencing factors of death in patients with CIR-PH ( $P < 0.05$ ). Multivariate Cox proportional hazard regression analysis showed that heparinase, NT-proBNP, mPAP and mRAP were independent influencing factors of death in patients with CIR-PH ( $P < 0.05$ ). ROC curve analysis showed that the AUC of heparinase in predicting death in CIR-PH patients was 0.784 [95%CI (0.688–0.879)], the optimal cut-off value was 10.4  $\mu\text{g/L}$ , the sensitivity was 0.500, and the specificity was 0.875; the AUC of NT-proBNP in predicting death in CIR-PH patients was 0.761 [95%CI (0.662–0.860)], the optimal cut-off value was 3 775 ng/L, the sensitivity was 0.357, and the specificity was 0.950. Pearson correlation analysis showed that heparinase was positively correlated with NT-proBNP ( $r=0.639$ ), APACHE II score ( $r=0.763$ ), mPAP ( $r=0.876$ ), PCWP ( $r=0.858$ ) and PVR ( $r=0.846$ ), and negatively correlated with CO ( $r=-0.702$ ) in CIR-PH patients ( $P < 0.001$ ). **Conclusion** Heparinase is an independent influencing factor of death in patients with CIR-PH, and it has certain predictive value for death in CIR-PH patients, and it is closely related to the disease severity of CIR-PH patients.

**【Key words】** Pulmonary arterial hypertension; Critical illness; Heparin lyase; Heparinase; Prognosis

肺动脉高压 (pulmonary hypertension, PH) 的主要特征是肺动脉压 (pulmonary artery pressure, PAP) 升高, 即静息时平均肺动脉压 (mean pulmonary artery pressure, mPAP)  $\geq 20$  mmHg (1 mmHg=0.133 kPa)、肺血管阻力 (pulmonary vascular resistance, PVR)  $\geq 3$  Wood单位<sup>[1]</sup>, 其发病机制复杂, 任何导致肺血流增快或PVR增加的结构和功能异常均可能引发PH。研究表明, PAP增高会加重右心后负荷, 导致右心室肥大、扩张及心功能障碍, 严重者甚至导致右心衰竭<sup>[2-3]</sup>。世界卫生组织数据显示, PH患者5年生存率为65.4%<sup>[4]</sup>, 提示PH患者预后极差, 特别是危重症相关肺动脉高压 (critical illness-related pulmonary hypertension, CIR-PH) 患者。因此, 筛选CIR-PH患者预后的生物标志物对改善其预后具有重要意义。目前, NT-proBNP是相关指南推荐的评估PH患者预后的唯一血清标志物<sup>[5]</sup>。肝素酶是一种 $\beta$ -D葡萄糖醛酸酯酶, 其能特异性地裂解细胞外基质中的硫酸乙酰肝素 (heparan sulfate, HS) 侧链, 并激活多种血管生长因子, 进而参与调控血管生成, 其在肺血管内皮细胞中发挥着重要作用<sup>[6]</sup>。研究表明, 肝素酶能参与PH的发生<sup>[7]</sup>, 但其与PH患者预后的关系尚未完全明确。基于此, 本研究旨在探讨肝素酶与CIR-PH患者预后及病情严重程度的关系, 现报道如下。

## 1 对象与方法

### 1.1 研究对象

回顾性选取2021年4月—2022年6月兰州大学第一医院重症医学科收治的108例CIR-PH患者为研究对象。纳入标准: (1) 年龄 $\geq 18$ 岁; (2) 危重症患者, 且符合WHO关于PH的诊断标准<sup>[8]</sup>。排除标准: (1) 无法行右心导管检查 (right heart catheterization, RHC) 者; (2) 超声

检查图像不清晰者; (3) 合并晚期肿瘤及严重急性或慢性疾病者, 如急性大面积脑梗死、终末期尿毒症或难治性心力衰竭等; (4) 接受手术治疗者; (5) 合并精神疾病者。本研究已获得兰州大学第一医院伦理委员会审核批准 (伦理号: LDYYLL2023-453)。本研究在中国临床试验注册中心 (<https://www.chictr.org.cn/>) 注册, 注册识别号为ChiCTR2300072241。

### 1.2 分组

出院后1年对患者进行电话随访, 根据预后情况将其分为死亡组 ( $n=28$ ) 和生存组 ( $n=80$ )。

### 1.3 观察指标

#### 1.3.1 一般资料

收集患者的一般资料, 包括年龄、性别、BMI、PH临床分类 (包括动脉性PH、心脏病导致PH、肺疾病和/或缺氧导致PH、肺动脉阻塞性病变导致PH、未知原因或多因素导致PH)、肝素酶、NT-proBNP及急性生理学和慢性健康状况评价系统II (acute physiology and chronic health evaluation II, APACHE II) 评分。其中肝素酶、NT-proBNP通过酶联免疫吸附试验获得。

#### 1.3.2 RHC结果

收集患者入院时RHC结果, 采用SWAN-GANZ导管, 主要指标为mPAP、肺毛细血管楔压 (pulmonary capillary wedge pressure, PCWP)、PVR、平均右心房压 (mean right atrial pressure, mRAP) 和心排血量 (cardiac output, CO)。

#### 1.3.3 超声心动图检查结果

收集患者入院时超声心动图检查结果, 主要指标为右心室直径 (right ventricle dimension, RVD)、右心房直径

(right atrium dimension, RAD)、肺动脉宽度(pulmonary artery width, PAW)、肺动脉流速(pulmonary artery velocity, PAV)、PAP、三尖瓣反流速度(tricuspid regurgitation velocity, TRV)。

#### 1.4 统计学方法

采用SPSS 26.0软件进行数据处理,采用Graph Pad Prism 9软件绘图。符合正态分布的计量资料以( $\bar{x} \pm s$ )表示,两组间比较采用成组 $t$ 检验;不符合正态分布的计量资料以 $M(P_{25}, P_{75})$ 表示,两组间比较采用秩和检验;计数资料以相对数表示,组间比较采用 $\chi^2$ 检验;CIR-PH患者预后的影响因素分析采用单因素、多因素Cox比例风险回归分析;采用ROC曲线分析肝素酶、NT-proBNP对CIR-PH患者死亡的预测价值;肝素酶与CIR-PH病情相关指标(NT-proBNP、APACHE II评分、mPAP、PCWP、PVR、CO)的相关性分析采用Pearson相关分析。以 $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 生存组与死亡组一般资料、RHC结果、超声心动图检查结果比较

生存组与死亡组性别、BMI、PH临床分类、PAW、PAV比较,差异无统计学意义( $P > 0.05$ );死亡组年龄、RVD、

RAD大于生存组,肝素酶、NT-proBNP、APACHE II评分、mPAP、PCWP、PVR、mRAP、PAP高于生存组,CO低于生存组,TRV快于生存组,差异有统计学意义( $P < 0.05$ ),见表1。

### 2.2 CIR-PH患者预后的影响因素

以表1中差异有统计学意义的项目为自变量,以CIR-PH患者预后(赋值:生存=0,死亡=1)为因变量,进行单因素Cox比例风险回归分析,结果显示,年龄、肝素酶、NT-proBNP、APACHE II评分、mPAP、PCWP、PVR、mRAP、CO、RVD、RAD、PAP、TRV可能是CIR-PH患者死亡的影响因素( $P < 0.05$ ),见表2。以上述影响因素为自变量(赋值同表2),以CIR-PH患者预后(赋值:生存=0,死亡=1)为因变量,进行多因素Cox比例风险回归分析,结果显示,肝素酶、NT-proBNP、mPAP、PAP是CIR-PH患者死亡的独立影响因素( $P < 0.05$ ),见表3。

### 2.3 肝素酶、NT-proBNP对CIR-PH患者死亡的预测价值

ROC曲线分析结果显示,肝素酶预测CIR-PH患者死亡的AUC为0.784〔95%CI(0.688~0.879)〕,最佳截断值为10.4  $\mu\text{g/L}$ ,灵敏度为0.500,特异度为0.875;NT-proBNP预测CIR-PH患者死亡的AUC为0.761〔95%CI

表1 生存组与死亡组一般资料、RHC结果、超声心动图检查结果比较  
Table 1 Comparison of general data, RHC results and echocardiography results between survival group and death group

项目	生存组( $n=80$ )	死亡组( $n=28$ )	检验统计量值	$P$ 值
年龄( $\bar{x} \pm s$ , 岁)	42.9 $\pm$ 8.1	49.3 $\pm$ 9.3	-3.446 <sup>a</sup>	0.001
性别(男/女)	44/36	15/13	0.017 <sup>b</sup>	0.896
BMI [ $M(P_{25}, P_{75})$ , kg/m <sup>2</sup> ]	23.1 (20.9, 24.7)	24.4 (21.2, 25.6)	-1.718 <sup>c</sup>	0.086
PH临床分类 [ $n(\%)$ ]			2.416 <sup>b</sup>	0.660
动脉性PH	14 (17.5)	4 (14.3)		
心脏病导致PH	23 (28.7)	7 (25.0)		
肺疾病和/或缺氧导致PH	17 (21.3)	9 (32.1)		
肺动脉阻塞性病变导致PH	14 (17.5)	6 (21.4)		
未知原因或多因素导致PH	12 (15.0)	2 (7.1)		
肝素酶( $\bar{x} \pm s$ , $\mu\text{g/L}$ )	9.1 $\pm$ 1.3	10.6 $\pm$ 1.4	-5.100 <sup>a</sup>	<0.001
NT-proBNP [ $M(P_{25}, P_{75})$ , ng/L]	1 490 (851, 2 500)	2 777 (1 812, 4 070)	-4.102 <sup>c</sup>	<0.001
APACHE II评分( $\bar{x} \pm s$ , 分)	16.1 $\pm$ 3.2	18.7 $\pm$ 3.5	-3.493 <sup>a</sup>	0.001
mPAP( $\bar{x} \pm s$ , mmHg)	40.0 $\pm$ 6.9	43.6 $\pm$ 8.1	-2.272 <sup>a</sup>	0.025
PCWP( $\bar{x} \pm s$ , mmHg)	10.7 $\pm$ 2.0	12.6 $\pm$ 3.2	-2.853 <sup>a</sup>	0.007
PVR [ $M(P_{25}, P_{75})$ , Wood单位]	15.2 (13.6, 16.9)	16.0 (14.4, 20.0)	-2.132 <sup>c</sup>	0.033
mRAP [ $M(P_{25}, P_{75})$ , mmHg]	7.0 (6.0, 8.0)	8.5 (6.3, 10.0)	-3.352 <sup>c</sup>	0.001
CO( $\bar{x} \pm s$ , L/min)	4.6 $\pm$ 1.0	3.9 $\pm$ 1.5	2.638 <sup>a</sup>	0.012
RVD( $\bar{x} \pm s$ , mm)	58.0 (56.0, 60.0)	60.0 (57.3, 62.8)	-2.812 <sup>a</sup>	0.005
RAD( $\bar{x} \pm s$ , mm)	52.4 $\pm$ 4.6	55.6 $\pm$ 4.6	-3.237 <sup>a</sup>	0.002
PAW [ $M(P_{25}, P_{75})$ , mm]	34.0 (33.0, 35.0)	35.0 (33.3, 36.0)	-1.719 <sup>c</sup>	0.086
PAV [ $M(P_{25}, P_{75})$ , m/s]	0.58 (0.53, 0.63)	0.58 (0.54, 0.63)	-0.562 <sup>c</sup>	0.574
PAP( $\bar{x} \pm s$ , mmHg)	38.4 $\pm$ 7.1	42.9 $\pm$ 6.3	-2.987 <sup>a</sup>	0.003
TRV( $\bar{x} \pm s$ , m/s)	2.9 $\pm$ 0.3	3.1 $\pm$ 0.3	-2.844 <sup>a</sup>	0.005

注:PH=肺动脉高压,APACHE II=急性生理学 and 慢性健康状况评价系统II,mPAP=平均肺动脉压,PCWP=肺毛细血管楔压,PVR=肺血管阻力,mRAP=平均右心房压,CO=心排量,RVD=右心室直径,RAD=右心房直径,PAW=肺动脉宽度,PAV=肺动脉流速,PAP=肺动脉压,TRV=三尖瓣反流速度;<sup>a</sup>表示 $t$ 值,<sup>b</sup>表示 $\chi^2$ 值,<sup>c</sup>表示 $Z$ 值。

表2 CIR-PH患者预后影响因素的单因素Cox比例风险回归分析

Table 2 Univariate Cox proportional hazard regression analysis of influencing factors of prognosis in patients with CIR-PH

变量	赋值	$\beta$	SE	Wald $\chi^2$ 值	P值	HR (95%CI)
年龄	实测值	0.064	0.020	10.180	0.001	1.066 (1.025 ~ 1.109)
肝素酶	实测值	0.578	0.131	19.555	<0.001	1.783 (1.380 ~ 2.303)
NT-proBNP	实测值	0.001	<0.001	15.667	<0.001	1.000 (1.000 ~ 1.001)
APACHE II 评分	实测值	0.159	0.049	10.699	0.001	1.172 (1.066 ~ 1.289)
mPAP	实测值	0.059	0.027	4.863	0.027	1.060 (1.007 ~ 1.117)
PCWP	实测值	0.243	0.073	11.013	0.001	1.275 (1.105 ~ 1.348)
PVR	实测值	0.174	0.063	7.514	0.006	1.190 (1.051 ~ 1.316)
mRAP	实测值	0.261	0.066	15.611	<0.001	1.298 (1.140 ~ 1.477)
CO	实测值	-0.089	0.171	7.318	0.007	0.915 (0.654 ~ 1.279)
RVD	实测值	0.216	0.067	10.328	0.001	1.242 (1.088 ~ 1.417)
RAD	实测值	0.136	0.042	10.403	0.001	1.146 (1.055 ~ 1.245)
PAP	实测值	0.080	0.027	8.615	0.003	1.083 (1.027 ~ 1.143)
TRV	实测值	1.648	0.636	6.724	0.010	5.196 (1.495 ~ 18.056)

表3 CIR-PH患者预后影响因素的多因素Cox比例风险回归分析

Table 3 Multivariate Cox proportional hazard regression analysis of influencing factors of prognosis in patients with CIR-PH

变量	$\beta$	SE	Wald $\chi^2$ 值	P值	HR (95%CI)
年龄	0.019	0.024	0.618	0.432	1.019 (0.972 ~ 1.069)
肝素酶	0.957	0.447	4.576	0.032	2.603 (1.083 ~ 6.252)
NT-proBNP	0.000	0.000	3.920	0.048	1.000 (1.000 ~ 1.001)
APACHE II 评分	0.042	0.122	0.121	0.728	1.043 (0.822 ~ 1.324)
mPAP	-0.444	0.129	11.893	0.001	0.641 (0.498 ~ 0.826)
PCWP	-0.037	0.205	0.033	0.856	0.964 (0.645 ~ 1.440)
PVR	-0.203	0.150	1.832	0.176	0.816 (0.608 ~ 1.095)
mRAP	0.109	0.155	0.498	0.481	1.116 (0.823 ~ 1.512)
CO	-0.256	0.294	0.758	0.384	0.774 (0.436 ~ 1.377)
RVD	0.095	0.084	1.275	0.259	1.099 (0.933 ~ 1.295)
RAD	0.073	0.051	2.042	0.153	1.075 (0.937 ~ 1.188)
PAP	0.271	0.134	4.089	0.043	1.311 (1.009 ~ 1.704)
TRV	0.247	0.748	0.109	0.742	1.280 (0.295 ~ 5.547)

(0.662 ~ 0.860) ]，最佳截断值为3 775 ng/L，灵敏度为0.357，特异度为0.950，见图1。

#### 2.4 肝素酶与CIR-PH病情相关指标的相关性分析

Pearson相关分析结果显示，肝素酶与CIR-PH患者NT-proBNP ( $r=0.639$ )、APACHE II 评分 ( $r=0.763$ )、mPAP ( $r=0.876$ )、PCWP ( $r=0.858$ )、PVR ( $r=0.846$ ) 呈正相关，与CO ( $r=-0.702$ ) 呈负相关 ( $P<0.001$ )，见图2。

#### 3 讨论

WHO数据显示，既往诊断和新诊断的PH患者1年生存率分别为90.4%、86.3%<sup>[4]</sup>。本研究结果显示，CIR-PH患者1年生存率为74.1%，低于WHO数据，分析原因为本研究纳入患者为危重症患者，病情较严重。PH的主要发病机制是肺血管内皮细胞改变引起肺血管重构<sup>[9]</sup>；此外，还包括炎症反应<sup>[10]</sup>、血液高凝状态和血栓形成<sup>[11]</sup>、肺血管纤维化<sup>[12]</sup>

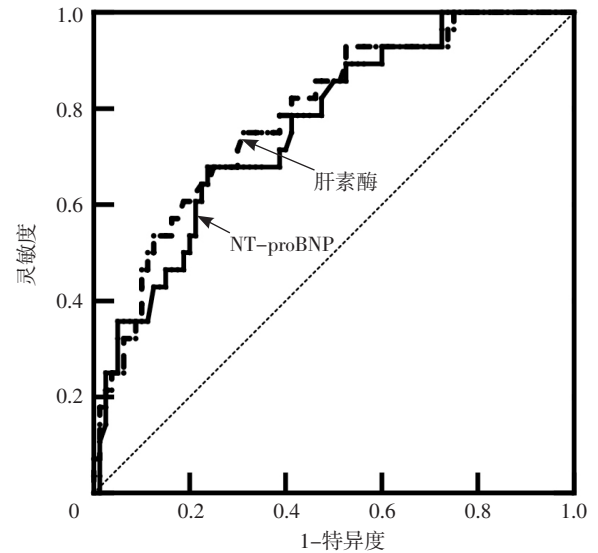


图1 肝素酶、NT-proBNP预测CIR-PH患者死亡的ROC曲线

Figure 1 ROC curve of heparinase and NT-proBNP in predicting the death of patients with CIR-PH

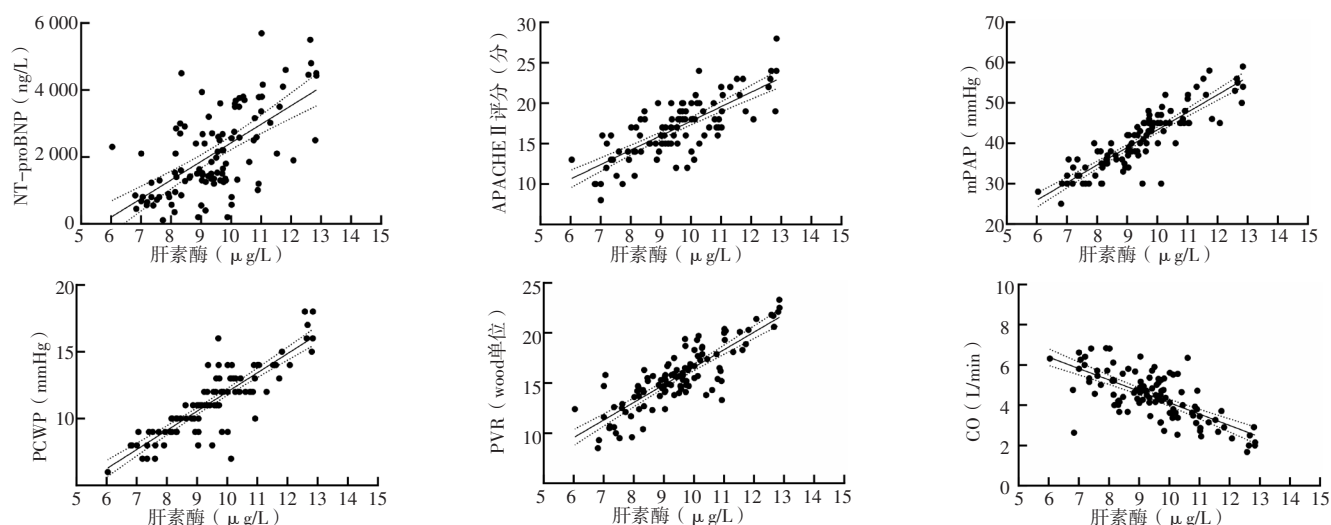
等。目前，诊断PH的“金标准”为RHC，但其属于侵入性操作；超声检查也常用于评估PH<sup>[13-14]</sup>。PH常导致右心室压力过载和右心衰竭，进而影响危重症患者预后。三尖瓣环收缩移位和Tei指数已被用于评估PH患者的右心功能<sup>[15-16]</sup>。BNP和NT-proBNP是PH风险分层的常用生物标志物<sup>[5, 17]</sup>。研究表明，BNP与PH患者死亡风险升高相关<sup>[18]</sup>。NT-proBNP作为BNP的前体，更加稳定，故常作为PAH诊断和预后评估的生物标志物<sup>[19]</sup>。

肝素酶是唯一能够降解细胞外基质中硫酸类肝素的糖苷酶<sup>[20]</sup>，其通过降解硫酸类肝素而激活内皮型一氧化氮合酶，进而在血流重塑中发挥重要作用<sup>[21-22]</sup>。同时，肝素酶可参与炎症反应<sup>[23]</sup>，增强局部凝血活性，包括从细胞表面解离组织因子通路抑制因子和诱导组织因子表达<sup>[24-25]</sup>。此外，肝素酶还可调节内皮细胞中的生长因子表达，如血管生成素，并参与肺部和其他器官纤维化，进而影响肺和其他器官的正常结构和功能<sup>[26-27]</sup>。

本研究结果显示，死亡组肝素酶和NT-proBNP高于生存组；多因素Cox比例风险回归分析结果显示，肝素酶、NT-proBNP是CIR-PH患者死亡的独立影响因素；ROC曲线分析结果显示，肝素酶预测CIR-PH患者死亡的AUC为0.784，NT-proBNP预测CIR-PH患者死亡的AUC为0.761。因此，肝素酶可能成为预测CIR-PH患者死亡的生物标志物。

众所周知，CIR-PH病情严重程度可直接影响患者预后。研究表明，NT-proBNP与PH病情严重程度呈正相关<sup>[28]</sup>。APACHE II 评分由急性生理评分、年龄评分及慢性健康评分构成，其分值越高表示患者病情越严重，预后越差<sup>[29]</sup>。mPAP、PCWP、PVR、CO为RHC结果，其中mPAP、PCWP、PVR是PH的诊断指标，其值越高提示PH患者病情越严重<sup>[30]</sup>。CO是血流动力学中最基本的指标之一，常用来评估心脏泵血功能，其值越低提示PH患者病情越严重<sup>[31]</sup>。本研究Pearson相关分析结果显示，肝素酶与CIR-PH患者NT-





注: APACHE II=急性生理学和慢性健康状况评价系统II, mPAP=平均肺动脉压, PCWP=肺毛细血管楔压, PVR=肺血管阻力, CO=心排量。

图2 肝素酶与CIR-PH病情相关指标关系的散点图

Figure 2 Scatter plot of the relationship between heparanase and CIR-PH disease-related indicators

proBNP、APACHE II评分、mPAP、PCWP、PVR呈正相关,与CO呈负相关,提示肝素酶与CIR-PH患者病情严重程度密切相关,肝素酶越高CIR-PH患者病情越严重,预后越差。

#### 4 结论

综上所述,肝素酶是CIR-PH患者死亡的独立影响因素,其对CIR-PH患者死亡有一定预测价值,且其与CIR-PH患者病情严重程度密切相关,这为进一步探索CIR-PH患者预后血清标志物提供了参考。但本研究尚存在一定局限性:(1)本研究为单中心回顾性、非随机对照研究,无法排除混杂因素影响;(2)本研究样本量较小。因此,未来仍需要扩大样本量、联合多中心研究进一步证实本研究结论。

作者贡献:王林军、刘丽平进行文章的构思与设计;李建春、陈娣进行研究的实施与可行性分析;岳建巍、李洪磊进行数据收集、整理、分析;王林军、冯菲进行结果分析与解释;王林军负责撰写、修订论文;刘丽平负责文章的质量控制及审校,对文章整体负责、监督管理。

本文无利益冲突。

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