不同年龄组重症社区获得性肺炎预后危险因素分析

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摘要　目的　探讨不同年龄组重症社区获得性肺炎(SCAP)预后危险因素。**方法**　采用多中心、前瞻性的研究方法,分析2017年12月至2021年10月,河南中医药大学第一附属医院等11家三甲医院收治的住院SCAP患者的临床资料。根据患者年龄分为老年组(≥65岁)和非老年组(18~64岁),分析SCAP临床特征。根据死亡与否分为存活组与死亡组,通过多因素Logistic回归分析确定SCAP死亡的危险因素。**结果**　170例SCAP患者被纳入研究,年龄20~93(65.75±15.23)岁,其中老年SCAP比例为58.82%(100/170)。非老年SCAP住院死亡率为24.3%(17/70),老年SCAP住院死亡率为28%(28/100)。与非老年SCAP相比,老年SCAP入院时病情严重程度评分更高,合并症更多,但入院时发热、呼吸频率增快症状表现更不明显。多因素Logistic回归分析显示,入院时肺炎严重指数(PSI)评分($P=0.016$, $OR=1.022$, 95% CI: 1.004~1.041)和有创机械通气($P=0.037$, $OR=4.543$, 95% CI: 1.092~18.898)为非老年SCAP住院死亡的独立危险因素,入院时序贯性脏器功能衰竭(SOFA)评分($P=0.006$, $OR=1.240$, 95% CI: 1.063~1.446)和合并冠心病($P=0.037$, $OR=2.834$, 95% CI: 1.066~7.534)为老年SCAP住院死亡的独立危险因素。**结论**　SCAP患者住院病死率高,入院时PSI评分和有创机械通气为非老年SCAP住院死亡的独立危险因素,入院时SOFA评分和合并冠心病为老年SCAP住院死亡的独立危险因素。

关键词　重症社区获得性肺炎;老年;病死率;危险因素;SOFA评分;PSI评分
中图分类号　R 563.1
文献标志码　A　**文章编号**　1000-1492(2025)03-0558-07
doi:10.19405/j.cnki.issn1000-1492.2025.03.024

社区获得性肺炎(community-acquired pneumonia, CAP)是世界范围内导致死亡最常见的感染性疾病,重症社区获得性肺炎(severe community-acquired pneumonia, SCAP)是死亡的主要原因[1]。尽管治疗理念和干预措施不断优化,重症肺炎30 d病死率仍高达27%[2]。早期对SCAP进行预后评估,对指导SCAP的临床治疗及降低病死率具有积极意义。国内一项关于老年重症肺炎的meta分析[3]显示,年龄、机械通气、APACHE Ⅱ评分等因素是影响老年重症肺炎预后的危险因素;欧洲一项研究[4]发现,男性和年龄是中重度CAP治疗失败的独立危险因素;巴西一项回顾性队列研究[5]发现,有创机械通气、年龄>65岁等是住ICU肺炎患者死亡的危险因素。国内外研究表明,年龄是SCAP死亡的影响因素,但目前尚无针对不同年龄组SCAP预后危险因素分析的研究。因此,该研究根据年龄将SCAP患者分为老年组和非老年组,分析不同年龄组SCAP预后危险因素。

1　资料与方法

1.1　病例资料　收集2017年12月至2021年10月,河南中医药大学第一附属医院等11家三甲医院呼吸与危重症学科及重症监护室(ICU)的住院SCAP患者的临床资料。纳入标准:① 年龄≥18岁;② 诊断标准参照《社区获得性肺炎诊断和治疗指南(2016版)》[6]。排除标准:① 合并恶性肿瘤;② 妊娠及哺乳期妇女;③ 严重免疫抑制;④ 真菌肺炎、HIV相关肺囊虫肺炎、肺结核;⑤ 感染新型冠状病毒肺炎(COVID-19);⑥ 拒绝签署知情同意书。

1.2　方法

1.2.1　研究类型　本研究为多中心前瞻性观察性研究。

1.2.2　资料收集及预后指标　各中心研究者在观察期间每日对受试者探视,了解受试者病情变化,通

2024-12-17 接收
基金项目:国家自然科学基金(编号:82074411、81774222);河南省高校科技创新团队支持计划(编号:22IRTSTHN029);河南省中医药科学研究专项课题重大专项(编号:20-21ZYZD04);河南省中医药拔尖人才培养项目(编号:2019ZYBJ05);河南省中医药科学研究专项课题(编号:2022ZYFY04)
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过病例报告(case report form, CRF)表对患者每天的资料进行采集和记录,CRF 表完成后及时在网络数据平台进行填报,组长单位(河南中医药大学第一附属医院)有专门负责人员每月定期对网络填报数据进行质量控制,同时建立课题实施工作群,每日进行课题实施工作的汇报,对课题实施过程中出现的问题随时在群里提出并讨论解决。资料收集:①基本信息:姓名、性别、年龄、住院前危险因素、合并症等;② 入院 1 d 临床资料:临床体征、重症患者序贯性脏器功能衰竭(sequential organ failure assessment, SOFA)评分、肺炎严重指数(pneumonia severity index, PSI)评分、CURB-65 评分、血气分析、病原学检查等;③预后结局指标,主要结局指标:病死率,包括住院病死率、28 d 病死率、PSI 分级Ⅴ级(PSI-Ⅴ)患者病死率、有创机械通气患者病死率、ICU 患者病死率;次要结局指标:治疗失败率、器官功能衰竭比例、有创机械通气比例、住院时间等。治疗失败包括早期治疗失败和晚期治疗失败,早期治疗失败定义为 72 h 内病情恶化(出现休克、需要气管插管,或死亡);晚期治疗失败定义为影像学进展(与入院时比较肺部渗出增加大于 50%),持续严重的呼吸衰竭(未有创机械通气的患者氧合指数 <26.7 kPa,呼吸频率≥30 次/min),出现休克、需要气管插管,或于 72 h 后死亡[7]。如上述临床指标在同一天内多次测量,则取最差值。

1.2.3 *研究分组* 根据患者年龄分为老年组(年龄≥65 岁)和非老年组(年龄 18 ~64 岁),评估不同年龄组 SCAP 临床特征和预后;根据住院存活情况分为存活组和死亡组,分析与 SCAP 住院死亡相关的危险因素。

1.2.4 *伦理及知情同意* 本研究符合赫尔辛基宣言(2013 年修订),所有患者均已签署知情同意,本研究经河南中医药大学第一附属医院伦理委员会批准(2017HL-002-01)。

1.2.5 *多中心合作及质量控制* 为保证多中心合作研究的数据质量及伦理,研究开始前组长单位(河南中医药大学第一附属医院)均与各中心签订合作协议书,同时制定《研究者工作手册》,对各中心的课题参加人员进行专门培训,并进行一致性检测。

1.3 统计学处理 采用 SPSS20.0 统计软件进行数据的统计分析。计数指标用频数和构成比描述,两组疗效比较采用 χ^2 检验或 Fisher 精确检验。计量指标用 $\bar{x} \pm s$ 描述,符合正态分布的计量资料两组疗效比较采用 t 检验,非正态分布的计量资料以采用 Mann-Whitney U 检验。首先对 SCAP 死亡因素进行单因素分析,对差异有统计学意义的相关因素采用 Forward LR 逐步法进行多因素 Logistic 回归分析,确定影响 SCAP 预后的相关因素。均采用双侧检验,P <0.05 为差异有统计学意义。

2 结果

2.1 不同年龄段 SCAP 患者临床特征 共纳入 186 例重症肺炎患者,观察中剔除 16 例,最终对 170 例 SCAP 患者进行分析。见图 1。其中男性 114 例(67.1%),年龄 20 ~93 (65.75 ± 15.23)岁,老年患者比例为 58.82% (100/170)。与非老年 SCAP 相比,老年 SCAP 患者身体质量指数(body mass index, BMI)、体温、呼吸频率更低,合并冠心病、心功能不全比例更高。对病情严重程度评估显示,老年 SCAP 患者 CURB-65 评分、PSI 评分更高。见表 1。

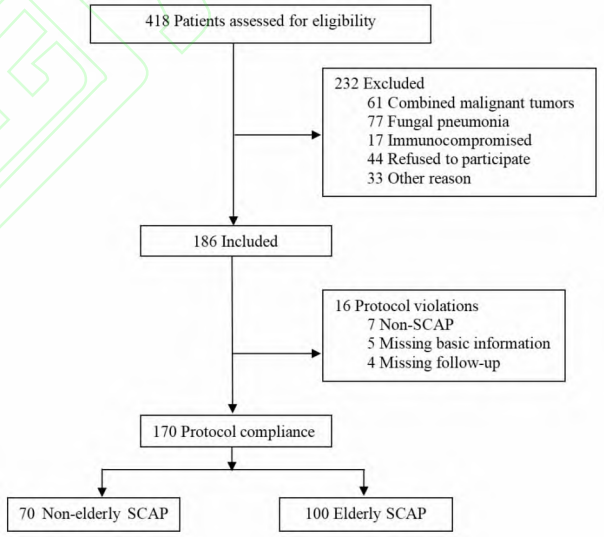

图 1 研究流程图

Fig. 1 Research flow diagram

2.2 不同年龄段 SCAP 患者病原学检查 采用痰培养和血培养进行病原学检查。170 例患者中仅 73 例患者检出了病原菌,检出率最高的依次为铜绿假单胞杆菌(19.2%),鲍曼不动杆菌(17.8%),肺炎克雷伯杆菌(15.1%),金黄色葡萄球菌(11.0%)。老年 SCAP 与非老年 SCAP 患者病原菌分布比较差异无统计学意义。见表 2。

2.3 不同年龄组 SCAP 患者预后 SCAP 患者住院死亡率为 26.5% (45/170),有创机械通气患者病死率最高,为 38.6% (34/88)。74 例 (43.5%)

表 1 不同年龄组 SCAP 患者临床特征[n(%),$\bar{x}\pm s$, $M(P_{25}, P_{75})$]

Tab. 1 Clinical characteristics of SCAP patients in different age groups[n(%),$\bar{x}\pm s$,$M(P_{25}, P_{75})$]

Characteristics	Non-elder <65years (n=70)	Elder≥65 years (n=100)	n=170	$\chi^2/t/Z$	P Value
Age	50.91±11.06	76.14±6.78	65.75±15.23		
Male	45(64.3)	69(69.0)	114(67.1)	0.414[b]	0.520
BMI(kg/m^2)	24.0(22.0,27.8)	22.0(20.0,24.0)	23.0(21.0,25.0)	−4.291	0.001*
Clinical signs					
Temperature(℃)	37.68±0.96	37.35±0.89	37.49±0.93	2.244[c]	0.026*
Respiratory rate(breaths/min)	25.57±5.74	23.69±6.06	24.46±5.98	2.009	0.046*
Heart rate(beats/min)	100.77±17.84	102.94±21.26	102.04±19.88	−0.696[c]	0.488
Systolic blood pressure(mmHg)	123.19±20.44	128.88±23.33	126.54±22.30	−1.647[c]	0.101
Diastolic blood pressure(mmHg)	71.42±13.17	70.61±14.44	70.95±13.90	0.369[c]	0.713
$PaCO_2$(mmHg)	36.4(31.65,43.25)	37.4(32.75,46.10)	37.0(32.35,43.90)	−0.706	0.480
PaO_2/FiO_2(mmHg)	176.0(135.5,227.0)	182.0(142.3,258.0)	181.0(142.0,248.0)	−1.155	0.248
Pre-hospitalization risk factors					
Received IV antibiotics for the last 30 days	29(41.4)	44(44.0)	73(42.9)	0.111[b]	0.739
Hospitalization ≥2 days in the last 90 days	15(21.4)	30(30.0)	45(26.5)	1.554[b]	0.213
Comorbidities					
Hypertension	25(35.7)	38(38.0)	63(37.1)	0.092[b]	0.761
Cerebrovascular disease	15(21.4)	31(31.0)	46(27.1)	1.911[b]	0.167
Diabetes mellitus	17(24.3)	28(28.0)	45(26.5)	0.292[b]	0.589
Coronary artery disease	11(15.7)	31(31.0)	42(24.7)	5.172[b]	0.023*
Cardiac insufficiency	9(12.9)	27(27.0)	36(21.2)	4.934[b]	0.026*
Severity criteria					
Confusion	36(51.4)	55(55.0)	91(53.5)	0.211[b]	0.646
Shock state	9(12.9)	22(22.0)	31(18.2)	2.309[b]	0.129
Invasive mechanical ventilation,	39(55.7)	49(49.0)	88(51.8)	0.743[b]	0.389
SOFA score	5.88±3.50	5.62±3.11	5.73±3.27	−0.269[c]	0.788
CURB-65 score	1.46±1.00	2.45±0.95	2.04±1.08	−5.730[c]	0.001*
PSI score	99.43±39.40	128.75±32.64	116.68±38.30	−5.289[c]	0.001*
PSI risk class[a]					
Ⅰ~Ⅲ	29(41.4)	13(13.0)	42(24.7)	17.889[b]	0.001*
Ⅳ	23(32.9)	45(45.0)	68(40.0)	2.530[b]	0.112
Ⅴ	18(25.7)	42(42.0)	60(35.3)	4.782[b]	0.029*

* P<0.05 there was statistically significant difference between the groups; [a]Risk classes Ⅰ~Ⅲ (≤90 points), risk class Ⅳ (91~130 points), risk class Ⅴ(>130 points); [b]:χ^2, [c]:t, Others are Z.

表 2 不同年龄组 SCAP 患者病原学检查[n(%)]

Tab. 2 Microbiologic identification of SCAP patients in different age groups[n(%)]

Microbiologic	Non-elder <65 years (n=30)	Elder≥65 years (n=43)	n=73	χ^2	P value
Gram-negative bacteria					
Pseudomonas aeruginosa	3 (10.0)	11 (25.6)	14 (19.2)	2.768	0.096
Acinetobacter baumannii	7 (23.3)	6 (14.0)	13 (17.8)	1.062	0.303
Klebsiella pneumoniae	5 (16.7)	6 (14.0)	11 (15.1)	0.102	0.752
Other *Gram-negative bacteria*	8 (26.7)	16 (37.2)	24 (32.9)	0.890	0.345
Gram-positive bacteria					
Staphylococcus aureus	4 (13.3)	4 (9.3)	8 (11.0)	0.294	0.588
Other *Gram-positive bacteria*	10 (33.3)	12 (27.9)	22 (30.1)	0.247	0.619

SCAP 患者合并了至少一种呼吸系统以外的脏器功能衰竭。老年 SCAP 与非老年 SCAP 患者预后差异无统计学意义。见表 3。

2.4 非老年 SCAP 患者住院死亡危险因素分析

对非老年 SCAP 住院死亡的危险因素进行单因素分析，显示意识障碍、有创机械通气、SOFA 评分、

CURB-65 评分、PSI 评分，死亡组与存活组比较差异有统计学意义。将住院死亡与否作为因变量，将上述因素作为自变量进行多因素 Logistic 回归分析。结果显示入院第一天的重症患者 PSI 评分、有创机械通气为非老年 SCAP 住院死亡的独立影响因素。见表 4。

2.5 老年 SCAP 患者住院死亡危险因素分析 对老年 SCAP 死亡的危险因素进行单因素分析显示，两组重症患者 SOFA 评分、CURB-65 评分、休克、意识障碍、合并冠心病、合并心功能不全比较差异有统计学意义。将住院死亡与否作为因变量，将上述因素作为自变量进行多因素 Logistic 回归分析显示，入院第一天的重症患者 SOFA 评分、合并冠心病为老年 SCAP 死亡的独立影响因素。见表 5。

3 讨论

这项前瞻性、多中心、观察性研究显示，非老年 SCAP 住院病死率为 24.3%，老年 SCAP 住院病死率为 28.0%；入院时 PSI 评分和有创机械通气为非老年 SCAP 住院死亡的独立危险因素，入院时 SOFA

表 3 不同年龄组 SCAP 患者预后[n(%)]

Tab.3 Prognosis of SCAP patients in different age groups[n(%)]

Outcomes	Non-elder < 65years (n = 70)	Elder ≥ 65 years (n = 100)	n = 170	χ^2/Z	P Value
Primary Clinical Outcome					
In-hospital mortality,	17 (24.3)	28 (28.0)	45 (26.5)	0.292	0.589
28-day mortality	15 (21.4)	23 (23.0)	38 (22.4)	0.059	0.809
Mortality in PSI-V [a]	8 (44.4)	14 (33.3)	22 (36.7)	0.670	0.413
Mortality in ivasive mechanical ventilation[b]	14 (35.9)	20 (40.8)	34 (38.6)	0.222	0.638
Mortality in ICU-SCAP[c]	14 (28.6)	24 (38.7)	38 (34.2)	1.249	0.264
Secondary Outcomes					
Treatment failure	22 (36.7)	41 (41.0)	63 (39.4)	0.295	0.587
Organ failure	26 (37.1)	48 (48.0)	74 (43.5)	1.975	0.160
Circulatory system failure	13 (18.6)	28 (28.0)	41 (24.1)	2.000	0.157
Renal failure	5 (7.1)	13 (13.0)	18 (10.6)	1.492	0.222
Liver failure	8 (11.4)	7 (7.0)	15 (8.8)	1.004	0.316
Length of stay (day, IQR)	15 (12, 23)	15 (9, 24)	15 (9, 24)	−0.557[d]	0.578

[a]: Mortality in SCAP with PSI classes V, $n_{\text{non-elder}}$ = 18, n_{elder} = 42; [b]: Mortality in SCAP with ivasive mechanical ventilation, $n_{\text{non-elder}}$ = 39, n_{elder} = 49; [c]: Mortality in SCAP admitted to the ICU, $n_{\text{non-elder}}$ = 49, n_{elder} = 62; [d]: Z, Others are χ^2.

表 4 非老年 SCAP 患者住院死亡危险因素分析

Tab.4 Univariate and multivariate analysis of variables associated with in-hospital mortality of non-elderly patients with SCAP

Factor	Univariate analysis			Multivariate analysis		
	Exp (B)	95% *CI*	P value	Exp (B)	95% *CI*	P value
PSI score	1.024	1.007 – 1.042	0.006	1.022	1.004 – 1.041	0.016
Invasive mechanical ventilation	5.227	1.343 – 20.335	0.017	4.543	1.092 – 18.898	0.037
SOFA score	1.178	1.006 – 1.380	0.042			
Confusion	4.239	1.220 – 14.728	0.023			
CURB-65 score	4.239	1.220 – 14.728	0.023			

表 5 老年 SCAP 患者住院死亡危险因素分析

Tab.5 Univariate and multivariate analysis of variables associated with in-hospital mortality of elderly patients with SCAP

Factor	Univariate analysis			Multivariate analysis		
	Exp(B)	95% *CI*	P Value	Exp(B)	95% *CI*	P Value
Combined with Coronary artery disease	3.235	1.291 – 8.110	0.012	2.834	1.066 – 7.534	0.037
Combined with Cardiac insufficiency	2.850	1.113 – 7.296	0.029			
Shock state	2.731	1.014 – 7.361	0.047			
Confusion	2.643	1.031 – 6.774	0.043			
SOFA score	1.238	1.065 – 1.439	0.005	1.240	1.063 – 1.446	0.006
CURB-65 score	1.723	1.055 – 2.814	0.030			

评分和合并冠心病为老年 SCAP 住院死亡的独立危险因素。

老年人群因为生理机能减退和组织器官衰老，免疫力低下，并发症较多，疾病进展迅速，病情复杂，与非老年患者在病理生理等方面有较大差别[8]。研究结果显示，与非老年 SCAP 相比，老年 SCAP 入院时 PSI 评分和 CURB-65 评分更高，合并冠心病和心功能不全比例更高。但临床体征方面，老年 SCAP 患者入院时发热、呼吸频率增快等症状表现更不典型，提示老年 SCAP 病情较重，但症状不典型，这与既往研究[9]结论一致。因此密切关注老年 SCAP 患者病情变化，早期对老年 SCAP 病情严重程度和死亡风险进行评估具有积极意义。

本研究中，SOFA 评分是老年 SCAP 患者住院死亡的独立影响因素。SOFA 包括了 6 个不同的系统的评分，反映器官功能衰竭程度[10]。既往多项研究[11]发现，SOFA 评分对老年 SCAP 住院死亡有很好的预测价值。近年来 SOFA 评分被越来越多地应用于临床指导重症患者的病情评估，与其他预后评估工具相比，SOFA 评分对重症患者的死亡风险预后价值更高[12]。合并冠心病是老年 SCAP 的独立危险因素。2013 年中国第五次卫生服务调查显示成年人冠心病患病率为 10.2‰，而 60 岁以上人群冠心病患病率为 27.8‰[13]。SCAP 主要的病理生理机制是感染导致的全身炎症反应综合征，炎症反应过程中释放的大量炎症因子可以导致心肌损伤，从而加重心脏负荷，而合并冠心病的老年患者心脏功能较差，容易出现病情的迅速进展，导致心肺功能衰竭[14-15]。研究[16]发现，COVID-19 重症患者多合并心血管疾病，COVID-19 死亡患者中，35%（14/40）的患者伴有心肌细胞的坏死。

本研究采用多中心前瞻性观察性的研究方法，将 SCAP 患者分为老年人群和非老年人群，对比分析不同年龄段的 SCAP 患者临床特征，同时采用 Logistic 分析，确定与非老年 SCAP 患者和老年 SCAP 患者死亡相关的危险因素。但本研究也存在一定的局限性。首先，本研究纳入病例既有普通病房患者，又有 ICU 患者，不同护理单元患者病情严重程度及治疗方案可能存在一定差异，因此纳入患者可能存在一定偏倚。其次，这是一项多中心研究，不同医院的临床医师可能根据他们的经验做出不同的临床决定，因此西医常规治疗可能存在一定差别。最后，本研究病例数相对较少，且仅观察住院期间的病死率，因此在分析生存相关影响因素时可能外推性较为局限。

综上，SCAP 患者中老年患者比例较高，与非老年 SCAP 患者相比，老年 SCAP 患者入院时病情严重程度更高，合并症更多，但入院临床症状表现更不明显。SCAP 住院病死率高，入院时 PSI 评分和有创机械通气为非老年 SCAP 住院死亡的独立危险因素，入院时 SOFA 评分和合并冠心病为老年 SCAP 住院死亡的独立危险因素。今后可开展大样本、高质量的临床研究，验证针对 SCAP 患者有创机械通气和合并冠心病的保护性干预措施是否可以使 SCAP 患者获益。

致谢（排名不分先后）：感谢孙同文、刘韶华（郑州大学第一附属医院）；赵丽敏、曹帆、忽新刚（河南省人民医院）；李利华（郑州人民医院）；汤兵祥、侯聪霞（河南省胸科医院）；何咏（郑州市中医院）；张华、徐超（郑州市中心医院）；朱慧志、张念志（安徽中医药大学第一附属医院）；封继宏（天津中医药大学第二附属医院）；耿立梅、闫红倩（河北省中医院）、王丁超、李文生（濮阳市中医院）对本研究的贡献。

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The risk factors of prognosis in patients with severe community-acquired pneumonia in different age groups

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Abstract ***Objective*** To explore the risk factors of prognosis in patients with severe community-acquired pneumonia (SCAP) in different age groups. ***Methods*** A multi-center and prospective study was conducted at 11 teaching hospitals in China from December 2017 to October 2021. Patients who met the criteria were assigned to the elderly group (≥65 years) and the non- elderly group (18 – 64 years) to demonstrate the clinical characteristics of SCAP. Patients were divided into survival group and death group according to whether they died in hospital, to determine the risk factors associated with mortality by multivariate logistic regression analysis. ***Results*** A total of 170 patients with SCAP were included in the study. The age of SCAP was 20 ~ 93 (65.75 ± 15.23) years old, and the proportion of SCAP in the elderly was 58.82% (100/170). In-hospital mortality of non-elderly SCAP was 24.3% (17/70), and the in-hospital mortality of elderly SCAP was 28% (28/100). Compared with non-elderly group, patients in elderly group had higher severity score and more complications on admission, but the symptoms of fever and respiratory rate at admission were less obvious. In multivariable logistic regression analysis, the factors significantly associated with in-hospital mortality of non-elderly SCAP were pneumonia severity index (PSI) score (P = 0.016, OR = 1.022, 95% CI: 1.004 – 1.041) and invasive mechanical ventilation (P = 0.037, OR = 4.543, 95% CI: 1.092 – 18.898) on admission, and the risk factors associated with in-hospital mortality in elderly SCAP were sequential organ failure assessment (SOFA) score (P = 0.006, OR = 1.240, 95% CI: 1.063 – 1.446) and

combined with coronary artery disease on admission ($P=0.037$, $OR=2.834$, 95% CI: 1.066 – 7.534). ***Conclusion*** In-hospital mortality for SCAP is high. PSI score and invasive mechanical ventilation are risk factors for in-hospital mortality of non-elderly patients with SCAP, and SOFA score and combined with coronary artery disease on admission are risk factors for in-hospital mortality of elderly patients with SCAP.

Key words severe community-acquired pneumonia; aged; mortality; risk factors; SOFA score; PSI score

Fund programs National Natural Science Foundation of China (Nos. 82074411,81774222); Science and Technology Innovation Team Support Program for Universities in Henan Province (No. 22IRTSTHN029); Major Program of Traditional Chinese Medicine Scientific Research of Henan Province (No. 2021ZYZD04); Traditional Chinese Medicine Scientific Research Program of Henan Province (No. 2019ZYBJ05); Outstanding Talent Training Program of Traditional Chinese Medicine of Henan Province (No. 2022ZYFY04)

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The laboratory biomarkers of disease activity in ankylosing spondylitis

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Abstract ***Objective*** To analyze the correlation between different laboratory biomarkers and disease activity in ankylosing spondylitis and to compare their specificity and sensitivity in assessing disease activity. ***Methods*** Spearman correlation or Pearson correlation was used to analyze the correlation between disease activity and laboratory biomarkers. Receiver operating characteristic (ROC) was used to compare the sensitivity and specificity of each laboratory biomarker in evaluating disease activity. ***Results*** Hypersensitive C-reactive protein, fibrinogen, D-dimer, erythrocyte sediment rate, C-reactive protein, immuno-inflammatory index (platelet count × neutrophil count/lymphocyte count), fibrinogen/albumin ratio, albumin and pro-albumin were correlated with disease activity. The ratio of fibrinogen to albumin, fibrinogen, erythrocyte sedimentation rate, immuno-inflammatory index, C-reactive protein and hypersensitive C-reactive protein had good values in determining the disease activity. ***Conclusion*** Different laboratory biomarkers are correlated with the disease activity of ankylosing spondylitis, and some of them have better discriminating values for the disease activity.

Key words ankylosing spondylitis; disease activity; laboratory biomarkers; specificity; sensibility

Fund programs National Natural Science Foundation of China (No. 81901668). Beijing Jishuitan Hospital Nova Program (No. XKXX – 202112)

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