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老年肺炎患者血清 Apelin-13 水平与疾病严重程度和预后的相关性研究*

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摘要 目的:探讨与研究老年肺炎患者血清 Apelin-13 水平与疾病严重程度和预后的相关性。**方法:**采用回顾性研究方法,2018 年 3 月到 2021 年 2 月选择在延安大学咸阳医院住院诊治的老年肺炎患者 78 例作为研究对象,检测血清 Apelin-13 水平,使用急性生理学及慢性健康状况评分系统(APACHE II)、CT 严重程度指数(CTSI)、序贯性器官功能衰竭评分(SOFA)评定患者的疾病严重程度,随访患者的预后并进行相关性分析。**结果:**所有患者随访到 2021 年 7 月 1 日,平均随访时间为 18.47±2.82 个月,死亡 18 例(死亡组),占比 23.1%。死亡组的性别、年龄、生活行为、体重指数、病程、合并疾病等与非死亡组对比无差异($P>0.05$),但血清 Apelin-13 表达水平具有差异,且死亡组较非死亡组低($P<0.05$)。死亡组的 APACHE II 评分、SOFA 评分、CTSI 评分高于非死亡组($P<0.05$)。在 78 例患者中,Pearson 分析显示血清 Apelin-13 水平与 APACHE II 评分、SOFA 评分、CTSI 评分存在负相关性($P<0.05$)。多因素 logistic 回归分析显示:血清 Apelin-13 水平($OR=3.770$)、APACHE II 评分($OR=3.624$)、SOFA 评分($OR=2.422$)、CTSI 评分($OR=1.842$)都为影响患者预后死亡的重要因素($P<0.05$)。**结论:**老年肺炎患者血清 Apelin-13 水平呈现低表达状况,与患者的 APACHE II 评分、SOFA 评分、CTSI 评分等疾病严重程度指标存在相关性,也是影响患者预后死亡的重要因素。

关键词:老年人肺炎;Apelin-13;急性生理学及慢性健康状况评分系统

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Study on the Correlation between Serum Apelin-13 Level and Disease Severity and Prognosis in Elderly Patients with Pneumonia*

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ABSTRACT Objective: To explore and study the correlation between serum Apelin-13 level and disease severity and prognosis in elderly patients with pneumonia. **Methods:** Used retrospective research methods, from March 2018 to February 2021, 78 cases of elderly patients with pneumonia who were hospitalized in Xianyang Hospital of Yan 'an University were selected as the research subjects. The serum Apelin-13 levels were detected and the APACHE II, CTSI, SOFA were used to assess the severity of the patient's disease, followed up the prognosis of the patient and given correlation analysis. **Results:** All patients were followed up until July 1, 2021. The average follow-up time were 18.47±2.82 months. There were 18 cases were died (death group), accounted for 23.1%. The gender, age, life behavior, body mass index, course of disease, and co-morbidities of the death group showed no difference compared with the non-death group ($P>0.05$), but the expression level of serum Apelin-13 in the death group was lower than that in the non-death group ($P<0.05$). The APACHE II scores, CTSI scores and SOFA scores of the death group were higher than that of the non-death group ($P<0.05$). In the 78 patients, Pearson analysis showed that there were negative correlation between serum Apelin-13 level and APACHE II scores, CTSI scores and SOFA scores. Logistic regression analysis showed that serum Apelin-13 level ($OR=3.770$), APACHE II score ($OR=3.624$), CTSI scores ($OR=2.422$) and SOFA scores ($OR=1.842$) were important factors affected the prognosis of death ($P<0.05$). **Conclusion:** The level of serum Apelin-13 in elderly patients with pneumonia presents low expression state, which are correlated with the APACHE II scores, CTSI scores and SOFA scores of the patient, and are also important factors affecting the prognosis and death of the patient.

Key words: Elderly pneumonia; Apelin-13; Acute physiology and chronic health status scoring system

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前言

肺炎是影响人类健康的重要疾病,多发病于老年人,具有极高的治疗费用、致残率与死亡率^[1]。老年肺炎在临床上主要表现为呼吸急促、意识丧失、发热、咳嗽、咳痰等症状,肺炎的病情复杂且进展快^[2-4]。程度较轻的老年肺炎患者可在门诊或普通住院病房治疗,但重症老年肺炎在短时间内便可出现呼吸窘迫、血流动力学不稳定,需立即住重症监护病房治疗,为此加强早期诊断与预后评估具有重要价值^[5,6]。目前已有多种评估肺炎严重程度度的工具,但均存在一定不足,或在操作上比较复杂^[7]。例如:血常规指标在肺炎患者中可表现异常情况,但对于肺炎的诊断敏感性与特异性有待提供^[8]。急性生理学及慢性健康状况评分系统(Acute physiology and chronic health evaluation scoring system, APACHE II)与 CT 严重程度指数(Computed Tomography Severity Index, CTSI)可用于对肺炎患者的病情严重程度进行分级,序贯性器官功能衰竭评分(Sequential Organ Failure Assessment, SOFA)是一种在肺炎中常用于反映疾病严重程度以及预测病情预后的系统,该系统可用于动态检测、反复评估病情,具有较高的预测价值。但 APACHE II 评分与 SOFA 评分存在操作复杂等局限性,为此在临床上需要寻找更加简单有效的生物学指标,希望在快速评估肺炎患者的病情、预后判断发挥价值^[9,10]。血清 Apelin 水平与心血管疾病的严重程度存在一定的相关性,能拮抗血管紧张素 II 的作用,与动脉斑块的发展及其稳定性有关^[11,12]。本文探讨与研究了老年肺炎患者血清 Apelin-13 水平与疾病严重程度和预后的相关性,旨在为老年肺炎临床诊治提供一定的思路。

1 资料与方法

1.1 研究对象

采用回顾性研究方法,选择 2018 年 3 月到 2021 年 2 月在延安大学咸阳医院住院诊治的老年肺炎患者 78 例作为研究对象。

纳入标准:年龄 60-90 岁;符合肺炎的诊断标准;临床资料完整;具有机械通气应用的指征;经医学伦理委员会批准;患者

知情同意本研究。

排除标准:长期使用华法林及低分子肝素者;合并有慢阻肺、肺结核、间质性肺病等肺部疾病者;合并有传染性疾病的患者;曾有新冠肺炎病史或者密切接触史的患者;合并有恶性肿瘤的患者;合并有肝肾功能衰竭的患者;入院后 24 h 内死亡者。

1.2 血清 Apelin-13 检测

采集所有患者的肘静脉血 2-3 mL,不抗凝,4℃放置 30 min,然后 3000 rpm/min 离心 10 min,取上层血清后,将其置于医用冰箱待用。采用酶联免疫法(试剂盒:北京北方伟业发展有限公司)检测血清 Apelin-13 水平。

1.3 调查资料

1.3.1 调查一般资料 调查患者的一般资料,包括病程、合并疾病、APACHE II 评分等。APACHE II 评分为四个维度评分之和,分别为年龄、存在严重脏器功能不全或免疫损害、格拉斯哥昏迷评分、生理指标等,分数越高,病情越差。

1.3.2 患者死亡与存活情况 所有患者随访到 2021 年 7 月 1 日,记录患者的死亡与存活情况。死亡标准:患者家属放弃治疗,自行出院,后经电话随访证明患者已死亡;治疗后患者症状或体征无好转,甚至病情加重,证实为临床死亡。

1.4 统计方法

选择 SPSS18.00 软件进行分析,计数资料以 n/%表示,计量资料采用($\bar{x} \pm s$)表示,对比采用 t 检验、 χ^2 检验分析等,采用 Pearson 分析进行相关性分析,采用 logistic 回归分析进行多因素分析,检验水准为 $\alpha=0.05$ 。

2 结果

2.1 预后情况

所有患者随访到 2021 年 7 月 1 日,平均随访时间为 18.47 ± 2.82 个月,死亡 18 例(死亡组),占比 23.1%,非死亡患者为 60 例,为非死亡组。

2.2 病理特征对比分析

死亡组的性别、年龄、生活行为、体重指数、病程、合并疾病等与非死亡组对比无差异($P>0.05$),但血清 Apelin-13 表达水平具有差异,且死亡组较非死亡组低($P<0.05$)。见表 1。

表 1 病理特征对比分析

Table 1 Comparative analysis of pathological features

Groups	n	Gender (male/female)	Age(years)	Smoking(n)	Drinking(n)	Body mass index(kg/m ²)	Duration (d)	Diabetes mellitus(n)	High blood pressure(n)	Apelin-13
Death group	18	9/9	69.25±1.68	9(50.0%)	11(61.1%)	22.17±1.48	9.73±0.34	5(27.8%)	7(38.9%)	246.30± 29.28
No death group	60	31/29	69.33±2.18	31(51.7%)	38(63.3%)	22.23±2.17	9.74±0.24	16(26.7%)	23(38.3%)	456.10± 31.00
t or χ^2		0.015	0.123	0.015	0.029	0.087	0.043	0.009	0.002	29.732
P		0.903	0.893	0.903	0.865	0.934	0.976	0.924	0.964	0.000

2.3 APACHE II 评分、SOFA 评分、CTSI 评分对比

死亡组的 APACHE II 评分、SOFA 评分、CTSI 评分高于非死亡组($P<0.05$)。见表 2。

2.4 相关性分析

在 78 例患者中,Pearson 分析显示血清 Apelin-13 水平与 APACHE II 评分、SOFA 评分、CTSI 评分存在负相关性($P<0.05$)。见表 3。

表 2 两组 APACHE II 评分、SOFA 评分、CTSI 评分对比(分,均数±标准差)

Table 2 Comparison of APACHE II score, SOFA score and CTSI score between the two groups (scores, mean ± standard deviation)

Groups	n	APACHE II score	SOFA score	CTSI score
Death group	18	30.04±3.28	12.48±1.82	6.69±0.63
No death group	60	18.76±4.16	6.28±0.78	4.66±0.33
t		13.742	11.024	8.173
P		0.000	0.000	0.005

表 3 老年肺炎患者血清 Apelin-13 水平与疾病严重程度的相关性(n=78)

Table 3 Association of serum Apelin-13 levels with disease severity in elderly patients with pneumonia (n=78)

Indicators	APACHE II score	SOFA score	CTSI score
r	-0.762	-6.485	-6.111
P	0.000	0.000	0.000

2.5 影响因素分析

在 78 例患者中,以随访预后死亡作为因变量,以血清 Apelin-13 水平与 APACHE II 评分作为自变量,多因素 logistic

回归分析显示:血清 Apelin-13 水平(OR=3.770)、APACHE II 评分(OR=3.624)、SOFA 评分(OR=2.422)、CTSI 评分(OR=1.842)都为影响患者预后死亡的重要因素($P<0.05$)。见表 4。

表 4 影响老年肺炎患者预后的多因素 logistic 回归分析(n=78)

Table 4 Multivariate Logistic regression analysis affecting prognosis of elderly patients with pneumonia (n=78)

Factors	OR	95%CI	P
Apelin-13	3.770	2.665-5.224	0.012
APACHE II score	3.624	1.156-5.392	0.009
SOFA score	2.422	1.333-5.681	0.013
CTSI score	1.842	1.111-4.824	0.018

3 讨论

肺炎是呼吸内科的常见疾病,易产生细胞缺氧、机体代谢功能障碍等,疾病的不断发展将会造成气管衰竭等,也是机体免疫与炎症反应失衡导致的疾病^[13]。该病多发生于老年人,存在多种基础疾病等情况,如果治疗不及时,患者严重情况下可导致死亡^[14]。特别是老年人由于高龄,身体机能弱化的同时,支气管黏膜逐渐萎缩,其腺体也增生肿大、纤毛运动减缓、肺泡弹性蛋白减少、胸廓和组织细胞的弹性降低,导致呼吸系统的功能逐渐退化,是各类细菌、病毒种植于肺部组织的重要原因^[15,16]。当前有关 Apelin-13 与肺炎的研究甚少,因此本研究创新的探究老年肺炎患者血清 Apelin-13 水平与疾病严重程度和预后的相关性。研究显示所有患者随访到 2021 年 7 月 1 日,平均随访时间为 18.47±2.82 个月,死亡 18 例(死亡组),占比 23.1%,表明老年肺炎患者存在一定的死亡率。

Apelin 是一种 G 蛋白耦联受体血管紧张素受体--AT I 相关受体蛋白的天然配体,广泛分布于体内多个器官和系统,人的 Apelin 基因包含 3 个外显子和 2 个内含子,信使 RNA 长度为 2673 bp,具有多个潜在的翻译后加工蛋白酶切位点,可被裂解成活性多肽,Apelin-13 属于该基因家族^[17]。Apelin-13 主要表达于人体乳腺、肺、脑、心脏、脂肪等组织,该基因被发现能作用于心肌肥大以及心房纤维化,也能抑制由 Ang II 基因所诱导产

生的心肌细胞肥大^[18]。Apelin-13 是健康人血浆的主要亚型,作为新型神经保护因子,该因子被发现能作用于神经细胞的凋亡,缓解损伤,并且能够阻滞心肌中缺血-再灌注对神经造成的损害,发挥其所特有的神经保护作用^[19]。本研究显示死亡组的性别、年龄、生活行为、体重指数、病程、合并疾病等与非死亡组对比无差异,但血清 Apelin-13 表达水平具有差异,且死亡组较非死亡组低。这一结果与 Dean P 的报道^[20]相符,表明性别、年龄、生活行为等与肺炎患者的影响较小。

近年来,肺炎患者的临床诊治水平虽得以长足发展,但降低肺炎死亡率仍是临床研究的重点^[21,22]。APACHE II 评分作为新兴的评分系统,具有科学性以及权威性,用于临床上评价危重患者病情状况,具有重要的指导作用,其评分与病情呈正比。通过该系统对患者病情的严重程度以及预后的情况进行评估,为临床上准确评估病情及预后开拓新的思路,并提供一定的借鉴^[23,24]。SOFA 评分与患者的重症比例呈相同趋势。CTSI 评分是早期评估胰腺及胰周情况将胰腺炎 CT 改变状况的评价系统,在预测疾病严重程度具有一定的优势。不过 CTSI 评分依赖影像学检查,对检查设备要求比较高,且其结果判读存在一定的主观性。本研究显示死亡组的 APACHE II 评分、SOFA 评分、CTSI 评分高于非死亡组。这一结果与 Maca J 等人一致^[25],即以上三种评分系统对于流感相关肺炎具有最佳的预测价值,表明以上三种评分系统在肺炎病情评定中具有一定的可行性,

但 APACHE II 评分、SOFA 评分、CTSI 评分需要收集患者的大量临床指标,在操作中比较复杂,在早期评估老年肺炎患者的病情时,具有局限性^[26]。特别是 APACHE II 评分较 SOFA 评分、CTSI 评分更为复杂,并且与其他评分系统相比,在临床实用性中受到一定限制。

由于受到人口老年化加剧、病原体不断变迁等因素的影响,当前老年肺炎的发病率不断增加^[27]。Apelin 在肺部组织中分布广泛,与许多呼吸系统的调节功能存在相关性^[28]。Apelin-13 能够激活 PI3K/Akt 信号通路,作用于脑缺血再灌注,进而抑制损伤,还可诱导表皮内钙增加,诱导肠道内分泌细胞 ERK1/2 的激活^[29]。同时 Apelin 的上调能够缓解由缺氧所导致的血管收缩,可调节下游蛋白抑制肺动脉高压的发生^[30,31]。本研究 Pearson 分析显示:老年肺炎患者的血清 Apelin-13 水平与 APACHE II 评分、SOFA 评分、CTSI 评分存在负相关性($r=-0.762, P=0.000$);多因素 logistic 回归分析显示:血清 Apelin-13 水平(OR=3.770)、APACHE II 评分(OR=3.624)、SOFA 评分(OR=2.422)、CTSI 评分(OR=1.842)都为影响患者预后死亡的重要因素。这一结果与 Ye C 等人^[32]的结果一致, Ye C 等人研究发现,经刺激 Apelin 表达,抑制炎症细胞因子,减轻肺炎症和纤维化。从机制分析原因可知, Apelin-13 可促进生成 NO, 参与炎症反应、抗氧化作用,从而抑制肺功能的恶化,导致患者预后变差,且 Apelin-13 可参与调节机体中免疫炎症因子的生成途径,从而对肺功能重构起积极作用,也可反映患者的病情^[33,34]。但本研究也存在一定的缺陷,所涉及的样本病例数目较少,且因年龄及体重等因素对 Apelin-13 的检测,故临床结果存在一定程度的偏倚,将在后续研究中继续进行机制等内容的深入分析。

总之,老年肺炎患者血清 Apelin-13 水平呈现低表达状况,与患者的 APACHE II 评分、SOFA 评分、CTSI 评分等疾病严重程度指标存在相关性,也是影响患者预后死亡的重要因素。

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