

doi: 10.3978/j.issn.2095-6959.2022.01.021

View this article at: <https://dx.doi.org/10.3978/j.issn.2095-6959.2022.01.021>

慢性阻塞性肺疾病急性加重期患者肺功能及血清细胞因子水平变化及其与吸烟、体重指数的相关性

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[摘要] 目的: 观察研究慢性阻塞性肺疾病急性加重期(acute exacerbation of chronic obstructive pulmonary disease, AECOPD)患者肺功能和血清细胞因子水平变化情况, 及其与患者吸烟、体重指数(body mass index, BMI)的相关性。方法: 选取2020年6月至2020年12月于海南省人民医院海南医学院附属海南医院接受治疗的102例AECOPD患者作为研究对象, 将吸烟的50例患者纳入吸烟组, 将已戒烟或无吸烟史的52例患者纳入非吸烟组, 同时选取50例院内同期进行身体检查的健康志愿者纳入对照组。测定比较3组对象的1秒用力呼气容积(forced expiratory volume in one second, FEV₁)和一氧化碳弥散量占预计值百分率(percentage of carbon monoxide diffusion to the predicted value, DLco%), 同时收集三组对象降钙素原(procalcitonin, PCT)、C反应蛋白(C-reactive protein, CRP)、白细胞介素-6(interleukin-6, IL-6)和肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)等血清细胞因子表达情况, 并分析肺功能及血清细胞因子水平与患者吸烟指数(smoking index, SI)和BMI之间的相关性。结果: 吸烟组AECOPD患者的FEV₁和DLco%均显著低于非吸烟组和对照组, 差异具有统计学意义($P < 0.05$)。吸烟组AECOPD患者PCT、CRP、IL-6和TNF- α 的血清表达水平均显著高于非吸烟组和对照组, 差异具有统计学意义($P < 0.05$)。高SI患者的FEV₁和DLco%均显著低于低SI患者, 差异具有统计学意义($P < 0.05$)。高SI患者PCT、CRP、IL-6和TNF- α 的血清表达水平均显著高于低SI患者, 差异具有统计学意义($P < 0.05$)。AECOPD患者的SI与PCT、CRP、IL-6和TNF- α 呈明显正相关性($P < 0.05$), 与肺功能情况呈明显负相关($P < 0.05$); AECOPD患者的BMI与PCT、IL-6和TNF- α 呈明显正相关($P < 0.05$), 与肺功能无明显相关($P > 0.05$)。结论: 长期吸烟的AECOPD患者PCT、CRP、IL-6和TNF- α 等血清细胞因子的表达水平显著更高, 而肺功能状况显著更差。AECOPD患者的吸烟情况和体质量状况均是衡量患者体内炎症因子表达的重要指标, 与患者血清细胞因子的变化具有明显相关性, 对于高BMI的吸烟患者应当予以更多关注。

[关键词] 慢性阻塞性肺疾病; 肺功能; 降钙素原; 超敏反应蛋白; 白细胞介素-6; 肿瘤坏死因子; 吸烟; 体重指数

收稿日期 (Date of reception): 2021-03-22

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基金项目 (Foundation item): 海南省卫生计生行业科研项目 (19A200037)。This work was supported by the Health and Family Planning Industry Research Project of Hainan Province, China (19A200037).

Changes of lung function and serum cytokine levels in acute exacerbation of chronic obstructive pulmonary disease patients and their correlation with smoking and body mass index

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Abstract

Objective: To observe and study the changes of lung function and serum cytokine levels in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) and their correlation with smoking and body mass index (BMI). **Methods:** A total of 102 patients with AECOPD who were treated in our hospital from June 2020 to December 2020 were selected as the research objects; 50 patients who smoked were included in the smoking group, and 52 patients who had quit or had no smoking history were included in the non-smoking group; at the same time, 50 healthy volunteers who underwent physical examinations in the hospital at the same time were selected into the control group. The forced expiratory volume in one second (FEV_1) and the percentage of carbon monoxide diffusion to the predicted value (DLco%) of the three groups of subjects were determined and compared; and the expression of serum cytokines such as procalcitonin (PCT), high-sensitivity C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) were collected in three groups at the same time, and the correlation between lung function and serum cytokine levels, smoking index (SI) and BMI were analyzed. **Results:** The FEV_1 and DLco% of AECOPD patients in the smoking group were significantly lower than those in the non-smoking group and the control group, and the difference was statistically significant ($P < 0.05$). From the perspective of serum cytokine expression, the serum expression levels of PCT, CRP, IL-6 and TNF- α in AECOPD patients in the smoking group were significantly higher than those in the non-smoking group and the control group, and the difference was statistically significant ($P < 0.05$). The FEV_1 and DLco% of high-SI patients were significantly lower than those of low-SI patients, and the difference was statistically significant ($P < 0.05$). In terms of serum cytokine expression, the serum expression levels of PCT, CRP, IL-6 and TNF- α in patients with high SI were significantly higher than those in patients with low SI, and the difference was statistically significant ($P < 0.05$). The SI of AECOPD patients was significantly positively correlated with PCT, CRP, IL-6 and TNF- α ($P < 0.05$), and was significantly negatively correlated with lung function ($P < 0.05$); and the BMI of AECOPD patients was significantly positively correlated with PCT, IL-6 and TNF- α ($P < 0.05$), but not significantly correlated with lung function ($P > 0.05$). **Conclusion:** AECOPD patients with long-term smoking history have significantly higher expression levels of serum cytokines such as PCT, CRP, IL-6 and TNF- α , while their lung function status is significantly worse. The smoking status and body mass status of AECOPD patients are important indicators to measure the expression of inflammatory factors in the patient's body, and have obvious correlation with the changes of patients' serum cytokines. More attention should be paid to smoking patients with high BMI.

Keywords

chronic obstructive pulmonary disease; lung function; procalcitonin; hypersensitivity protein; interleukin-6; tumor necrosis factor; smoking; body mass index

慢性阻塞性肺疾病(chronic obstructive pulmonary disease, COPD)是目前呼吸科门诊中较为常见的一种疾病, 临床医学调查^[1-3]显示: COPD的发病率正逐年上升, 由于COPD的发病会导致不完全可逆的呼吸系统损伤, 因此开展COPD相关的流行病学调查和患病相关因素、危险因素分析具有重要意义。在临床诊疗实践中, 许多COPD患者往往有多年吸烟史, 且伴有其他基础代谢疾病, 病例个体呈现出较为多样化的特点, 但总体来看, COPD患者的血液检查结果往往呈现明显的炎症因子高表达, 而在慢性阻塞性肺疾病急性加重期(acute exacerbation of chronic obstructive pulmonary disease, AECOPD)患者中则更甚, 血清细胞炎症因子的表达情况往往与患者病情发展相关^[4-5]。本研究以AECOPD患者为基本研究对象, 对比分析患者血清细胞因子水平的变化情况与患者吸烟状况、体重指数(body mass index, BMI)之间的相关性, 以期对AECOPD患者的诊疗分析提供参考借鉴。

1 对象与方法

1.1 对象

选取2020年6月至2020年12月于海南省人民医院海南医学院附属海南医院接受治疗的102例AECOPD患者作为研究对象, 所有纳入研究的患者对象均符合下列筛选标准。纳入标准: 1)既往COPD病史, 此次就医确诊为AECOPD; 2)临床症状和指征符合2021年修订版《慢性阻塞性肺疾病诊治指南》中的相关诊断标准^[6]; 3)参与研究前1周内无明显病情加重; 4)意识状态良好, 能够较好地配合研究开展。排除标准: 1)合并存在严重脏器功能不足或器质性病变; 2)患者病历资料不全, 无法开展研究; 3)合并存在其他严重基础代谢疾病或肺部疾病; 4)合并恶性肿瘤。将患者分为吸烟组和非吸烟组(非吸烟患者为无吸烟史或已戒烟3年以上患者), 吸烟组共50例患者, 非吸烟组52例患者, 同时选取50例同期在海南省人民医院海南医学院附属海南医院接受身体检查的健康志愿者纳入对照组, 对照组均为排除COPD及其他疾病的健康志愿者, 且无吸烟史或已戒烟3年以上。

1.2 方法

1.2.1 肺功能检测

利用比利时Medisoft生产的肺功能仪5500作为肺功能检查仪器, 由具有丰富操作经验的同一熟练程度的医师进行检测操作, 按照最新肺功能检

查指南^[7]对受试者进行检查, 在受试者吸入硫酸沙丁胺醇气雾剂300 μg 后20 min对患者进行1秒用力呼气容积(forced expiratory volume in one second, FEV₁)测试, 再进行一口气弥散功能检测, 测定患者的一氧化碳弥散量占预计值百分率(percentage of carbon monoxide diffusion to the predicted value, DLco%), 测定时受试者最大屏气时间不超过7 s, 每项各测定2次取平均值作为检测结果。

1.2.2 血清细胞因子水平检测

1)降钙素原(procalcitonin, PCT)检测: 在受试者确认参与研究后1周内进行排序检测, 于检测当天早上8点抽取受试者静脉, 取1/2静置后进行血浆离心获得血清, 采用罗氏诊断产品有限公司生产的601全自动电化学发光测定仪测定血清PCT水平, 试剂盒采用罗氏诊断产品有限公司生产的降钙素原检测试剂盒。2)C反应蛋白(C-reactive protein, CRP)检测: 取余下1/2标本利用雅培C16000E全自动生化分析仪测定对象的CRP水平, 试剂盒采用德赛诊断系统有限公司生产的C-反应蛋白测定试剂盒(免疫透射比浊方法)。3)白细胞介素-6(interleukin-6, IL-6)和肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)检测: 再次抽取受检者静脉血5 mL, 于离心机内离心后获得血清送检, 采用ELISA法测定TNF- α 和IL-6的质量浓度, 试剂盒为上海科敏生物科技有限公司产品, 测定过程严格按照相关说明完成。

1.3 观察指标

1)比较吸烟组AECOPD患者、非吸烟组AECOPD患者和对照组志愿者的FEV₁、DLco%以及PCT、CRP、IL-6和TNF- α 的血清表达水平。2)比较高吸烟指数(SI)患者(SI \geq 400)和低SI患者(SI<400)的FEV₁、DLco%以及PCT、CRP、IL-6和TNF- α 的血清表达水平。3)分析AECOPD患者SI、BMI与患者肺功能状况、血清细胞因子(PCT、CRP、IL-6和TNF- α)水平的相关性。

1.4 统计学处理

应用SPSS 18.0统计软件分析数据, 计量资料以均数 \pm 标准差($\bar{x}\pm s$)表示, 两两比较 t 检验, 多组均数比较采用方差 F 检验, 相关性分析采用Pearson分析, 以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 各组基线资料情况比较

吸烟组、非吸烟组与对照组性别比、年龄等

表4 AECOPD患者SI与患者肺功能状况、血清细胞因子水平的相关性分析

Table 4 Correlation analysis of SI, lung function status and serum cytokine levels in patients with AECOPD

指标	<i>r</i>	<i>P</i>
PCT	0.591	<0.0001
CRP	0.483	<0.05
IL-6	0.625	<0.0001
TNF- α	0.574	<0.05
FEV ₁	-0.490	<0.05
DLco%	-0.387	<0.05

表5 AECOPD患者BMI与肺功能状况、血清细胞因子水平的相关性分析

Table 5 Correlation analysis of BMI with lung function status and serum cytokine levels in AECOPD patients

指标	<i>r</i>	<i>P</i>
PCT	0.489	<0.05
CRP	0.172	>0.05
IL-6	0.518	<0.05
TNF- α	0.475	<0.05
FEV ₁	-0.069	>0.05
DLco%	-0.124	>0.05

3 讨论

COPD是目前临床上较为严重的呼吸系统疾病, 由于COPD会给患者带来严重的肺功能损伤, 使患者生活质量下降, 长期的COPD患病还会严重增加患者的病死率^[8-10], 且随着病程的延长, 许多COPD患者的预后也随之变差, 因此, COPD的医治和相关因素分析对于减轻病情和提升患者生活质量具有重要意义。年龄过大、吸烟、肥胖以及其他基础代谢疾病均为COPD发病的独立危险因素^[11-12], 但由于患者个体的差异, 许多患者的基础代谢疾病也会对研究造成影响, 探知COPD患者肺功能情况以及血清细胞因子变化情况与SI指数、BMI等量化指标之间的关系, 对于制订和修正诊疗方案具有重要价值, 以提升患者的治愈率并改善预后。

从COPD的发病机制来看^[13-15], COPD的发生

常常与气管上皮细胞的长期损伤有关, 患者往往呈现明显的支气管炎或肺气肿症状, 且由于受患者工作环境或个人习惯的影响, 长期吸入某些有毒有害气体颗粒物, 患者的呼吸功能也存在进行性受限的趋势。不同的病情发展周期呈现出不同的特点, 尤其处于病情发展期的AECOPD患者, 其呼吸功能障碍更加明显, 患者生活质量严重下降, 但COPD的发生牵涉许多方面的原因, 单一归因于吸烟所带来的理化刺激或是不良生活习惯无益于患者的诊断和治疗, 只有深入探究和分析AECOPD患者吸烟情况和体重对血清细胞因子水平和肺功能影响, 对患者进行针对性的治疗和处理则更具价值。

从本研究所选取的观察指标来看, PCT是目前感染医学研究中最为常用的研究指标之一^[16-17], 对反映患者细胞内毒素水平具有较高的灵敏性, 且能区分于患者的正常免疫表达, 在衡量AECOPD患者受吸烟或是其他环境因素影响程度上具有重要意义; CRP和IL-6是经典的炎症反应标志物, 在许多临床研究中均被选取为首要标志检测物^[18-19], 由于两者在中性粒细胞中均发挥慢性炎症的介质作用, 因此两者在评估AECOPD炎症中均具有良好的价值; 而TNF- α 则是关键的COPD炎症因子, 在COPD的形成机制中占据重要地位, 可以在临床检查中作为AECOPD基础的判断因素^[20-21]。上述指标的选取均能从不同的角度来评估患者的炎症情况, 从而为临床治疗提供参考依据。

从研究结果来看, 吸烟组AECOPD患者的肺功能指标均弱于非吸烟组和对照组, 同时吸烟组AECOPD患者血清PCT、CRP、IL-6和TNF- α 等表达水平均高于非吸烟组和对照组, 可见吸烟患者在患病后炎症更加严重。而高SI患者的肺功能指标均显著低于低SI患者, 高SI患者PCT、CRP、IL-6和TNF- α 的血清表达水平均高于低SI患者, 这些结果均提示了高SI患者较低SI患者存在更加严重的炎症反应, 在入院时可以通过SI指数筛查来对患者作出更加全面的判断。而从相关性分析结果来看, AECOPD患者的SI与PCT、CRP、IL-6和TNF- α 呈明显正相关性, 与肺功能情况呈明显负相关; 但AECOPD患者的BMI与PCT、IL-6和TNF- α 呈明显正相关, 与肺功能无明显相关性, 可见患者的炎症反应与SI和BMI具有重要关系, 而患者的肺功能更多与SI的变化有关, 但与BMI这一较为粗略的身体指标无明显相关性, 推测BMI在AECOPD患者群体中差异较大, 因此其相关性有限。

综上所述, 长期吸烟的AECOPD患者PCT、

CRP、IL-6和TNF- α 等血清细胞因子的表达水平显著更高, 而肺功能显著更差。AECOPD患者的吸烟情况和体质量状况均是衡量患者体内炎症因子表达的重要指标, 但AECOPD患者的体质量状况与患者肺功能状况无明显关系, 因此对于高BMI和高SI的AECOPD患者应当在前期接诊时予以更多的关注。

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本文引用: 洗少静, 陈庆芸. 慢性阻塞性肺疾病急性加重期患者肺功能及血清细胞因子水平变化及其与吸烟、体重指数的相关性[J]. 临床与病理杂志, 2022, 42(1): 144-150. doi: 10.3978/j.issn.2095-6959.2022.01.021

Cite this article as: XIAN Shaojing, CHEN Qingyun. Changes of lung function and serum cytokine levels in acute exacerbation of chronic obstructive pulmonary disease patients and their correlation with smoking and body mass index[J]. Journal of Clinical and Pathological Research, 2022, 42(1): 144-150. doi: 10.3978/j.issn.2095-6959.2022.01.021