

下肢动脉硬化闭塞症患者血清 IL-17 和 TNF- α 水平表达及其临床意义

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摘要: 目的 探讨下肢动脉硬化闭塞症 (arteriosclerosis obliterans, ASO) 患者血清白细胞介素 (interleukin, IL) -17 和肿瘤坏死因子 (tumor necrosis factor, TNF) - α 水平检测及临床意义。方法 选取 2016 年 5 月~2020 年 1 月于鞍山市鞍钢总医院住院治疗的下肢动脉硬化闭塞症患者 90 例为研究对象 (病例组), 其中正常组 78 例, 狭窄组 12 例; 选取同期健康体检者 92 例作为对照组。采用 Pearson 法分析患者血清 IL-17 与 TNF- α 的相关性。结果 病例组 IL-17 (812.94 ± 103.75 pg/ml) 和 TNF- α (74.28 ± 4.96 ng/L) 高于对照组 (421.58 ± 97.46 pg/ml, 30.44 ± 2.79 ng/L), 差异有统计学意义 ($t=26.235, 73.696$, 均 $P < 0.05$)。下肢动脉硬化闭塞症患者血清 IL-17 与 TNF- α 呈正相关 ($r=0.527$, $P < 0.05$)。狭窄组血清 IL-17 (894.27 ± 110.34 pg/ml) 和 TNF- α (79.26 ± 3.71 ng/L) 水平高于正常组 (653.29 ± 98.16 pg/ml, 53.18 ± 2.94 ng/L), 差异有统计学意义 ($t=7.790, 27.604$, 均 $P < 0.05$)。结论 下肢动脉硬化闭塞症患者血清 IL-17 和 TNF- α 明显增高, 二者与患者分期及预后均相关, 可能共同参与了下肢动脉硬化闭塞症的发生、发展。

关键词: 下肢动脉硬化闭塞症; 白细胞介素; 肿瘤坏死因子 - α

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Expression and Clinical Significance of Serum Levels of IL-17 and TNF- α in Patients with Arteriosclerosis Obliterans of Lower Extremity

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Abstract: Objective To investigate the serum levels of interleukin (IL)-17 and tumor necrosis factor (TNF) - α in patients with arteriosclerosis obliterans (ASO) of lower extremity and their clinical significance. **Methods** From May 2016 to January 2020, 90 patients with ASO in Ansteel Group General Hospital of Anshan City were selected as the research objects (case group), 78 cases in normal group and 12 cases in stenosis group. A total 92 healthy subjects were selected as the control group. Pearson method was used to analyze the correlation between serum IL-17, TNF- α and related indexes in patients with lower extremity ASO. **Results** IL-17 (812.94 ± 103.75 pg/ml) and TNF- α (74.28 ± 4.96 ng/L) in the case group were higher than those in the control group (421.58 ± 97.46 pg/ml, 30.44 ± 2.79 ng/L), the differences were statistically significant ($t=26.235, 73.696$, all $P < 0.05$). There was a positive correlation between serum IL-17 and TNF- α ($r=0.527, P<0.05$). The levels of serum IL-17 (894.27 ± 110.34 pg/ml) and TNF- α (79.26 ± 3.71 ng/L) in the stenosis group were higher than those in the normal group (653.29 ± 98.16 pg/ml, 53.18 ± 2.94 ng/L), and the differences were statistically significant ($t=7.790, 27.604$, all $P<0.05$). **Conclusion** IL-17 and TNF- α were highly expressed in the serum of patients with lower extremity ASO, and they were related to the stage and prognosis of patients, and may participate in the occurrence and development of ASO of lower limbs.

Keywords: lower extremity arteriosclerosis obliterans; interleukin-17; tumor necrosis factor- α

下肢动脉硬化闭塞症 (arteriosclerosis obliterans, ASO) 是临床血管外科常见疾病, 其发病率随年龄的增长而增加, 常给患者生活质量造成严重影响^[1]。Fontaine 分期在指导下肢动脉硬化闭塞症临床治疗中有重要意义, 但其无法准确用于分期诊断、病情风险及预后评估^[2-3]。因此, 寻找合适的生物标志物正确评估下肢动脉硬化闭塞症疾病进展, 对于疾病的治疗十分必要。白细胞介素 (interleukin, IL) -17 是一种由 T 淋巴细胞亚群分泌的促炎因子,

可间接参与动脉粥样硬化的形成^[4]。肿瘤坏死因子 (tumour necrosis factor, TNF) - α 不仅是调节粒细胞激活的重要细胞因子, 还是体内重要的炎症介质, 参与动脉粥样硬化的发生、发展^[5-6]。IL-17, TNF- α 均与动脉粥样硬化有关, 但二者与下肢动脉硬化闭塞症分期及预后的相关性有待进一步研究。本研究通过分析不同分期及预后下肢动脉硬化闭塞症患者血清 IL-17, TNF- α 表达水平, 以期对疾病的早期预测及预后改善提供参考指标, 现报道

如下。

1 材料与方法

1.1 研究对象 选取2016年5月~2020年1月于鞍山市鞍钢集团总医院住院治疗的90例下肢动脉硬化闭塞症患者为研究对象(病例组),男性48例,女性42例,年龄42~78(61.37 ± 10.03)岁;吸烟45例,饮酒36例;同期选取健康体检者92例作为对照组,男性46例,女性46例,年龄42~78(60.28 ± 9.46)岁;吸烟42例,饮酒32例。对照组和病例组年龄、性别、吸烟、饮酒情况比较,差异均无统计学意义(均 $P > 0.05$)。

纳入标准:①符合下肢动脉硬化闭塞症诊治指南^[7];②病例资料齐全,且经本院临床研究伦理委员会批准,所有研究对象均为自愿参加;③无影像学检查禁忌症者;④入组前1个月内均未服用过激素类、免疫抑制剂等。排除标准:①有多发性大动脉炎、血栓闭塞性脉管炎等其他原因引起的动脉闭塞性疾病者;②并发有心脏病、严重肝肾功能损伤、全身感染或恶性肿瘤等疾病者;③处于月经期女性。**1.2 仪器与试剂** IL-17 ELISA试剂盒(滁州仕诺达生物科技有限公司,货号:SND-H1814), TNF- α ELISA试剂盒(上海瓦兰生物科技有限公司,货号:E01593),全波长酶标仪(北京赛百奥科技有限公司,型号:Multiskan GO)。

1.3 方法

1.3.1 样品采集及保存:采集健康体检者体检当天、下肢动脉硬化闭塞症患者入院第二天晨起空腹静脉血样,3 000 r/min离心15 min后收集血清,置于 -80°C 保存待测。

1.3.2 血清IL-17, TNF- α 水平测定:采用酶联免疫吸附试验(enzyme linked immunosorbent assay, ELISA)法检测血清IL-17, TNF- α 水平,操作步骤严格按照试剂盒说明书进行。

1.3.3 下肢动脉硬化闭塞症患者Fontaine分期及预后评定^[7-8]:根据Fontaine分期标准,将患者分为I期组14例,II期组38例,III期组26例,IV期组12例。I期患者主要表现为无症状及体征或仅自述下肢轻微不适,动脉阻塞为单一部分,轻度受累;II期患者主要表现为间歇性或中重度跛行、红斑、趾温下降、动脉阻塞为单一部分,中重度受累或多部位轻度受累;III期患者主要表现为静息痛,肢体萎缩、紫绀,多部位、多水平受累;IV期患者主要表现为缺血性溃疡或坏疽,严重多部位、多水平受累。

患者行支架植入痊愈后再狭窄判定标准:支架内或支架两端5 mm内管腔直径狭窄 $\geq 50\%$ 。根据是否出现再狭窄,将患者分为正常组78例,狭窄

组12例。

1.4 统计学分析 利用SPSS 23.0对数据进行统计学分析,计量资料符合正态分布,以均数 \pm 标准差($\bar{x} \pm s$)表示,两组间比较行 t 检验,多组间比较采用单因素方差分析,进一步两两比较采用SNK- q 检验;计数资料以 n 表示,组间比较采用卡方检验;采用Pearson法分析下肢动脉硬化闭塞症患者血清IL-17与TNF- α 的相关性。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 对照组与病例组血清IL-17, TNF- α 水平表达比较 病例组血清IL-17($812.94 \pm 103.75\text{pg/ml}$), TNF- α ($74.28 \pm 4.96\text{ng/L}$)水平高于对照组($421.58 \pm 97.46\text{pg/ml}$, $30.44 \pm 2.79\text{ng/L}$),差异均有统计学意义($t=26.235$, 73.696 , 均 $P < 0.05$)。

2.2 下肢动脉硬化闭塞症患者血清IL-17与TNF- α 的相关性 见图1。Pearson法分析结果显示,下肢动脉硬化闭塞症患者血清IL-17与TNF- α 呈正相关($r=0.527$, $P < 0.05$)。

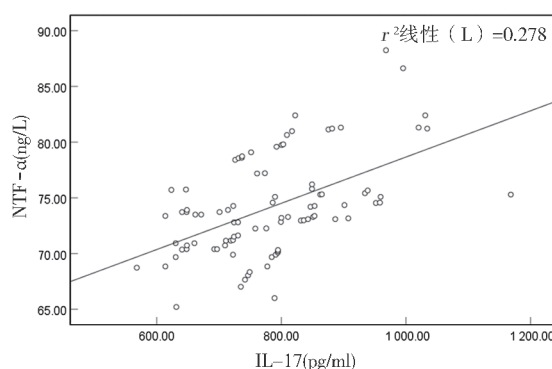


图1 下肢动脉硬化闭塞症患者血清IL-17与TNF- α 的相关性

2.3 不同Fontaine分期下肢动脉硬化闭塞症患者血清IL-17, TNF- α 水平表达比较 见表1。IV期组血清IL-17, TNF- α 水平均高于I期组、II期组和III期组,差异有统计学意义($t=10.631$, 44.078 ; 8.831 , 49.022 ; 2.879 , 15.308 , 均 $P < 0.001$)。III期组血清IL-17, TNF- α 水平均高于I期组和II期组,差异有统计学意义($t=9.586$, 36.192 ; 3.754 , 21.545 , 均 $P < 0.001$)。II期组血清IL-17, TNF- α 水平均高于I期组,差异有统计学意义($t=6.188$, 15.555 , 均 $P < 0.001$)。

2.4 不同预后组血清IL-17, TNF- α 水平表达比较 狭窄组血清IL-17($894.27 \pm 110.34\text{pg/ml}$), TNF- α ($79.26 \pm 3.71\text{ng/L}$)水平高于正常组($653.29 \pm 98.16\text{pg/ml}$, $53.18 \pm 2.94\text{ng/L}$),差异均有统计学意义($t=7.790$, 27.604 , 均 $P < 0.05$)。

表1 不同 Fontaine 分期组下肢动脉硬化闭塞症患者血清 IL-17, TNF- α 水平表达比较 ($\bar{x} \pm s$)

项目	Fontaine 分期				F	P
	I 期组 (n=14)	II 期组 (n=38)	III 期组 (n=26)	IV 期组 (n=12)		
IL-17 (pg/ml)	626.54 \pm 81.37	764.26 \pm 93.13	852.74 \pm 109.83	924.26 \pm 121.74	23.612	0.000
TNF- α (ng/L)	48.16 \pm 2.75	59.83 \pm 3.12	76.95 \pm 3.81	89.77 \pm 3.92	454.951	0.000

3 讨论

动脉粥样硬化始动因素可能是炎症反应, 血管内皮细胞损伤, 而下肢动脉硬化闭塞症是动脉粥样硬化病变的重要肢体表现^[9-10]。支架置入术是治疗下肢动脉硬化闭塞症的重要手段, 但术后再次狭窄仍是目前临床医师面临的重难点^[11]。

IL-17 可通过降解细胞外基质破坏动脉粥样硬化斑块稳定性, 在炎症反应中发挥重要作用^[12-13]。TNF- α 可通过诱发循环中及自身的单核细胞产生多种促炎因子, 促进炎症连锁反应^[14-15]。既往研究显示^[16-18], IL-17, TNF- α 与动脉粥样硬化有密切联系, 而本研究中下肢动脉硬化闭塞症患者血清 IL-17, TNF- α 水平高于健康人群, 与既往文献 IL-17, TNF- α 的表达趋势一致。提示血清 IL-17, TNF- α 水平表达异常可能与下肢动脉硬化闭塞症的发生有关。推测其可能是由于疾病初期, 患者体内炎症反应增加, 而 IL-17, TNF- α 作为炎症反应中的关键起始因子, 其水平表达均增加。本研究中血清 IL-17, TNF- α 表达水平随 Fontaine 分期增加而升高, 与韩玉明等^[19] 结果具有一致性。提示 IL-17, TNF- α 在下肢动脉硬化闭塞症的发病过程中可能起到重要作用, 临床可考虑将 IL-17, TNF- α 作为下肢动脉硬化闭塞症严重程度的评估指标, 指导疾病治疗。IL-17 与 TNF- α 的相关性结果进一步提示二者在下肢动脉硬化闭塞症疾病进展中可能发挥协同作用。此外, 下肢动脉硬化闭塞症术后血清 IL-17, TNF- α 水平升高可能造成机体炎症反应剧烈, 而术中机械性压力会导致内皮细胞和血管壁受损, 影响患者手术疗效, 增加再狭窄几率。

综上所述, IL-17, TNF- α 在下肢动脉硬化闭塞症患者血清中均呈高表达, 且随患者病情程度加深, 二者表达水平呈升高趋势。此外, 血清 IL-17, TNF- α 表达水平与下肢动脉硬化闭塞症患者术后再狭窄有一定的联系, 有可能成为预后预测及疾病治疗的潜在靶点。临床上可通过密切监测血清 IL-17, TNF- α 水平变化, 制定相应的干预措施, 避免患者发生支架内再狭窄, 降低支架置入术带来的高风险。本研究的不足之处为样本量较少, 今后将增加样本量进一步验证 IL-17, TNF- α 的具体作用机制及实际临床应用价值。

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