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# 血清肿瘤坏死因子 $\alpha$ 水平与肺癌患者疼痛程度的相关性研究\*

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**摘要 目的:**探究肺癌患者血清肿瘤坏死因子 $\alpha$ (tumor necrosis factor- $\alpha$ , TNF- $\alpha$ )水平与其疼痛程度的相关性。**方法:**选取2015年1月-2018年1月于我院进行治疗的53例肺癌患者为研究组,另选取60例同期于我院进行体格检查的健康个体为对照组,对比两组研究对象血清TNF- $\alpha$ 水平,使用视觉模拟量表(visual analogue scale, VAS)评估研究组患者的疼痛度,分析研究组患者的VAS评分、临床病理特征与其血清TNF- $\alpha$ 水平的相关性。**结果:**(1)研究组VAS评分及血清TNF- $\alpha$ 水平均明显高于对照组( $P<0.05$ );(2)肺癌患者血清TNF- $\alpha$ 水平与其VAS评分之间呈显著正相关( $r=0.986, P<0.05$ );(3)肺癌患者血清TNF- $\alpha$ 水平与其临床分期、浸润深度、是否存在淋巴结转移均显著相关( $P<0.05$ ),但与其年龄、性别无显著相关性( $P>0.05$ )。**结论:**肺癌患者血清TNF- $\alpha$ 水平与其疼痛度呈正相关,通过检测肺癌患者血清TNF- $\alpha$ 水平可辅助评估其疼痛度及临床预后。

**关键词:** TNF- $\alpha$ ; 肺癌; 疼痛度**中图分类号:** R734.2 **文献标识码:** A **文章编号:** 1673-6273(2019)16-3172-03

## Correlation of the serum Tumor Necrosis Factor Alpha Levels with the Pain in Patients with Lung Cancer\*

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**ABSTRACT Objective:** To investigate the correlation between the level of serum tumor necrosis factor-alpha (TNF- $\alpha$ ) and the degree of pain in patients with lung cancer. **Methods:** 53 patients with lung cancer who were treated in our hospital from January 2015 to January 2018 were selected as the study group, and 60 healthy individuals who underwent physical examination at the same time were selected as the control group. The levels of serum TNF- $\alpha$  were compared between the two groups. Visual analogue scale (VAS) was used to evaluate the degree of pain in the study group, and the correlation between VAS score, clinicopathological features and the levels of serum TNF- $\alpha$  was analyzed. **Results:** (1) The VAS score and serum TNF- $\alpha$  level in the study group were significantly higher than those in the control group ( $P<0.05$ ); (2) There was a significant positive correlation between serum TNF- $\alpha$  level and VAS score in lung cancer patients ( $r=0.986, P<0.05$ ); (3) The levels of serum TNF- $\alpha$  were significantly correlated with clinical stage, depth of invasion and lymph node metastasis ( $P<0.05$ ), but not with age and sex ( $P>0.05$ ). **Conclusion:** The level of serum TNF- $\alpha$  in patients with lung cancer was positively correlated with the degree of pain. Detecting the level of serum TNF- $\alpha$  in patients with lung cancer can help to evaluate the degree of pain and clinical prognosis.

**Key words:** TNF- $\alpha$ ; Lung cancer; Pain intensity**Chinese Library Classification(CLC):** R734.2 **Document code:** A**Article ID:** 1673-6273(2019)16-3172-03

### 前言

肺癌是呼吸系统中最常见的恶性肿瘤之一,其发病率具有恶性肿瘤首位,其中非小细胞癌为最为常见的病理类型。统计数据显示,2012年全球癌症发病数为1.41亿例,而肺癌发病例数为1600万,约占总数的12.9%,同年死于肺癌的人数高达1600万例<sup>[1-3]</sup>。肺癌的临床症状包括咳嗽、胸痛、气急、声音嘶哑

等,其中晚期肺癌患者最为突出的临床表现就是疼痛。有研究显示晚期肺癌患者的触发疼痛几率高达91%<sup>[4-6]</sup>,疼痛症状会造成患者出现诸如无法饮食、睡觉和活动、食欲下降、免疫力下降等症状<sup>[7]</sup>。随着人们对于医护工作质量要求的提高,肺癌患者的疼痛管理成为评价医护水平的重要方面。本研究结果显示肺癌患者血清TNF- $\alpha$ 水平与其疼痛度呈正相关,通过检测血清TNF- $\alpha$ 水平有助于量化其疼痛度及临床预后,结果报道如下。

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## 1 资料与方法

### 1.1 一般资料

选取 2015 年 1 月-2018 年 1 月于我院进行治疗的 53 例肺癌患者为研究组,另选取 60 例同期于我院进行体格检查的健康个体为对照组。研究组中,男性 27 例,女性 26 例,年龄最小 35 岁,最大 64 岁,平均年龄( $42.36 \pm 10.15$ )岁,对照组中,男性 30 例,女性 30 例,年龄最小 34 岁,最大 63 岁,平均年龄( $41.96 \pm 11.56$ )岁,两组一般资料比较差异均无统计学意义( $P > 0.05$ ),具有可比性。

纳入标准:(1)经病理检查证实为肺癌;(2)意识清醒能够配合进行调研者;(3)病历资料齐全者;(4)患者及其家属知情同意;(5)调研经医院伦理学会批准实施。

排除标准:(1)合并精神疾病患者;(2)前期已进行抗癌治疗者;(3)合并其他器质性疾病如冠心病、肾衰竭等;(4)依从性差者;剔除标准:(1)干预过程中死亡病例;(2)患者或其家属主动要求退出调研者。

### 1.2 方法

空腹采集静脉血 5 mL,离心机离心后留取上层清液,置于  $-20^{\circ}\text{C}$  条件下保存,待标本收集完毕后统一检测,使用酶联免疫吸附法(ELISA)测量两组患者血清 TNF- $\alpha$  水平。

### 1.3 观察指标及评测标准

疼痛度的测量选择视觉模拟量表进行;TNF- $\alpha$  水平的测量即以试剂盒检测结果为准。

### 1.4 统计学方法

使用 SPSS22.0 对采集的数据进行处理,计量资料以均数 $\pm$ 标准差( $\bar{x} \pm s$ )表示,组间对比采用  $t$  检验;计数资料以  $n(\%)$  的形式表示,组间比较采用  $\chi^2$  检验。以  $P < 0.05$  为差异具有统计学意义。

## 2 结果

### 2.1 两组疼痛度及血清 TNF- $\alpha$ 水平对比

研究组 VAS 评分及血清 TNF- $\alpha$  水平明显高于对照组 ( $P < 0.05$ ),见表 1。

表 1 两组研究对象疼痛度及血清 TNF- $\alpha$  水平对比

Table 1 Comparison of the pain level and serum TNF- $\alpha$  level between two groups of subjects

| Groups         | Case | VAS score       | TNF- $\alpha$ (pg/mL) |
|----------------|------|-----------------|-----------------------|
| Research Group | 53   | $6.23 \pm 0.51$ | $35.69 \pm 6.21$      |
| Control group  | 60   | $2.13 \pm 0.91$ | $10.01 \pm 1.65$      |
| $t$            | -    | 3.699           | 6.559                 |
| $P$            | -    | $<0.05$         | $<0.05$               |

### 2.2 肺癌患者的疼痛度及血清 TNF- $\alpha$ 水平的相关性

经相关性分析结果显示:肺癌患者血清 TNF- $\alpha$  水平与其 VAS 评分之间存在显著正相关( $r=0.986, P < 0.05$ )。

肺癌患者血清 TNF- $\alpha$  水平与其临床分期、浸润深度、是否淋巴结转移均显著相关( $P < 0.05$ ),但与其年龄、性别均无显著相关性( $P > 0.05$ ),见表 2。

### 2.3 血清 TNF- $\alpha$ 水平与肺癌患者临床病理特征的相关性

表 2 血清 TNF- $\alpha$  水平与肺癌患者的临床病理特征的相关性

Table 2 Correlation between the serum TNF- $\alpha$  level with the clinicopathological features of lung cancer patients

| Clinical case characteristics |           | n  | TNF- $\alpha$ level | $t$   | $P$     |
|-------------------------------|-----------|----|---------------------|-------|---------|
| Sex                           | male      | 27 | $19.68 \pm 2.11$    | 0.986 | $>0.05$ |
|                               | female    | 26 | $21.39 \pm 2.18$    |       |         |
| Age (year)                    | $\leq 55$ | 30 | $21.96 \pm 1.98$    | 0.781 | $>0.05$ |
|                               | $>55$     | 23 | $20.96 \pm 2.17$    |       |         |
| TNM staging                   | I-II      | 16 | $14.12 \pm 2.11$    | 3.641 | $<0.05$ |
|                               | III-IV    | 37 | $41.63 \pm 2.98$    |       |         |
| Depth of infiltration         | T1-T3     | 31 | $23.69 \pm 3.26$    | 3.956 | $<0.05$ |
|                               | T4        | 22 | $39.98 \pm 0.44$    |       |         |
| Lymph node metastasis         | Yes       | 26 | $23.32 \pm 2.11$    | 8.591 | $<0.05$ |
|                               | No        | 27 | $43.63 \pm 1.96$    |       |         |

## 3 讨论

肺癌属于癌症中较常见的一种,其发病率和致死率一直位

列肿瘤前茅。统计数据显示我国近些年肺癌的发病率和致死率呈现逐年递升趋势,已经成为威胁居民生命健康的重要因素。有研究指出,空气污染、吸烟等因素是诱发肺癌发生的重要原

因,且肺癌的发病率会随着年龄的增长而上升,提示肺癌会成为未来影响我国经济和社会发展的一个重要影响因素<sup>[8]</sup>。疼痛是癌症患者一种较为常见的临床症状,一般是由肿瘤组织的膨胀性生长或溃破、感染等使末梢神经或神经干受到刺激或压迫,疼痛的出现往往提示癌症已经发展到了中、晚期。早期癌症患者一般表现为隐痛或钝痛,而后随病情逐渐加重,且不间断的出现,尤其夜间更为明显,一般的止痛药镇痛效果不明显<sup>[9-12]</sup>。疼痛不仅会给患者的生活带来极大的负面影响,同时还会影响治疗的顺利进行,增加患者的不良情绪,甚至诱发自杀事件<sup>[13-15]</sup>。因此,准确的疼痛评估对肺癌的治疗具有重要意义。

传统的疼痛评估方式包括单维度疼痛评估量表、疼痛性质评估量表、神经电生理测试、痛阈测量等,但量表检测其信度及效度有限,而神经电生理测试等方式检测仪器较昂贵,难以推广使用<sup>[16-19]</sup>。TNF- $\alpha$ 是目前已发现的直接杀伤肿瘤细胞的生物活性最强的因子之一,其能够直接杀伤肿瘤细胞而对正常细胞无明显毒性的细胞因子,已有多名学者对血清 TNF- $\alpha$  水平与个体疼痛度之间的关系进行了论述<sup>[20-23]</sup>。有研究者将 62 例行髋关节置换术老年患者进行分组干预,发现患者术后 VAS 评分越低,其血清 TNF- $\alpha$  水平也就越低,相关性分析显示二者之间存在正相关<sup>[24]</sup>。Daoust R 等也通过对 42 例伴有躯体疼痛与 79 例不伴有躯体疼痛抑郁症患者的分析发现伴发躯体疼痛的患者其血清 TNF- $\alpha$  水平明显高于对照组,且血清 TNF- $\alpha$  水平与患者 VAS 评分、HAMD 评分及 HAMA 评分均呈正相关性<sup>[25]</sup>。

本研究中,肺癌患者疼痛度及血清 TNF- $\alpha$  水平明显高于健康对照组个体,同时其 VAS 评分与血清 TNF- $\alpha$  水平呈显著正相关性,分析原因,我们认为肿瘤细胞的快速分裂会对正常细胞产生压迫、破坏,造成正常细胞的凋亡,TNF- $\alpha$  属于炎症反应的使动因子,在免疫调节中发挥着重要作用,病理状态下其水平的上升会对机体器官、免疫系统产生较大的损害。已有多项研究指出血清 TNF- $\alpha$  水平与肺癌的病理发生发展过程呈一定相关性<sup>[27-29]</sup>。而另有研究指出 TNF- $\alpha$  能够透过血脑屏障,激活下丘脑室旁核中的神经元,从而影响机体的痛阈<sup>[30]</sup>。因此,血清 TNF- $\alpha$  的水平在一定程度上能够反映机体的疼痛程度。

总而言之,肺癌患者血清 TNF- $\alpha$  水平与其疼痛度呈正相关,通过检测肺癌患者血清 TNF- $\alpha$  水平可辅助评估其疼痛度及临床预后。

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(上接第 3174 页)

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