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## 血清 CEA, CA125 及 CA199 在肺结核诊断中的价值

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**[摘要]** 目的: 探讨肺结核患者血清肿瘤标志物癌胚抗原(carcinoembryonic antigen, CEA)糖类抗原125(carbohydrate antigen 125, CA125)、糖类抗原199(carbohydrate antigen 199, CA199)水平变化及其临床价值。方法: 选取111例肺结核患者(肺结核组)、60例肺癌患者(肺癌组)以及60例健康体检者(对照组), 检测并比较各组血清肿瘤标志物CEA, CA125, CA199水平, 评估各肿瘤标志物在肺结核中的诊断价值。结果: 各组血清CEA, CA125, CA199水平比较, 差异有统计学意义(均 $P<0.05$ )。肺癌组血清CEA, CA199水平明显高于肺结核组和对照组( $P<0.05$ ); 肺结核组血清CA125明显高于肺癌组和对照组(均 $P<0.01$ ); 肺癌组CA199水平明显高于对照组( $P<0.05$ )。血清CA125的受试者工作特征曲线下面积(AUC)值为0.745(95%CI: 0.711~0.861,  $P<0.001$ ), 其灵敏度为81.8%, 特异度为62.3%。各肿瘤标志物联合检测的AUC值为0.776(95%CI: 0.703~0.849,  $P<0.001$ ), 其灵敏度为85.6%, 特异度为65.3%。结论: 血清CA125可作为肺结核的重要鉴别诊断指标, 联合检测CEA, CA125及CA199可明显提高肺结核诊断的灵敏度。

**[关键词]** 肺结核; 癌胚抗原; 糖类抗原125; 糖类抗原199

## Value of serum CEA, CA125, and CA199 in diagnosis of pulmonary tuberculosis

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**Abstract** **Objective:** To investigate the changes of serum tumor markers carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125) and carbohydrate antigen 199 (CA199) in patients with pulmonary tuberculosis and their clinical value. **Methods:** A total of 112 patients with pulmonary tuberculosis (pulmonary tuberculosis), 30 patients with lung cancer (the lung cancer group) and 30 healthy subjects (the control group) were selected. The serum tumor markers CEA, CA125 and CA199 were detected and compared. The diagnostic value of three tumor markers in tuberculosis were analyzed. **Results:** The levels of serum CEA, CA125 and CA199 in each group were significantly different (all  $P<0.05$ ). The levels of serum CEA and CA199 in lung cancer group were significantly higher than those in tuberculosis group and control group (all  $P<0.05$ ). The serum CA125 level in tuberculosis group was significantly higher than that in lung cancer group and control group (all  $P<0.01$ ); the level of CA199

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in lung cancer group was significantly higher than that in the control group (all  $P < 0.05$ ). The area under the ROC curve (AUC) of serum CA125 was 0.745 (95% CI: 0.711 to 0.861,  $P < 0.001$ ) with a sensitivity of 81.8% and a specificity of 62.3%. The combined detection of each tumor marker showed an AUC value of 0.776 (95% CI: 0.703 to 0.849,  $P < 0.001$ ) with a sensitivity of 85.6% and a specificity of 65.3%. **Conclusion:** Serum CA125 can be used as an important differential diagnosis index for tuberculosis. Combined detection of CEA, CA125 and CA199 can significantly improve the sensitivity of tuberculosis diagnosis.

**Keywords** pulmonary tuberculosis; carcinoembryonic antigen; carbohydrate antigen 125; carbohydrate antigen 199

近年来, 血清肿瘤标志物已成为筛查肿瘤的常用临床方法。研究<sup>[1-2]</sup>表明: 肺结核患者中血清肿瘤标志物糖类抗原125(carbohydrate antigen 125, CA125)、神经元特异度烯醇化酶、癌胚抗原(carcinoembryonic antigen, CEA)等指标的血清水平高于正常人群。肿瘤标志物可能对肺结核的诊断具有潜在的临床价值。然而, 关于肿瘤标志物的预测能力以及哪种肿瘤标志物在肺结核诊断中具有更高灵敏度和特异度尚不清楚。本研究旨在评估血清CEA, CA125及糖类抗原199(carbohydrate antigen 199, CA199)在肺结核鉴别诊断中的临床应用价值。

## 1 对象与方法

### 1.1 对象

选取2018年8月至2019年3月中国人民解放军总医院第八医学中心收治的肺结核患者111例, 作为肺结核组; 经病理诊断确诊的肺癌患者60例, 作为肺癌组。其中肺结核组男80例, 女31例, 年龄( $51.2 \pm 5.4$ )岁; 肺癌组男39例, 女21例, 年龄( $53.2 \pm 4.3$ )岁。同期选择60例门诊健康体检者作为对照组, 其中男40例, 女20例, 年龄( $50.4 \pm 3.7$ )岁。各组在性别、年龄等方面比较, 差异无统计学意义(均 $P > 0.05$ )。

### 1.2 血清学指标检测

所有受试者在早晨空腹采集静脉血5 mL, 离心后取上清液。采用德国罗氏全自动化学发光仪(Cobas e601), 所用试剂盒为配套罗氏进口试剂, 正常值范围按照说明书设置CEA(0~5 ng/mL)、CA125(0~35 U/mL)、CA199(0~27 U/mL)。检测受试者血清。

### 1.3 统计学处理

采用SPSS 18.0统计软件进行数据分析, 计量资料采用均数±标准差( $\bar{x} \pm s$ )表示, 组间比较采用方差分析, 计数资料采用百分数来表示, 采用卡方检验,  $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 各组血清 CEA, CA125, CA199 水平比较

方差分析结果显示: 各组血清CEA, CA125, CA199水平比较, 差异有统计学意义( $P < 0.05$ )。其中, 肺癌组血清CEA, CA199水平明显高于肺结核组 and 对照组( $P < 0.05$ ); 肺结核组血清CA125明显高于肺癌组 and 对照组( $P < 0.01$ ); 肺癌组CA199水平明显高于对照组( $P < 0.05$ ), 而肺结核组CEA, CA199水平稍高于对照组, 差异无统计学意义( $P > 0.05$ , 表1)。

表1 各组血清CEA, CA125, CA199水平比较

Table 1 Comparison of serum CEA, CA125 and CA199 levels in each group

组别	<i>n</i>	CEA/(ng·mL <sup>-1</sup> )	CA125/(U·mL <sup>-1</sup> )	CA199/(U·mL <sup>-1</sup> )
肺结核组	111	3.31 ± 3.09	86.02 ± 79.04	13.18 ± 15.15
肺癌组	60	5.98 ± 3.52	57.90 ± 44.65	18.84 ± 15.13
对照组	60	1.75 ± 0.81	9.58 ± 3.57	8.30 ± 6.20
<i>F</i>		16.523	15.939	4.258
<i>P</i>		<0.001	<0.001	0.016

## 2.2 各肿瘤标志物单独检测对肺结核的诊断价值

通过受试者工作特征(receiver operating characteristic, ROC)曲线分析各肿瘤标志物对肺结核的诊断价值, 结果显示: 血清CA125的ROC曲线下面积(AUC)值为0.745(95%CI: 0.711~0.861,  $P < 0.001$ ), 其灵敏度为81.8%, 特异度为62.3%(图1, 表2)。

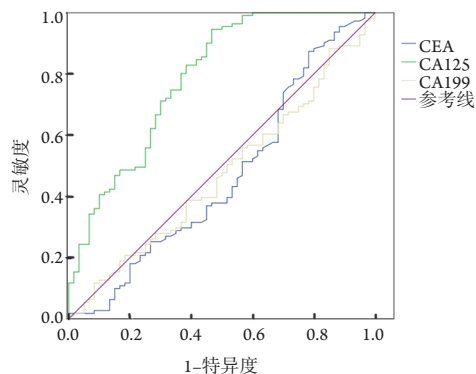


图1 各肿瘤标志物对肺结核诊断的ROC曲线分析

Figure 1 ROC curve analysis of the diagnosis of tuberculosis by various tumor markers

表2 各肿瘤标志物对肺结核的诊断价值分析

Table 2 Diagnostic value of various tumor markers for pulmonary tuberculosis

指标	AUC	P	95%CI	灵敏度	特异度
CEA	0.465	0.455	0.37~0.56	0.734	0.346
CA125	0.745	<0.001	0.711~0.861	0.818	0.623
CA199	0.473	0.560	0.383~0.563	0.478	0.469

## 2.3 各肿瘤标志物联合检测对肺结核诊断的价值

根据Logistic回归模型分析, 将CEA, CA125和CA199纳入肺结核诊断模型中, 得出的预测概率进行ROC曲线分析, 结果显示: 各肿瘤标志物联合检测的AUC值为0.776(95%CI: 0.703~0.849,  $P < 0.001$ ), 其灵敏度为85.6%, 特异度为65.3%(图2)。

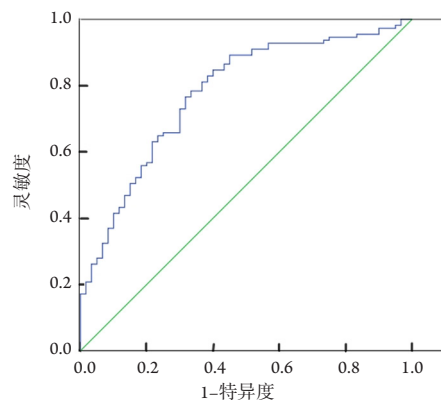


图2 联合检测肿瘤标志物对肺结核诊断的ROC曲线分析

Figure 2 ROC curve analysis of combined detection of tumor markers for diagnosis of pulmonary tuberculosis

## 3 讨论

由于结核病传染期很长, 早期诊断对减少其传播显得尤为重要。结核病的治疗取决于其诊断检测结果。血清肿瘤标志物是结核病的潜在有用的诊断工具<sup>[3-4]</sup>。本研究探讨了3种常见临床血清肿瘤标志物的诊断价值, 即CEA, CA125和CA199, 结果显示: 在肺结核组中CEA, CA125显著高于对照组, 但只有CA125对于肺结核的诊断具有一定的临床意义, 其AUC值为0.745, 其灵敏度为81.8%, 特异度为62.3%。进一步分析发现, 联合检测的AUC值为0.776, 其灵敏度为85.6%, 特异度为65.3%, 表明联合检测CEA, CA125, CA199可明显提高肺结核诊断的灵敏度。

CA125主要在胎儿肺中合成, 存在于气管、支气管、细支气管及末端细支气管上皮中, 作为参与促进卵巢癌细胞生长的细胞表面糖蛋白, 它被认为是卵巢癌的特异度生物标志物。然而, 有研究<sup>[5-6]</sup>发现: 血清CA125在肺癌、肺结核、肺炎等患者中也有不同程度升高, 严重的肺结核与支气管上皮细胞破坏有关, 这导致肺结核患者的CA125水平升高。此外, 炎症性间皮细胞增殖可诱导结核患者CA125的分泌。如果由于炎症或肿瘤破坏了这些细胞, CA125将被释放, 并且在血清中增加。Ma等<sup>[7]</sup>研究发现: 肺结核患者血清CA125, CA199和CEA水平显著高于对照组。初始治疗组和再治疗组之间3种肿瘤标志物无显著差异。Logistic

回归分析显示: CA125是肺结核的影响因素; ROC分析显示: CA125的AUC为0.966 (95%CI: 0.951~0.981), 其截断值为10.30 U/mL, 敏感性、特异度分别为95.6%和85.0%。表明血清CA125对肺结核具有潜在的良好诊断性能。赵维群<sup>[8]</sup>的研究显示: 肺结核组CA125检测值及阳性率均高于正常组, CA125可为不同类型肺结核患者临床诊治提供参考。此外, 血清CA125水平可以作为了解继发性肺结核患者病情进展和评价治疗效果的指标。

CEA是一种高分子糖蛋白, 可在多种肿瘤组织中表达, 在肺癌中可显著升高。本研究中CEA的AUC仅为0.465。因此用CEA诊断肺结核不是一种好方法。CA199是呼吸系统肿瘤细胞株分泌的低聚糖肿瘤相关抗原, 正常成人表达水平极低, 目前CA199主要是诊断胰腺癌、胃癌的常见临床肿瘤标志物。在肺癌、肺结核、支气管结核中, CA199明显增高<sup>[9]</sup>。梁曼曼等<sup>[10]</sup>研究发现: CA199水平在继发性肺结核治疗前、治疗后及正常对照组间差异均无统计学意义。本研究中肺癌组血清CA199水平明显高于肺结核组和对照组, 而肺结核组CA199与对照组比较, 差异无统计学意义。

本研究尚有一些局限性, 如纳入的样本数量偏少, 且仅为肺结核患者, 因此结果可能不适用于其他类型的结核等。血清肿瘤标志物与肺结核的相关机制尚有待进一步探索。综上, 血清CA125可能是肺结核重要的鉴别诊断指标之一, 联合检测CEA, CA125及CA199可明显提高肺结核诊断的灵敏度。

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