·论著·胸部·

基于炎症指标和肿瘤标志物CEA、CYFRA21-1、CA19-9对肺癌远处转移的预测价值

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【摘要】**目的** 探讨炎症指标和肿瘤标志物癌胚抗原(CEA)、细胞角蛋白19片段(CYFRA21-1)、糖类抗原19-9(CA19-9)对肺癌远处转移的预测价值。**方法** 选取2021年2月至2024年2月在开封市肿瘤医院内科就诊的肺癌患者82例，依据患者是否发生远处转移分为远处转移组(n=20)和未远处转移组(n=62)，多因素Logistic回归分析影响肺癌远处转移因素，ROC曲线分析炎症指标和肿瘤标志物对肺癌远处转移的预测价值。**结果** 两组年龄、NLR、CEA、CA19-9、CYFRA21-1水平比较差异显著(*P*<0.05)；多因素Logistic回归分析显示，高龄、高水平NLR、CEA、CA19-9、CYFRA21-1均为肺癌远处转移的危险因素(*P*<0.05)；ROC曲线分析显示炎症指标联合肿瘤标志物预测肺癌远处转移的AUC为0.881，95%CI为0.803~0.960，*P*<0.001，灵敏度为0.950，特异度为0.758。**结论** NLR、CEA、CYFRA21-1及CA19-9是肺癌远处转移的独立危险因素，其联合检测可显著提升远处转移的预测效能，有助于优化个体化诊疗策略。

【关键词】肺癌；远处转移；炎症；肿瘤标志物；预测
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Predictive Value of Tumor Markers CEA, CYFRA21-1 and CA19-9 for Distant Metastasis of Lung Cancer Based on Inflammatory Indicators and Tumor Markers

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Abstract: ***Objective*** To investigate the predictive value of CEA, CYFRA21-1 and CA19-9 in distant metastasis of lung cancer. ***Methods*** A total of 82 lung cancer patients who visited the Internal Medicine Department of Kaifeng Cancer Hospital from February 2021 to February 2024 were selected and divided into the distant metastasis group (n=20) and the non-distant metastasis group (n=62) based on whether distant metastasis occurred. Multivariate Logistic regression analysis was conducted to analyze the factors influencing distant metastasis of lung cancer. The ROC curve was used to analyze the predictive value of inflammatory indicators and tumor markers for distant metastasis of lung cancer. ***Results*** There were significant differences in age, NLR, CEA, CA19-9 and CYFRA21-1 levels between the two groups (*P*<0.05), but no significant differences in gender, pathological type between the two groups (*P*>0.05). Multivariate Logistic regression analysis showed that old age, high level of NLR, CEA, CA19-9 and CYFRA21-1 were risk factors for distant metastasis of lung cancer (*P*<0.05). ROC curve analysis showed that the AUC of inflammatory indexes combined with tumor markers for predicting distant metastasis of lung cancer was 0.881, 95%CI was 0.803-0.960, *P*<0.001, sensitivity was 0.950, specificity was 0.758. ***Conclusion*** NLR, CEA, CYFRA21-1 and CA19-9 are independent risk factors for distant metastasis of lung cancer. Their combined detection can significantly improve the predictive efficacy of distant metastasis and help optimize individualized diagnosis and treatment strategies.

Keywords: Lung Cancer; Distant Metastasis; Inflammation; Tumor Markers; Forecast

肺癌是全球范围内最常见的恶性肿瘤之一，其发病率和死亡率均居恶性肿瘤之首[1]。据统计[2]，全球每年有超过180万人因肺癌死亡，其中中国是肺癌死亡人数最多的国家之一。虽然近年来肺癌治疗手段得到了不断改进和创新，但由于肺癌隐匿性强、易侵犯周围组织、易发生远处转移等特点，使得肺癌的治疗难度依然较大[3-4]。肺癌远处转移是肺癌治疗中的重要问题，也是影响病人预后的主要因素之一[5]。研究表明[6-7]，约30%~50%的肺癌患者会出现远处转移，其中以骨、肝、脑等部位的转移最为常见。一旦发生远处转移，患者的生存期和治疗效果均会受到严重的影响。因此，为优化个体化治疗决策并改善患者生存结局，亟需建立可靠的方法来预测和评估肺癌远处转移。近年来，研究发现炎症反应与肿瘤转移密切相关[8]。慢性炎症是驱动肿瘤发生、发展乃至转移全过程的关键因素，对于调节肿瘤微环境、激活炎症介质、诱导血管新生、影响免疫反应等都有重要作用[9-10]。肿瘤标志物则是肿瘤特异性或非特异性生物标志物，是诊断肿瘤、监测治疗效果和预后判断的重要指标。在肺癌中，CEA、CA19-9、CYFRA21-1等标志物的检测已被广泛应用于临床诊断和治疗过程中[11-12]。本研究旨在探讨炎症指标和肿瘤标志物CEA、CYFRA21-1、CA19-9对肺癌远处转移的预测价值，为肺癌的诊断和治疗提供一定的参考依据，内容如下。

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1 资料与方法

1.1 一般资料 选取2021年2月至2024年2月在开封市肿瘤医院内科就诊的肺癌患者82例。

纳入标准：年龄在18岁及以上的患者；诊断为原发性肺癌或转移性肺癌的患者。排除标准：孕妇或哺乳期妇女；存在其他严重疾病(如肝肾功能衰竭、严重心脏病等)的患者；患有其他恶性肿瘤的患者；曾接受过放疗或化疗治疗的患者；有严重的呼吸道感染或肺部炎症的患者；具有自身免疫性疾病、重度过敏或自体免疫疾病的患者；患有晚期肺癌的患者等。依据美国癌症联合委员会第8版指南[13]明确患者是否发生远处转移分为远处转移组(n=20)和未远处转移组(n=62)。远处转移包括脑转移、骨转移、肝转移、肾转移、多发转移等。

1.2 方法

1.2.1 资料收集 经电子病历系统采集患者一般资料和生化资料等，如性别、年龄、病理类型(NSCLC、SCLC)、NLR、CEA、CA19-9、CYFRA21-1。

1.2.2 炎症指标和肿瘤标志物检测 于患者治疗前采集清晨静脉血5mL，离心，3000r/min，10min，采用ELISA法检测NLR，电化学发光法检测CEA、CA19-9、CYFRA21-1水平。

1.3 统计学方法 本研究应用 SPSS 27.0进行数据处理与分析，符合正态分布的连续性变量以($\bar{x}\pm s$)描述，组间比较使用独立样本t检验，分类变量以[n(%)]表示，比较用 χ^2检验，采用多因素 Logistic 回归模型识别肺癌远处转移的独立风险因素，通过绘制ROC曲线并计算AUC值，评价NLR和肿瘤标志物(CEA,CA19-9,CYFRA21-1)对远处转移的预测效能，所有统计检验均为双侧检验，*P*<0.05认为具有统计学显著性。

2 结 果

2.1 两组临床资料比较 两组患者在年龄分布及所有检测的血清学指标(NLR、CEA、CA19-9、CYFRA21-1)水平上均存在显著差异(*P*<0.05)。而在性别构成和病理类型分布方面，两组间未见统计学显著差异(*P*>0.05)，见表1。

2.2 多因素Logistic回归分析影响肺癌远处转移因素 年龄(>60岁)、NLR水平升高、CEA水平升高、CA19-9水平升高以及CYFRA21-1水平升高均是肺癌发生远处转移的独立危险因素(所有*P*值均<0.05)，见表2。

2.3 炎症指标和肿瘤标志物对肺癌远处转移的预测价值 炎症指标联合肿瘤标志物预测肺癌远处转移的AUC为0.881，95%CI为0.803~0.960，*P*<0.001，灵敏度为0.950，特异度为0.758，见表3和图1。

表1 两组临床资料比较[例(%)]

项目	转移组(n=20)	未转移组(n=62)	t/χ^2	*P*
性别			1.129	0.288
男性	12(60.00)	45(72.58)		
女性	8(40.00)	17(27.42)		
年龄(岁)			10.871	0.001
≤60	8(40.00)	49(79.03)		
>60	12(60.00)	13(20.97)		
病理类型			2.076	0.150
NSCLC	6(30.00)	30(48.39)		
SCLC	14(70.00)	32(51.61)		
NLR	4.11±0.25	3.03±0.21		19.076
<0.001				
CEA(ng/mL)	8.62±1.16	3.63±0.65	24.223	<0.001
CA19-9(U/mL)	11.27±1.11	5.21±0.72	28.413	<0.001
CYFRA21-1(ng/mL)	7.32±0.51	2.75±0.37	43.597	<0.001

表2 肺癌远处转移影响因素

自变量	B	标准误差	Wald χ^2	*P*	OR	95%CI
年龄	1.732	0.553	9.818	0.002	5.654	1.913~16.709
NLR	1.889	0.554	11.616	<0.001	6.616	2.232~19.610
CEA	0.438	0.115	14.399	<0.001	1.550	1.236~1.944
CA19-9	0.441	0.107	16.949	<0.001	1.555	1.260~1.919
CYFRA21-1	0.587	0.136	18.545	<0.001	1.799	1.377~2.351

表3 炎症指标和肿瘤标志物对肺癌远处转移的预测价值

检验变量	AUC	*P*	95%CI		灵敏度	特异度	最佳阈值
			下限	上限			
NLR	0.692	0.010	0.529	0.856	0.650	0.887	3.530
CEA	0.796	<0.001	0.686	0.906	0.800	0.806	4.235ng/mL
CA19-9	0.810	<0.001	0.701	0.920	0.900	0.710	5.665U/mL
CYFRA21-1	0.791	<0.001	0.663	0.919	0.650	0.887	5.115ng/mL
联合预测	0.881	<0.001	0.803	0.960	0.950	0.758	-

3 讨 论

本研究发现，肺癌患者中年龄、NLR、CEA、CA19-9和CYFRA21-1水平在远处转移组与未远处转移组之间存在显著差异，这些指标的显著差异提示它们可能在肺癌远处转移的发生和进展中起着重要的作用。随年龄递增，免疫细胞功能活性与组织修复相关细胞的再生潜能均呈现衰减趋势，从而使得肺癌

细胞在血液和淋巴系统中更容易发生远处转移，部分归因于免疫老化的现象。免疫老化是指随着年龄增长，机体免疫系统功能逐渐减退和失调的过程，包括免疫细胞数量和功能的变化，免疫调节的异常以及免疫应答的降低等，这种情况下，机体对肿瘤细胞的监测和清除能力减弱，使得肺癌细胞更容易逃避免疫监视以及免疫毁灭[14-15]；机体组织修复能力随增龄呈进行性减退，细胞修复和再生能力下降，不仅对正常组织和器官的维持产生影响，同时也削弱了对肿瘤细胞扩散和侵袭的阻击力，肺癌细胞在血液和淋巴系统中更容易存活、逃逸和定植远处器官，从而促进了肺癌的远处转移[16-17]。炎症指标NLR[18]。反映了机体的炎症状态和免疫功能[19]。研究表明[20-21]，高水平的NLR与肿瘤的侵袭性和预后不良相关。肺癌患者中高NLR水平可能与肿瘤相关的炎症反应和免疫逃逸有关，这些因素可能促进肿瘤细胞的远处转移[22-23]。它能够促进血管生成、细胞迁移和侵袭，并增强肿瘤细胞的远处转移能力[24]。

CEA、CA19-9和CYFRA21-1水平的升高可反映肿瘤细胞的增殖和代谢活性增加，以及肿瘤组织对周围环境的侵袭和破坏能力。CEA是一种胎儿抗原，普遍存在于胚胎期和胎盘组织中，但在正常成人组织中的表达极低[25]。而在肺癌等恶性肿瘤中，CEA的表达显著增加。研究发现[26]，高水平的CEA与肺癌细胞的侵袭和迁移能力相关，它可以通过促进细胞粘附、降解基底膜、增强细胞的迁移和侵袭等机制，促进肺癌细胞的远处转移。CA19-9是一种糖链抗原，其表达也显著增加在许多恶性肿瘤中，包括肺癌[27]。CA19-9的升高可反映肺癌细胞的增殖和浸润能力增加，与肺癌的生长和扩散密切相关。研究表明[28]，CA19-9通过增强细胞粘附、调节细胞信号传导和介导细胞间相互作用等机制，促进肺癌细胞的迁移和远处转移。CYFRA21-1是一种角质化细胞间黏附蛋白的降解产物，在肺癌等多种实体肿瘤中表达增加[29]。高水平的CYFRA21-1与肺癌细胞的浸润和转移能力增强相关。研究发现[30]，CYFRA21-1能够促进肺癌细胞的胶原酶的活性、细胞周期和基质金属蛋白酶的表达等，从而改变肺癌细胞的侵袭和迁移能力，促进远处器官的转移。ROC曲线分析结果显示，炎症指标和肿瘤标志物的联合应用在预测肺癌远处转移方面具有较高的准确性和可靠性，可以作为临床决策和治疗方案制定的重要参考依据。

综上所述，血清炎症指标NLR联合肿瘤标志物CEA、CYFRA21-1、CA19-9构建的预测模型对肺癌远处转移具有良好预测价值，可作为辅助临床风险分层的重要工具。

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