

肿瘤标志物预测NSCLC患者EGFR突变概率数学模型的建立与评价

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Title: Establishment and evaluation of a mathematical model for predicting the EGFR gene mutation probability of non-small cell lung cancer with tumor markers

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摘要: 目的: 利用血清肿瘤标志物建立预测非小细胞肺癌 (NSCLC) 患者表皮生长因子受体 (EGFR) 基因突变概率的数学模型, 并评价其临床应用价值。方法: 回顾性分析我院经病理学确诊的NSCLC患者107例, 对组织标本采用扩增阻滞突变系统实时荧光定量PCR (ARMS-PCR) 技术检测EGFR基因突变, 采集外周静脉血用化学发光法检测血清肿瘤标志物水平。多因素回归分析筛选出EGFR突变的独立预测因子, 建立Logistic回归模型。绘制受试者工作特征曲线 (ROC) 并计算曲线下面积 (AUC), 以评价模型准确性和临床价值。结果: 107例NSCLC患者中43.9%为EGFR突变型, 56.1%为EGFR野生型。Logistic回归分析显示吸烟史、CEA、CA199和CYFRA21-1在EGFR突变型和野生型组间差异有统计学意义, 是EGFR突变的独立预测因子。由此建立预测模型: $P = \frac{e^X}{1+e^X}$, $X = -3.664 + (3.246 \times \text{吸烟史}) + (2.441 \times \text{CEA}) + (1.866 \times \text{CA199}) - (1.918 \times \text{CYFRA21-1})$, e 为自然对数; 当截点 P 为0.478时, 模型的敏感度为85.1%, 特异性为65.0%。该模型的AUC为0.734 (95%CI: 0.637 ~ 0.830)。结论: 非吸烟、CEA和CA199高表达及CYFRA21-1低表达是NSCLC患者EGFR基因突变的独立预测因子。由此建立的数学预测模型准确度较高, 可为EGFR基因突变的预测提供有利帮助。

Abstract: Objective: To establish and evaluate a mathematical model for predicting the epidermal growth factor receptor (EGFR) gene mutation probability of non-small cell lung cancer (NSCLC) with the tumor markers. Methods: The clinical data of 107 patients with a clear pathological diagnosis of NSCLC were retrospectively analyzed from the Fourth Affiliated Hospital of China Medical University. The amplification refractory mutation system PCR (ARMS-PCR) technique was used to detect EGFR gene mutations. The series of tumor markers were detected by taking the peripheral venous blood with electrochemiluminescence method. To estimate the independent predictors of EGFR gene mutation, multivariate analysis was used. A Logistic regression prediction model was subsequently created. Receiver operating characteristic (ROC) curve was performed and the area under the curve (AUC) was calculated to evaluate model accuracy and clinical value. Results: In 107 NSCLC patients, EGFR gene mutation type rate was 43.9% and 56.1% was wild type. Logistic regression analysis showed that there were significant differences in smoking history, CEA, CA199, and CYFA21-1 levels between subgroups with EGFR gene mutation type and wild type ($P < 0.05$). These factors were identified as independent predictors of EGFR gene mutation. Our prediction model was $P = \frac{e^X}{1+e^X}$, $X = -3.664 + (3.246 \times \text{smoking history}) + (2.441 \times \text{CEA}) + (1.866 \times \text{CA199}) - (1.918 \times \text{CYFRA21-1})$. The goodness of fit of the model was fairly good. When the optimal cut-off point P was 0.478, the sensitivity was 85.1% and specificity was 65.0%. The AUC was 0.734 (95%CI: 0.637 ~ 0.830) in our model. Conclusion: Non-smokers, high expression level of CEA and CA199 and low expression level of CYFRA21-

1 are independent predictors of EGFR gene mutations in NSCLC patients. Our research shows that the mathematics model has high accuracy and can provide help for predicting EGFR gene mutation.

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