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切除修复交叉互补基因1、核苷酸还原酶M1亚基和β-微管蛋白III的表达对Ⅰ～Ⅲ期非小细胞肺癌术后辅助化疗疗效的预测意义

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Expression and Predictive Role of Excision Repair Cross Complementation Group 1, Ribonucleotide Reductase Subunit M1, and β-tubulinIII in Postoperative Patients with Non-small Cell Lung Cancer Receiving Adjuvant Chemotherapy

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摘要 参考文献 相关文章

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摘要 目的探讨切除修复交叉互补基因1（ERCC1）、核苷酸还原酶M1亚基（RRM1）和β-微管蛋白III与接受不同辅助化疗方案的非小细胞肺癌患者预后的关系。方法回顾性分析2004年1月至2007年12月我院接受手术治疗且术后行辅助化疗的Ⅰ～Ⅲ期非小细胞肺癌病例。利用免疫组织化学法检测ERCC1、 RRM1和β-微管蛋白III的表达，分析所有患者的临床病理特征、治疗特征、分子特征与生存规律的关系。结果ERCC1、RRM1和β-微管蛋白III的高表达率分别为36.4%、43.7%和38.4%，三者表达程度无相关性，ERCC1（P=0.008）和RRM1（P=0.028）在腺癌中的高表达率显著低于非腺癌，而β-微管蛋白III在腺癌中的高表达率显著高于非腺癌（P=0.001）。所有患者中位随访时间35.8个月，80例出现复发或转移，40例死亡，中位生存期未达到，中位无疾病生存期（DFS）为24.1个月。单因素分析显示男性（P=0.036）、临床分期早（P=0.001）及非腺癌（P=0.004）患者较女性、临床分期晚及腺癌患者中位DFS显著延长，而年龄、吸烟与否、化疗方案的类型及ERCC1、RRM1和β-微管蛋白III的表达程度对DFS无影响。分层分析显示，RRM1高表达时，含吉西他滨方案组较其他方案组DFS有缩短的趋势（P=0.054）[β-微管蛋白III高表达时，紫杉类方案组较长春瑞滨和吉西他滨组DFS有缩短的趋势（P=0.076）。而在RRM1或β-微管蛋白III低表达以及ERCC1不同表达程度层中，各化疗方案组对DFS的影响无差异。COX多因素分析显示，腺癌与否和临床分期是影响DFS的独立预后因素。结论对于接受手术治疗及术后辅助化疗的非小细胞肺癌患者，RRM1高表达者对吉西他滨耐药，而β-微管蛋白III高表达者对紫杉类耐药，在耐药人群中使用其他方案似乎能给患者带来更多的生存获益。免疫组织化学法检测ERCC1、RRM1和β-微管蛋白III的表达有助于筛选辅助化疗药物及预测化疗疗效。

关键词： 非小细胞肺癌 切除修复交叉互补基因1 核苷酸还原酶M1亚基 β-微管蛋白III 辅助化疗

Abstract: ObjectiveTo determine the predictive value of excision repair cross complementation group 1(ERCC1), ribonucleotide reductase subunit M1(RRM1), and β-tubulinIII expressions in postoperative patients with stage Ⅰ-Ⅲ non-small cell lung cancer(NSCLC)receiving adjuvant chemotherapy. MethodsAll NSCLC patients received surgery therapy followed by at least one cycle of adjuvant chemotherapy in our hospital from January 2004 to December 2007. The expressions of ERCC1, RRM1, and β-tubulinIII were detected by immunohistochemical methods. The relationships among clinicopathologic characteristics, chemotherapy regimens, biomarkers' expressions and disease-free survival （DFS） were analyzed. ResultsThe high-expression rates of ERCC1, RRM1, and β-tubulinIII were 36.4%, 43.7%, and 38.4%, respectively. The expressions of these three biomarkers were not correlated. After a median follow-up of 35.8 months, 80 patients experienced metastatic or recurrent tumors and 40 patients died. The median overall survival was not reached and the median DFS was 24.1 months. Univariate survival analysis showed that sex, clinical stage, and adenocarcinoma or not were related to DFS, while age, smoke history, chemotherapy regimens, and expression levels of ERCC1, RRM1, and β-tubulinIII has no prognostic significance in these surgically resected NSCLC patients who were receiving adjuvant chemotherapy. Male （P=0.036）, earlier clinical stage(P=0.001), and non-adenocarcinoma(P=0.004)predicted better DFS. Stratified analysis indicated that in RRM1 high-expression strata, the regimens with gemcitabine had curtailed DFS compared with other regimens(P=0.054); in β-tubulinIII high-expression strata, the regimens containing taxane(including paclitaxel and docetaxel subgroups)had curtailed DFS compared with other regimens(P=0.076), although there was no statistical significance. However, there were no similar predictive significance in RRM1 and β-tubulinIII low-expression strata or in ERCC1 strata with different expression levels. COX proportional regression analysis showed that adenocarcinoma or not and clinical stage were independent risk factors of DFS in this population. ConclusionsIn postoperative NSCLC patients who are receiving adjuvant chemotherapy, patients with high expression of RRM1 tends to be resistant to gemcitabine and patients with high expression of β-tubulinIII tends to

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be resistant to taxane drugs. ERCC1, RRM1, and β-tubulinⅢ detected by immunohistochemistry can be biomarkers to help to choose better chemotherapy regimen and predict the effectiveness of adjuvant chemotherapy.

Keywords: non-small cell lung cancer excision repair cross complementation group 1 ribonucleotide reductase subunit M1 β-tubulinⅢ adjuvant chemotherapy

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