RESEARCH ARTICLE

Clinical Value of Eukaryotic Elongation Factor 2 (eEF2) in Non-small Cell Lung Cancer Patients

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Abstract

Background: The purpose of this study was to evaluate a new type of tumor biomarker, eukaryotic elongation factor 2 (eEF2), in serum for the early diagnosis, confirmative diagnosis as well as assessment of treatment of non-small cell lung cancer (NSCLC). Methods: 130 patients with NSCLC and 50 healthy individuals undergoing physical examination in our hospital provided the observation and healthy control groups. An enzyme linked immune sorbent assay (ELISA) method was applied to determine serum eEF2 levels. Serum neuron specific enolase (NSE) and squamous cell carcinoma antigen (SCC) levels in the observation group were assessed with an automatic biochemical analyzer. Results: The median levels of eEF2 in the serum of NSCLC patients was found to be significantly higher than the healthy control group ($p < 0.01$) and it was markedly higher in stages III, IV than stages I, II ($p < 0.05$). eEF2 was higher with tumor size ≥2 cm than <2 cm ($P< 0.01$). Furthermore, two weeks after surgery patients showed a significant trend for eEF2 decrease ($p < 0.05$). Conclusions: The eukaryotic elongation factor 2 (eEF2) has certain clinical values for early diagnosis, verification, and prognosis as well as classification of lung cancer patients.

Keywords: Non-small cell lung cancer - eukaryotic elongation factor 2 - clinical value

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Introduction

Lung cancer is a heterogeneous disease with currently still unknown mechanisms of development (Massion et al., 2003). Lung cancer is the leading cause of cancer death in the word (Adcock et al., 2011). In 2012, there will be an estimated 226,000 new cases of lung cancer diagnosed in this country and over 160,000 individuals are expected to die from this disease (Siegel et al., 2012). Most patients will be diagnosed with locally advanced (stage III) or (stage IV) disease (Karp et al., 2013). So we wanted to find a way to early diagnosis of lung cancer. And a new markers that could guide therapeutic.

Materials and Methods

130 patients diagnosed as NSCLC by pathology or cytology admitted in our hospital from Sept. 2009 to Jun. 2013.50 were selected as observation group, in which there were 25 males and 25 females. They were 46-82 years old, and the mean was (66.1±6.5) years old. Other 50 healthy people underwent physical examination at the same period were chosen as control group. They were 47-78 years old, and the mean age was (68.4±7.5) years old. There were no significant differences in general data like the age and gender, indicating that there was comparability between two groups (p >0.05). All the patients were diagnosed with cancer for the first time, and none previously received chemotherapy or radiation therapy.

ELISA for serum eEF2

Serum eEF2 was analysed with enzyme linked immune sorbent assay (ELISA) kits (B&D, USA). All the operation method according to the manufacturer's instructions. At morning exsanguinate limosis venous blood and kept at room temperature for about 20 minutes, and then centrifuged at 3000 rpm for 5 minutes. Then the serum collected, and divided into aliquots stored frozen at -80°C.

Statistical Analysis

Most of the data were normally distributed, so the average level eef2, 2 groups were compared using t-test, receiver operating characteristic (ROC) curve drawing, he valued the sensitivity on the false-positive rate (1-specificity) generate assessment diagnostic accuracy of serum eEF2. receiver operating characteristic (ROC) curves were measured, the test area under the curve (AUC) roc exceeding 0.5. if not, no further assessment of diagnostic testing is necessary. In this study, the statistical significance set at P<0.05, p values reported are 2-sides. All analyzes were performed using SPSS v.17.0 for windows (USA).

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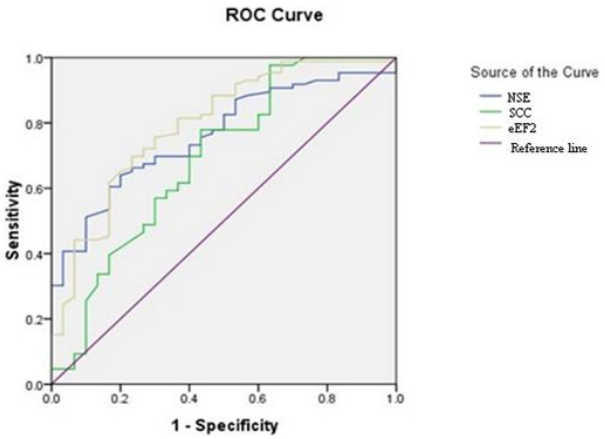

Figure 1. ROC Curves Was Generated from the Serum eEF2, SCC and NSE of 130 Patients with NSCLC. The eEF2, SCC and NSE areas under the curves were 0.763, 0. 671 and 0.702 for eEF2, SCC and NSE ($P < 0$ .05)

Results

The median serum eEF2 level was significantly higher in patients with NSCLC compared with healthy controls. It was further observed that eEF2 is markedly higher in stages III and IV than stages I and II ($p < 0.05$) and eEF2 is increased with tumor size ($p < 0.05$). Furthermore whereas patients had surgical operation two weeks later showed a significant trend of eEF2 decrease whereas patients (Table 1). The value of the eEF2, SCC, NSE in the lung cancer was evaluated with ROC curve analysis the AUC for the serum eEF2, SCC and NSE were 0.763 (95% CI: 0.673-0.853; $P < 0.01$), 0.671 (95 % CI: 0.572-0.810; $P < 0.01$), and 0.702 (95% CI: 0.700-0.889; $P < 0.01$) (Figure 1). The Cut-off value of eEF2, SCC and NSE were 0.542 mg/L, 9.24 μg/L, 21.8 μg/L. The serum eEF2 had a sensitivity of 97%, a specificity of 82%, yet the SCC and NSE had sensitivity were 67%, 78% specificity were 56%, 69%.

Discussion

Lung cancers are common malignancies and leading causes of cancer death in the world (Adcock et al., 2011; Hensing et al., 2013). Clinical outcome of these cancers still remains unsatisfactory despite recent progress in diagnosis and medical treatments (Hensing et al., 2013; Liang et al., 2013). A wide range of alterations in gene expression have been identified in cancers. Eukaryotic initiation factor is reported in some cancer (Nakamura et al., 2009; Chen et al., 2011; Leprivier et al., 2013) but the mechanisms of eEF2 in lung cancer was not clear. Our results show that eEF2 is highly expressed in non-small cell lung cancer (NSCLC). The median serum eEF2 level was significantly higher in patients with NSCLC compared with healthy controls and it was further observed that eEF2 is markedly higher in stages III, IV than stages I , II. eEF2 was increased with tumor size too; Furthermore whereas patients had surgical operation two weeks later showed a significant trend of eEF2 decrease. Indicating that eEF2 was associated with NSCLC. We also draw the conclusion that patients with high eEF2 expression had a significantly worse prognosis. It was further showed that eEF2 is higher in adenocarcinoma than in squamous-cell carcinoma, it illustrated that eEF2 was elated to the Pathological classification of lung cancer.

Table 1. General Data of Observation Groups

Groups	No.	mg/L	*P* value
Observation Group	130	0.831±0.036	$p < 0.01$
Healthy Control Group	90	0.486±0.039	
Pathological types			$p < 0.05$
Squamous cell carcinoma	78	0.621±0.024	
Adenocarcinoma	52	0.874±0.035	
Stage			$p < 0.05$
Stage I-II	43	0.514±0.071	
Stage III-IV	87	0.828±0.071	
Tumor size			$p < 0.01$
≥2cm	75	0.718±0.072	
<2cm	55	0.465±0.034	
Before Surgery	95	0.698±0.063	$p < 0.05$
After Surgery	95	0.564±0.029	

ROC analysis showed that the AUC for eEF2 could as a tumour monitor. The value of the eEF2, SCC, NSE in the f lung cancer was evaluated with ROC curve analysis the AUCs for the serum eEF2, SCC and NSE were 0.763, 0.671, and 0.702 the cut-off value of eEF2, SCC and NSE were 0.542 mg/L9.24 μg/L, 21.8 μg/L. The serum eEF2 had a sensitivity of 97%, a specificity of 82%, yet the SCC and NSE had sensitivity were 67%, 78% specificity were 56%, 69%. As a result , according to the AUC of t he ROC curve, eEF2 was better than CEA, SCC and NSE. Further our data demonstrate d that eEF2 might be a useful lung cancer-marker for NSCLC. Our results showed that increased eEF2 is strongly associated with NSCLC and correlated with NSCLC progression.

The clinical value of eef2 for early diagnosis of validation, prognosis and classification of patients. Therefore, it is necessary that eef2 as a new and different parameters used to evaluate the cost-effectiveness of non-small cell lung cancer diagnosis and treatment has been widely deployed. Eef2 Had a higher specificity, than NSE and SCC for non-small cell lung cancer (NSCLC), especially for Lung adenocarcinoma. But our study were limited by sample size, future larger prospective studies are needed to do.

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