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Clinical Value of Serum Carcinoembryonic Antigen (CEA) in Predicting EGFR Mutations in Lung Adenocarcinoma

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Abstract

Objective To evaluate the predictive value of serum carcinoembryonic antigen (CEA) levels and routine clinical characteristics for EGFR gene mutations in patients with lung adenocarcinoma. **Methods** A retrospective analysis was conducted on 98 patients with lung adenocarcinoma. Clinical data, including sex, smoking history, age, tumor stage, presence of distant organ and/or lymph node metastasis, and serum CEA levels, were analyzed to explore their association with EGFR mutation status. **Results** No statistically significant differences in sex, smoking history, age, tumor stage, or distant organ and/or lymph node metastasis were observed between the EGFR mutant and wild-type groups ($P > 0.05$). Compared with the EGFR wild-type group, the mutant group exhibited a higher serum CEA positivity rate. Further subgroup analyses based on mutation types revealed no statistically significant differences in CEA levels among the subgroups ($P > 0.05$). When stratified by abnormal CEA concentration (5–10 ng/mL and ≥10 ng/mL), no statistically significant difference in EGFR mutation rate was found between the concentration subgroups ($P > 0.05$). Receiver operating characteristic (ROC) curve analysis showed that the area under the curve (AUC) for CEA in predicting EGFR mutations was 0.637. **Conclusion** Serum CEA level has a certain clinical value in predicting EGFR gene mutations in patients with lung adenocarcinoma and may serve as a reference to guide targeted therapy decisions for this patient population.

Keywords Carcinoembryonic Antigen (CEA); Lung Adenocarcinoma; EGFR Gene; Predictive Value

1 Introduction

Lung cancer remains one of the most common malignancies worldwide. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases, with nearly 80% of patients diagnosed at an advanced stage[1]. The main histological subtypes of NSCLC include adenocarcinoma, squamous cell carcinoma, and large cell carcinoma[2], with adenocarcinoma being the most prevalent subtype[3]. Patients with lung cancer, particularly those with advanced disease, experience high postoperative recurrence rates; even after curative-intent surgery, prognosis remains poor[4]. Carcinoembryonic antigen (CEA) is a sensitive and clinically practical tumor marker used for cancer diagnosis, prognosis assessment, and treatment monitoring[5]. Currently, serum CEA is widely used in the diagnosis and treatment evaluation of NSCLC, especially adenocarcinoma[6], and changes in its levels are closely associated with chemotherapy response and prognosis[7]. CEA also serves as an important predictor of gefitinib sensitivity and survival: among

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patients receiving tyrosine kinase inhibitor (TKI) therapy, those with higher pretreatment CEA levels demonstrate longer survival and better outcomes compared to those with lower levels[8-9]. Studies have confirmed that epidermal growth factor receptor-tyrosine kinase inhibitors (EGFR-TKIs) possess clear antitumor activity and a high response rate, establishing them as first-line therapy for NSCLC patients with EGFR mutations[5]. However, for patients with EGFR wild-type status, the efficacy of TKI therapy is only 10%–15%. Therefore, determining EGFR mutation status before TKI treatment is crucial. Unfortunately, not all patients can undergo EGFR mutation testing, and the actual detection rate is lower than expected due to factors such as high costs, insufficient tumor tissue samples, technical challenges, and poor patient health status[10-11]. Consequently, identifying a simple and feasible clinical screening method is of great importance. Multiple studies have shown that serum CEA levels are closely associated with EGFR mutation status in patients with lung adenocarcinoma, suggesting that CEA may be a convenient predictor of EGFR mutations[7,12]. This study aims to analyze the correlation between serum CEA expression levels and EGFR mutations in patients with lung adenocarcinoma and to further evaluate its clinical value.

2 Patients and Methods

2.1 Patient Population

This retrospective study included patients with lung adenocarcinoma admitted to the Seventh Affiliated Hospital of Sun Yat-sen University between January 2020 and November 2024. Among them, 63 patients with EGFR gene mutations were assigned to the EGFR mutant group, and 35 patients with EGFR wild-type were assigned to the EGFR wild-type group. Inclusion criteria were: (1) pathologically confirmed diagnosis of lung adenocarcinoma by the Seventh Affiliated Hospital of Sun Yat-sen University; (2) newly diagnosed with no prior history of lung cancer-related treatment; and (3) availability of complete clinical data, including serum tumor markers and driver gene mutation analysis. Exclusion criteria were: (1) presence of other primary malignancies in other organs or pulmonary metastatic tumors; and (2) presence of liver or renal dysfunction, autoimmune diseases, or hematologic disorders that may potentially affect the study results. Baseline characteristics: EGFR mutant group: Mean age, 61.22 ± 10.43 years; 27 males, 36 females; 8 patients with smoking history, 55 without; clinical stage: stage I–II in 30 patients, stage III–IV in 33 patients. EGFR wild-type group: Mean age, 60.86 ± 10.33 years; 20 males, 15 females; 8 patients with smoking history, 27 without; clinical stage: stage I–II in 22 patients, stage III–IV in 13 patients.

2.2 Methods

2.2.1 EGFR Mutation Detection

Lung adenocarcinoma tissue samples fixed in neutral buffered formalin and embedded in paraffin were analyzed using next-generation sequencing (NGS) based on targeted region probe capture combined with the Illumina high-throughput sequencing platform. Cases with mutations detected in any exon of the EGFR gene were classified as mutant; those without detected mutations were classified as wild-type.

2.2.2 Tumor Marker Measurement

Fasting venous blood (2.0 mL) was collected from each patient. After centrifugation for 10 minutes, the supernatant was obtained, and serum CEA levels were measured using a chemiluminescence method. The normal reference value for CEA was <5.0 ng/mL. Values exceeding the normal range were considered positive; otherwise, they were considered negative.

2.3 Statistical Analysis

Statistical analyses were performed using SPSS version 23.0. Normally distributed continuous data were expressed as mean ± standard deviation (mean ± SD), and between-group comparisons were conducted using the *t*-test. Non-normally distributed continuous data were expressed as median (interquartile range) [M (P25, P75)], with between-group comparisons performed using nonparametric tests. Categorical variables were expressed as counts (percentages) [n (%)], and between-group comparisons were conducted using the chi-square (χ^2) test or Fisher's exact test. A P-value <0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of serum CEA for EGFR mutations in lung adenocarcinoma.

3 Results

3.1 EGFR Mutation Profile

Among the 63 patients with lung adenocarcinoma harboring EGFR mutations, a single-site mutation was identified in 57 cases (90.47%). Mutation spectrum analysis revealed that exon 21 L858R point mutation (exon 21 L858R) was the most common alteration, detected in 28 cases (44.44%), followed by exon 19 deletion mutation (exon 19 del) in 25 cases (39.68%). Additionally, exon 20 insertion mutations (exon 20 ins) were observed in 3 cases (4.76%), and an exon 21 L861Q mutation (exon 21 L861Q) was identified in 1 case (1.59%). Furthermore, double-site mutations were detected in 6 cases (9.52%) among all mutation-positive patients. The specific double-site mutation types included: 21 p.L858R/19 p.K757R, 21 p.L858R/20 p.T790M, 21 p.L858R/20 p.R776H, 21 p.L858R/18 p.E709K, 21 p.L858R/7 p.T263P, and 20 p.S768I/20 p.V774M. In summary, EGFR gene mutations were predominantly characterized by exon 21 L858R point mutations and exon 19 deletions. The detailed distribution of each mutation type is presented in Table 1.

Table 1. Specific Types of EGFR Gene Mutations in 63 Patients with Lung Adenocarcinoma

EGFR mutation variants	example number（n/N）	The percentage of mutation cases (%)
Exon 19 (19del)	25/63	39.68%
Exon 21 (L858R)	28/63	44.44%
Exon 21 (L861Q)	1/63	1.59%
21 p.L858R/19 p.K757R	1/63	1.59%
21 p.L858R/20 p.T790M	1/63	1.59%
21 p.L858R/20 p.R776H	1/63	1.59%
21 p.L858R/18 p.E709K	1/63	1.59%
21 p.L858R/7 p.T263P	1/63	1.59%
Exon 20（p.D770_N771insGD）	1/63	1.59%
Exon 20（p.H773_V774insPHPH）	1/63	1.59%
Exon 20（p.H773dup）	1/63	1.59%
20 p.S768I/20 p.V774M	1/63	1.59%

3.2 Association Between EGFR Mutation Status and Clinical Characteristics

A total of 63 patients with EGFR mutations and 35 patients with EGFR wild-type were included in this study. The mean ages of the two groups were 61.22 ± 10.43 years and 60.86 ± 10.33 years, respectively. Statistical analysis revealed that EGFR mutation status was not significantly associated with age, sex, smoking history, clinical stage, or the presence of distant organ and/or lymph node metastasis (all P > 0.05). Detailed data are presented in Table 2.

Table 2. Association Between EGFR Mutation Status and Clinical Characteristics in Patients with Lung Adenocarcinoma

Item	Characteristics	EGFR (n=98)		t or χ^2 value	P value
		The mutation group	The wild-type group		
Age (years)	Age (years), mean ± SD	61.22±10.43	60.86±10.33	0.167	0.862
	≤60	26 (41.27%)	16 (45.71%)	0.181	0.670
	>60	37 (58.73%)	19 (54.29%)		
Gender	Male	27 (42.86%)	20 (57.14%)	1.840	0.175
	Female	36 (57.14%)	15 (42.86%)		
Smoking	Yes	8 (12.70%)	8 (22.86%)	1.700	0.192
	No	55 (87.30%)	27 (77.14%)		
Clinical stage	I–II	30 (47.62%)	22 (62.86%)	2.098	0.148
	III–IV	33 (52.38%)	13 (37.14%)		
Distant organ and/or lymph node metastasis	Yes	34 (53.97%)	14 (40.00%)	1.757	0.185
	No	29 (46.03%)	21 (60.00%)		

3.3 Association Between EGFR Mutation and CEA Levels

The CEA positivity rate in the EGFR mutant group (49.21%) was significantly higher than that in the wild-type group (28.57%), with a statistically significant difference (P = 0.047). EGFR mutation was positively correlated with CEA levels (r = 0.200), as shown in Table 3. Further subgroup analysis was performed by stratifying EGFR mutant patients into the following groups: exon 19 mutation group, exon 21 mutation group, other single-site mutation group, and double/multiple-site mutation group. The results showed no statistically significant differences in CEA levels among these subgroups (P > 0.05), as presented in Table 4. Stratified analysis based on CEA concentration was also conducted. Among patients with abnormally elevated CEA levels (≥ 5 ng/mL), no statistically significant difference in EGFR mutation rate was observed between the 5 ng/mL - 10 ng/mL subgroup and the ≥ 10 ng/mL subgroup (P > 0.05). Detailed results are shown in Table 5.

Table 3. Association Between EGFR Mutation Status and Serum CEA Levels in Patients with Lung Adenocarcinoma

Item	Tumor marker	EGFR ($n = 98$)		t or χ^2 value	P value	r value
		Mutation group	Wild-type group			
CEA	Positive	31 (49.21%)	10 (28.57%)	3.937	0.047	0.200
	Negative	32 (50.79%)	25 (71.43%)			

Table 4. Association Between Serum CEA Levels and EGFR Mutation Subtypes in Patients with Lung Adenocarcinoma

Item	Tumor marker	EGFR mutation subgrouping				χ^2 value	P value
		Exon 19 mutation group	Exon 21 mutation group	Other single-site mutation group	Double/multiple-site mutation group		
CEA	Positive	14 (56.00%)	15 (51.72%)	0 (0.00%)	2 (33.33%)	3.662	0.324
	Negative	11 (44.00%)	14 (48.28%)	3 (100%)	4 (66.67%)		

Table 5. EGFR Mutation Rate by CEA Concentration Subgroup in CEA-Positive Patients

CEA concentration (ng/mL)	n	Mutation group	Wild-type group	χ^2 value	P value
5 ng/mL–10 ng/mL	13	8 (25.81%)	5 (50.00%)	1.079	0.299
≥ 10 ng/mL	28	23 (74.19%)	5 (50.00%)		

3.4 ROC Curve Analysis of CEA Levels for Predicting EGFR Mutations

A receiver operating characteristic (ROC) curve was constructed to evaluate the predictive value of pre-treatment serum CEA levels for EGFR mutation status. The results showed that the area under the curve (AUC) for CEA in predicting EGFR mutations was 0.637 (P = 0.025), indicating modest predictive performance. The optimal cutoff value was determined using the Youden index. At a CEA cutoff value of 16.51 ng/mL, the corresponding sensitivity was 34.9% and specificity was 94.3%. Detailed results are presented in Figure 1.

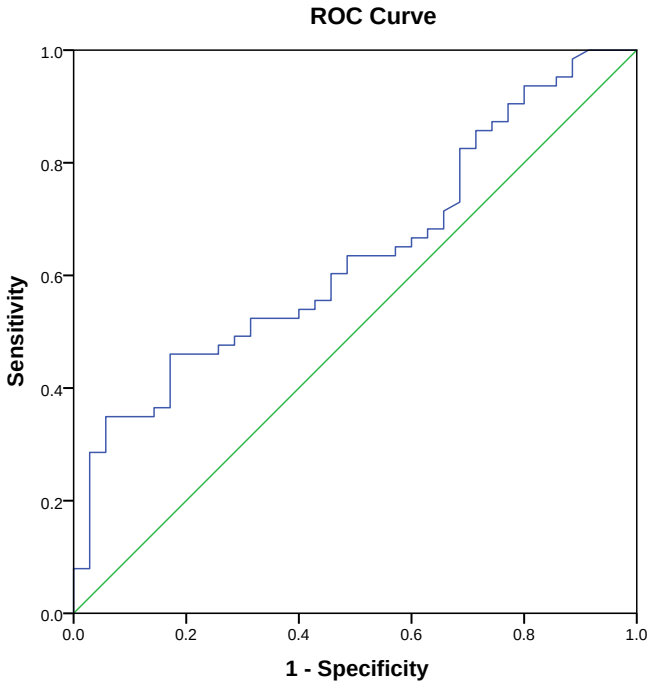


Figure 1: ROC curve of CEA levels for predicting EGFR mutations

4 Discussion

The treatment of lung cancer has now entered the era of "precision medicine." EGFR gene mutations are not only closely associated with the biological characteristics of the disease but also significantly influence patient responses to specific therapeutic regimens. With advances in molecular biology, precise identification of EGFR mutations has become a critical turning point in the treatment of non-small cell lung cancer (NSCLC). Previous studies have demonstrated that EGFR gene mutation status is one of the important biomarkers for predicting the efficacy of EGFR-TKI therapy[13]. Therefore, determining EGFR mutation status holds significant reference value for the diagnosis and treatment of patients with NSCLC. However, the high cost and stringent technical requirements of EGFR gene testing limit its widespread clinical application. Exploring effective methods for predicting EGFR mutations may help improve the efficacy of EGFR-TKI targeted therapy and provide a scientific basis for prognosis assessment in NSCLC patients.

Multiple international multicenter studies have confirmed that EGFR mutations occur at higher frequencies in specific clinical and demographic populations, particularly among Asian individuals, patients with adenocarcinoma histology, females, and never-smokers[14-16]. The present study, which included 98 patients with lung adenocarcinoma, showed no significant associations between EGFR mutation status and age, sex, smoking history, clinical stage, or the presence of distant organ and/or lymph node metastasis

(all P > 0.05). Discrepancies between our findings and those of some previous studies may be attributable to differences in sample size, racial and geographic distribution characteristics of the study populations, inclusion criteria, or statistical model specifications. Consequently, the association between clinical characteristics and EGFR mutation status warrants further validation through rigorously designed, large-scale, multicenter prospective clinical studies.

Tumor markers are substances synthesized and released by tumor cells that play important roles in cancer diagnosis, treatment efficacy assessment, and recurrence prediction. The literature reports a high positivity rate of CEA in lung adenocarcinoma, a histological subtype that also exhibits a high frequency of EGFR mutations, suggesting a potential intrinsic link between the two. The present study found a higher CEA positivity rate in the EGFR mutant group compared with the wild-type group, and serum CEA levels were positively correlated with EGFR mutation status. These findings are consistent with multiple previous studies[17-19], supporting the potential clinical utility of CEA in assessing the risk of EGFR mutations. From a molecular pathology perspective, EGFR gene mutations may continuously activate tyrosine kinase activity, promote phosphorylation of downstream signaling molecules such as Akt and STAT3, and subsequently initiate anti-apoptotic pathways. As an important effector molecule in this pathway, CEA expression levels are closely associated with EGFR mutation status[6,20].

Relevant studies[7] have confirmed a significant correlation between CEA levels and EGFR mutation positivity, and have further noted that patients with higher CEA levels are more likely to harbor exon 19 mutations. However, Cai et al.[17] analyzed 296 patients with non-small cell lung cancer and found no statistically significant differences between exon 19 or exon 20 mutations and serum CEA levels. This finding is consistent with the results of the present study, suggesting that serum CEA concentration may not be clearly associated with specific EGFR mutation sites (e.g., L858R or exon 19 deletion). Although the present study failed to confirm such an association, this negative finding requires further validation with an expanded sample size given the limitations of the current sample. ROC curve analysis further evaluated the predictive value of CEA levels for EGFR mutations, yielding an AUC of 0.637 with a cutoff value of 16.51 ng/mL, indicating an increased risk of mutation when CEA exceeds 16.51 ng/mL. The moderate AUC value suggests that other important variables have not yet been incorporated into the model, such as radiomic features, circulating tumor DNA (ctDNA) mutation profiles, or tissue proteomic information.

In summary, serum CEA level may serve as an auxiliary biomarker for predicting EGFR mutation status in patients with lung adenocarcinoma and has potential value for clinical application. However, given its moderate predictive performance and inability to distinguish between mutation subtypes, the current findings do not support the use of CEA alone as a basis for targeted therapy decisions. Future research should focus on integrating multi-dimensional data to construct more accurate predictive models, thereby advancing the development of precision medicine in lung cancer.

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References

[1]Yang B, Ji H S, Zhou C S, et al. 18F-fluorodeoxyglucose positron emission tomography/computed tomography-based radiomic features for prediction of epidermal growth factor receptor mutation status and prognosis in patients with lung adenocarcinoma[J]. Translational Lung Cancer Research, 2020, 9(3): 563.

[2]Jiang R, Wang X, Li K. Predictive and prognostic value of preoperative serum tumor markers is EGFR mutation-specific in resectable non-small-cell lung cancer[J]. Oncotarget, 2016, 7(18): 26823.
[3]Zou J, Lv T, Zhu S, et al. Computed tomography and clinical features associated with epidermal growth factor receptor mutation status in stage I/II l Ung adenocarcinoma[J]. Thoracic Cancer, 2017, 8(3): 260-270.
[4]Tetsuya I ,Hiroyuki I ,Haruhiko N , et al. Efficacy of Platinum-Based Adjuvant Chemotherapy on Prognosis of Pathological Stage II/III Lung Adenocarcinoma based on EGFR Mutation Status: A Propensity Score Matching Analysis. [J]. Molecular diagnosis & therapy, 2019, 23 (5): 657-665.
[5]Gao Y, Song P P, Li H, et al. Elevated serum CEA levels are associated with the explosive progression of lung adenocarcinoma harboring EGFR mutations[J]. BMC cancer, 2017, 17(1): 484.
[6]Gu J, Xu S, Huang L, et al. Value of combining serum carcinoembryonic antigen and PET/CT in predicting EGFR mutation in non-small cell lung cancer[J]. Journal of Thoracic Disease, 2018, 10(2): 723.
[7]Jin B, Dong Y, Wang H, et al. Correlation between serum CEA levels and EGFR mutations in Chinese nonsmokers with lung adenocarcinoma[J]. Acta Pharmacologica Sinica, 2014, 35(3): 373-380.
[8]Jung M, Kim S H, Hong S, et al. Prognostic and predictive value of carcinoembryonic antigen and cytokeratin-19 fragments levels in advanced non-small cell lung cancer patients treated with gefitinib or erlotinib[J]. Yonsei medical journal, 2012, 53(5): 931-939.
[9]Ko K H, Hsu H H, Huang T W, et al. Value of 18F-FDG uptake on PET/CT and CEA level to predict epidermal growth factor receptor mutations in pulmonary adenocarcinoma[J]. European journal of nuclear medicine and molecular imaging, 2014, 41(10): 1889-1897.
[10]Zhang J, Zhao X, Zhao Y, et al. Value of pre-therapy 18F-FDG PET/CT radiomics in predicting EGFR mutation status in patients with non-small cell lung cancer[J]. European journal of nuclear medicine and molecular imaging, 2020, 47(5): 1137-1146.
[11]Wang S, Ma P, Ma G, et al. Value of serum tumor markers for predicting EGFR mutations and positive ALK expression in 1089 Chinese non-small-cell lung cancer patients: a retrospective analysis[J]. European Journal of Cancer, 2020, 124: 1-14.
[12]Wang Z, Yang S, Lu H. Preoperative serum carcinoembryonic antigen levels are associated with histologic subtype, EGFR mutations, and ALK fusion in patients with completely resected lung adenocarcinoma[J]. OncoTargets and therapy, 2017: 3345-3351.
[13]Pan Z, Wang K, Wang X, et al. Cholesterol promotes EGFR-TKIs resistance in NSCLC by inducing EGFR/Src/Erk/SP1 signaling-mediated ERRα re-expression[J]. Molecular cancer, 2022, 21(1): 77.
[14]Shi Y, Li J, Zhang S, et al. Molecular epidemiology of EGFR mutations in Asian patients with advanced non-small-cell lung cancer of adenocarcinoma histology–mainland China subset analysis of the PIONEER study[J]. PloS one, 2015, 10(11): e0143515.
[15]Thi A M, Tin Tin S, McKeage M, et al. Utilisation and determinants of epidermal growth factor receptor mutation testing in patients with non-small cell lung cancer in routine clinical practice: a global systematic review[J]. Targeted Oncology, 2020, 15(3): 279-299.
[16]Seow W J, Matsuo K, Hsiung C A, et al. Association between GWAS-identified lung adenocarcinoma susceptibility loci and EGFR mutations in never-smoking Asian women, and comparison with findings from Western populations[J]. Human molecular genetics, 2017, 26(2): 454-465.
[17]Cai Z. Relationship between serum carcinoembryonic antigen level and epidermal growth factor receptor mutations with the influence on the prognosis of non-small-cell lung cancer patients[J]. OncoTargets and therapy, 2016: 3873-3878.
[18]Feng L X, Wang J, Yu Z, et al. Clinical significance of serum EGFR gene mutation and serum tumor markers in predicting tyrosine kinase inhibitor efficacy in lung adenocarcinoma[J]. Clinical and Translational Oncology, 2019, 21(8): 1005-1013.

[19]Weng Q, Hui J, Wang H, et al. Radiomic feature-based nomogram: a novel technique to predict EGFR-activating mutations for EGFR tyrosin kinase inhibitor therapy[J]. Frontiers in Oncology, 2021, 11: 590937.

[20]Tomoya T ,Miku K ,Ayaka S , et al. Gefitinib Enhances Mitochondrial Biological Functions in NSCLCs with EGFR Mutations at a High Cell Density. [J]. Anticancer research, 2017, 37 (9): 4779-4788.