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ORIGINAL ARTICLE

Effect of molecular targeted therapy combined with radiotherapy on the expression and prognostic value of COX-2 and VEGF in bone metastasis of lung cancer

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Summary

Purpose: *This study aimed to explore the effect of molecular targeted therapy combined with radiotherapy on the expression and prognostic value of cyclooxygenase-2 (COX-2) and vascular endothelial growth factor (VEGF) in bone metastasis of lung cancer.*

Methods: *82 patients with bone metastases of lung cancer who underwent targeted therapy combined with radiotherapy in Hubei Cancer Hospital were regarded as the experimental group, and another 64 patients with bone metastases of lung cancer who underwent conventional radiotherapy were regarded as the control group. Serum VEGF and COX-2 levels were measured by enzyme-linked immunosorbent assay (ELISA) before and after the treatment. The efficacy and adverse reactions of both groups were compared.*

Results: *The levels of COX-2 and VEGF in serum of both groups were significantly lower than those before treatment ($p<0.05$). The effective rate and local tumor efficiency of the experimental group were significantly higher than those of the control group ($p<0.05$). The diarrhea and asthenia and vomiting events in the experimental group were significantly lower than those in the control group ($p<0.05$). No significant differences were found between the two groups in other adverse reactions ($p>0.05$). A significant positive correlation was found between COX-2 and VEGF in serum in the two groups before and after treatment; the survival rate of COX-2 and VEGF high expression group was significantly lower than in the low expression group ($p<0.05$); ECOG score, pathological type, COX-2 and VEGF level were independent risk factors of death in the experimental group.*

Conclusion: *Targeted therapy combined with radiotherapy has a strong inhibitory effect on the expression of COX-2 and VEGF in bone metastasis of lung cancer. There was a significant positive correlation between the expression of COX-2 and VEGF, and the use of targeted therapy combined with radiotherapy can significantly improve the efficacy and quality of life and to prolong survival.*

Key words: *bone metastasis of lung cancer, COX-2, molecular targeted therapy, prognosis, radiotherapy, VEGF*

Introduction

Lung cancer, a very common malignant tumor, has the highest morbidity and mortality rates, and the non-small cell lung cancer (NSCLC) accounts for approximately 80% of all types of lung cancers [1]. Because the symptoms of lung cancer are not apparent in the early stage, most patients are already in advanced stage at the time of initial diagnosis [2]. Bone metastases often occur in lung cancer, which is normally associated with adenocarcinoma. Approximately 30-65% of patients with advanced lung cancer suffer from bone metastases, most of which are osteolytic, and the severe pain and functional disorders cause a serious impact on the patient quality of life [3]. Currently, bone metastasis of lung cancer is mainly treated with radiation, which can reduce the pain and improve

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the quality of life of patients. However, the disadvantage is that the treatment cannot significantly improve the patient survival [4,5]. Targeted therapy is the treatment by key molecules or genes on various molecular signaling pathways during cell division, proliferation and metastasis [6]. Gefitinib, an oral-type molecular targeted therapy, belongs the small molecule epidermal growth factor receptor tyrosine kinase inhibitor (EGFR tyrosine kinase, EGFR-TKI) [7]. EGFR-TKI is radiosensitized, so the combination of radiotherapy in the advanced NSCLC is a promising treatment [8-10]. However, further research is required for the specific effects of targeted therapy combined with radiotherapy for bone metastasis of lung cancer.

Cyclooxygenase (COX), an important rate-limiting enzyme that catalyzes the conversion of arachidonic acid to prostaglandins, has an important effect in many pathophysiological processes. Among them, cyclooxygenase-2 (COX-2) is an inducible enzyme with a 'rapid response gene' and low expression levels, however, its expression is upregulated in inflammation and tumor tissues [11]. Studies have shown that COX-2 positive expression is closely related to NSCLC lymph node metastasis and lung adenocarcinoma prognosis [12]. Vascular endothelial growth factor (VEGF) has an important effect in various physiological and pathological processes, such as placental formation and angiogenesis, and is an important angiogenesis-inducing agents [13]. Jin et al [14] also found that the clinical stage and lymph node metastasis of tumors are accompanied with overexpression of VEGF in NSCLC tumor tissues.

Enzyme-linked immunosorbent assay (ELISA) was maninly used to detect the effect of molecular targeted therapy combined with radiotherapy on serum VEGF and COX-2 levels in patients with bone metastases of lung cancer. Also the correlation between VEGF and COX-2 in bone metastasis of lung cancer and the role of molecular targeted drug therapy were further studied, which has a great significance in the clinical treatment of patients with bone metastases of lung cancer.

Methods

General information

A retrospective analysis method was used. Eight-two patients with bone metastases of lung cancer who were treated with molecular targeted therapy combined with radiotherapy in Hubei Cancer Hospital were regarded as the experimental group, including 54 males, 28 females, aged 32-78 years (mean±SD 54.27±13.67), a 3-24 months of follow-up time (mean±SD 16.47±3.12). What's more, 64 patients with bone metastases of lung cancer treated with conventional radiotherapy were regarded as the control group, including 41 males, 23 females, aged between 30-77 years (mean±SD 53.87±13.17) with an average follow-up time of 15.65±3.09 months.

Inclusion criteria

Lung cancer patients diagnosed with cytological and histopathological examinations; Patients with pain in bones; Patients with bone metastases who were diagnosed with bone lesions after CT, MRI, X-ray and Skelton ECT scan; All patients with normal ECG, routine urine, liver and kidney function, coagulation function, blood pressure and blood routine tests before treatment; Patients with a predicted survival longer than 3 months; Patients who had no history of surgery and trauma in the past 4 weeks; Patients with no serious vascular invasion observed in imaging examination results; Patients with Karnofsky performance score (KPS) > 50 [15].

Exclusion criteria

Patients with liver and kidney dysfunctions or severe cardiac insufficiency and mental illness; Patients with contraindications to chemotherapy; Patients with defects in the autoimmune system; Pregnant or lactating women; Patients who received other antitumor treatments within one month prior to treatment; Patients with poor compliance during treatment or incomplete data; Patients with allergic history; All other patients with osteoarthritis or traumatic fractures.

The study was approved by the ethics committee of Hubei Cancer Hospital and the patient experimental content was described in detail. All patients agreed and signed a complete informed consent form.

Methods of treatment

The control group: conventional radiotherapy was used as the main method, and certain patients with deep lesions were given three-dimensional conformal radiotherapy. Target area confirmation: CT showed bone destruction and peripheral soft tissue shadows, with soft tissue shadow 1.5 cm outside the field, otherwise, the bone was destroyed by 1.5 cm outside the field. For those who needed three-dimensional conformal radiotherapy, the CTV was 0.5 cm outside the GTV, and the PTV was 0.5 cm outside the CTV; also 95% of the PTV volume was required to receive 95% of the prescribed dosage. The total prescribed dosages were 30GY/3GY/10F. Most patients were given 4 mg of zoledronic acid (Jiangsu Osei Kang Pharmaceutical Co., Ltd., National Pharmaceutical Standard H20064298). It was dissolved in 100 ml of 0.9% normal saline, then intravenous infusion was applied for 15-20 min and the injection was repeated once every 4 weeks, and administered continuously for 2 times.

The experimental group: On the basis of the control group, the molecular targeted drug gefitinib (AstraZeneca Co., Ltd., Guoxun Zhuxu J20070047) was given orally for more than 6 months with 250 mg/d. The patient should stop taking the drug if there was intolerable toxic side reactions during the medication or when the disease progressed.

Collection of serum specimen

Two ml of elbow venous blood (with at least 8 h empty stomach) was extracted by a vacuum lancet from the patient 1 day before and after the treatment; then the blood was centrifuged. Centrifugation conditions: 3000 r/min, 15 min. The slurry in the test tube was then carefully aspirated to obtain serum and stored in a refrigerator at -80°C for future use.

Enzyme-linked immunosorbent assay (ELISA) for the detection of serum VEGF and COX-2 levels

Serum VEGF and COX-2 levels were measured by ELISA, and the VEGF and COX-2 kits were provided by Shanghai Jingkang Bioengineering Co., Ltd. and the batch number was JLC7456, JLC6322-96T, respectively. The instrument was BS-1101 enzyme label analyzer of Beijing Linmao Technology Co., Ltd. Steps: 50 µl of different concentration standards were added. Only one hole was set in the blank well and 50 µl of distilled water were added to the sample well for test. Also 40 µl of the sample dilution were added to the well and 10 µl of the sample were added and incubated in a 37°C water bath or incubator for 30 min. In addition to the blank wells, 50 µl of the enzyme labeling reagent in the kit was added to each well. Then, 50 µl of each of the developers A and B was sequentially added to each well, and the liquid in each well was gently mixed and was developed at 37°C for 15 min in the dark. Fifty µl of the reaction termination solution were added to each well, and the reaction was terminated, and yellow color appeared in the reaction well. Within 15 min, the blank hole was used as the zero reference value, and the OD value of each well was measured at a wavelength of 450 nm. A standard curve was used to calculate the concentration of VEGF and COX-2 in the sample. The specific operation was strictly in accordance with the kit instructions.

Follow-up and observation indicators

The two groups were followed up by on-site visit and telephone for 3 years. The survival conditions were recorded, the concentrations of VEGF and COX-2 were compared between the two groups before and after treatment and the correlation between VEGF and COX-2 was analyzed. The therapeutic effects of the two groups were compared. The adverse reactions that occurred in the two groups were compared to explore risk factors affecting the prognosis of patients with bone metastases from lung cancer.

Efficacy evaluation criteria [16]

Assessment was according to the response evaluation criteria in solid tumor (RECIST): complete response (CR): All lesions completely disappeared and maintained for 4 weeks; Partial response (PR): The total lesion diameter was reduced by ≥30% and maintained for 4 weeks; Progressive disease (PD): The total diameter of the lesion in-

Table 1. General information in both groups

	Experiment group (n=82) *n (%)*	*Control group (n=64)* *n (%)*	x^2/t	*p*
Gender			0.051	0.822
Male	54 (65.9)	41 (64.1)		
Female	28 (34.1)	23 (35.9)		
Age, years			0.015	0.901
≤60	44 (53.7)	35 (54.7)		
>60	38 (46.3)	29 (45.3)		
Weight (kg)			0.724	0.395
<50	23 (28.0)	14 (21.9)		
≥50	59 (72.0)	50 (78.1)		
Smoking status			0.137	0.712
Smoking	54 (65.9)	44 (68.8)		
Non-smoking	28 (34.1)	20 (31.2)		
ECOG score			0.017	0.896
≤2	21 (25.6)	17 (26.6)		
>2	61 (74.4)	47 (73.4)		
Metastasis types			0.030	0.999
Skull metastasis	10 (12.2)	8 (12.5)		
Rib metastasis	13 (15.9)	10 (15.6)		
Pelvis metastasis	26 (31.7)	21 (32.8)		
Spinal metastasis	33 (40.2)	25 (39.1)		
Incidence types			0.015	0.901
Single	44 (53.7)	35 (54.7)		
Multiple	38 (46.3)	29 (45.3)		

creased by ≥20% or new lesion(s) appeared; Stable disease (SD): The total diameter of the lesion decreased but did not reach PR or increased but did not reach PD. Effectiveness= (CR + PR) / total number of cases × 100%; local control rate of tumor= (CR + PR + SD) / total number of cases.

Statistics

Statistical analyses of experimental data was performed using SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA), The count data were expressed in n (%). Chi-square test was used for comparison between groups, mean±standard deviation was used to indicate the measurement data, the independent sample t-test was used for comparisons between groups, and the paired t-test was used to compare the data before and after treatment. Correlation between COX-2 and VEGF expression was performed using Pearson correlation coefficient. Survival analysis was performed using the Kaplan-Meier method and the Log-rank test. Univariate and multivariate Cox regression analyses were used to analyze the factors influencing the survival of patients with bone metastases from lung cancer. P<0.05 was considered statistically significant.

Results

General information in both groups

There were no significant differences (p>0.05) between the two groups in terms of gender, age, weight, smoking status, ECOG score, tumor metastasis type, single or multiple incidence, and the two groups were comparable (Table 1).

Serum levels of COX-2 and VEGF in bone metastasis of lung cancer before and after treatment

There was no significant difference in serum COX-2 and VEGF levels between the two groups before treatment (p>0.05). The serum levels in the experimental group were significantly lower than those before treatment (p<0.05). The serum levels in the control group decreased significantly after treatment (p<0.05). Figure 1 shows that the serum levels of COX-2 and VEGF in the experimental group were significantly lower than those in the control group after treatment (p<0.05).

Comparison of the efficacy in the two groups of treatment

All the patients in the two groups completed all the treatment and follow-ups. Comparing the effective and local efficiency of the experimental group and the control group the results showed that the effective rate and local tumor efficiency of the experimental group were significantly higher than those of the control group (p<0.05), and the difference was statistically significant (Table 2).

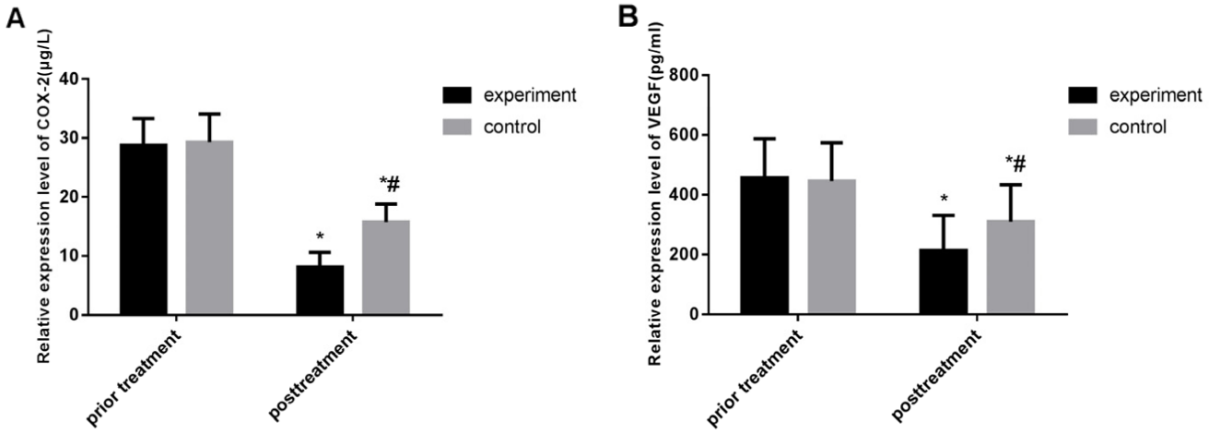

Figure 1. Contents of COX-2 and VEGF in serum of bone metastasis before and after treatment between the two groups. **A:** Comparison of serum COX-2 level of the experimental group and the control group before and after treatment. **B:** Comparison of serum VEGF level between the experimental group and the control group before and after treatment. *vs* before treatment, *p<0.05; #*vs* the experimental group, p<0.05.

Table 2. Comparison of the therapeutic effects between both groups

Groups	*n*	*CR* *n (%)*	*PR* *n (%)*	*SD* *n (%)*	*PD* *n (%)*	*Effective rate* %	*Local tumor efficiency* %
Experimental group	82	32 (39.0)	34 (41.5)	10 (12.2)	6 (7.3)	80.5	92.7
Control group	64	17 (26.6)	24 (37.5)	9 (14.1)	14 (21.9)	64.1	78.1
x^2						7.248	9.074
p value						0.007	0.003

Comparison of adverse reactions between the two groups

The diarrhea, asthenia and vomiting in the experimental group were significantly lower than those in the control group (p<0.05). However, they were mild and could be relieved spontaneously. There were no significant differences between the two groups in the other adverse reactions (p>0.05) (Table 3).

Correlation between the expression of COX-2 and VEGF

Before treatment, there was a significant positive correlation between the expression of COX-2 and VEGF in the serum of the experimental group and the control group (r=0.6218, 0.5038, p<0.05). After treatment, there was a significant positive correlation between the expression of COX-2 and VEGF in the serum of the experimental group and the control group (r=0.7554, 0.6118, p<0.05), as shown in Figure 2.

Comparison of survival rates between the two groups

The survival rate of the experimental group at 12 and 24 months was 54.88% and 25.61%, respectively, and the median survival time was 16

Table 3. Comparison of adverse reactions in the two groups

	Rash *n (%)*	*Diarrhea* *n (%)*	*Fever* *n (%)*	*Asthenia and vomit* *n (%)*	*Digestive tract reaction* *n (%)*
Experimental group	7 (8.5)	6 (7.3)	3 (3.7)	16 (19.5)	4 (4.9)
Control group	4 (6.3)	15 (23.4)	4 (6.3)	22 (34.4)	7 (10.9)
x^2	0.270	7.585	0.529	4.124	1.894
P	0.604	0.006	0.467	0.042	0.169

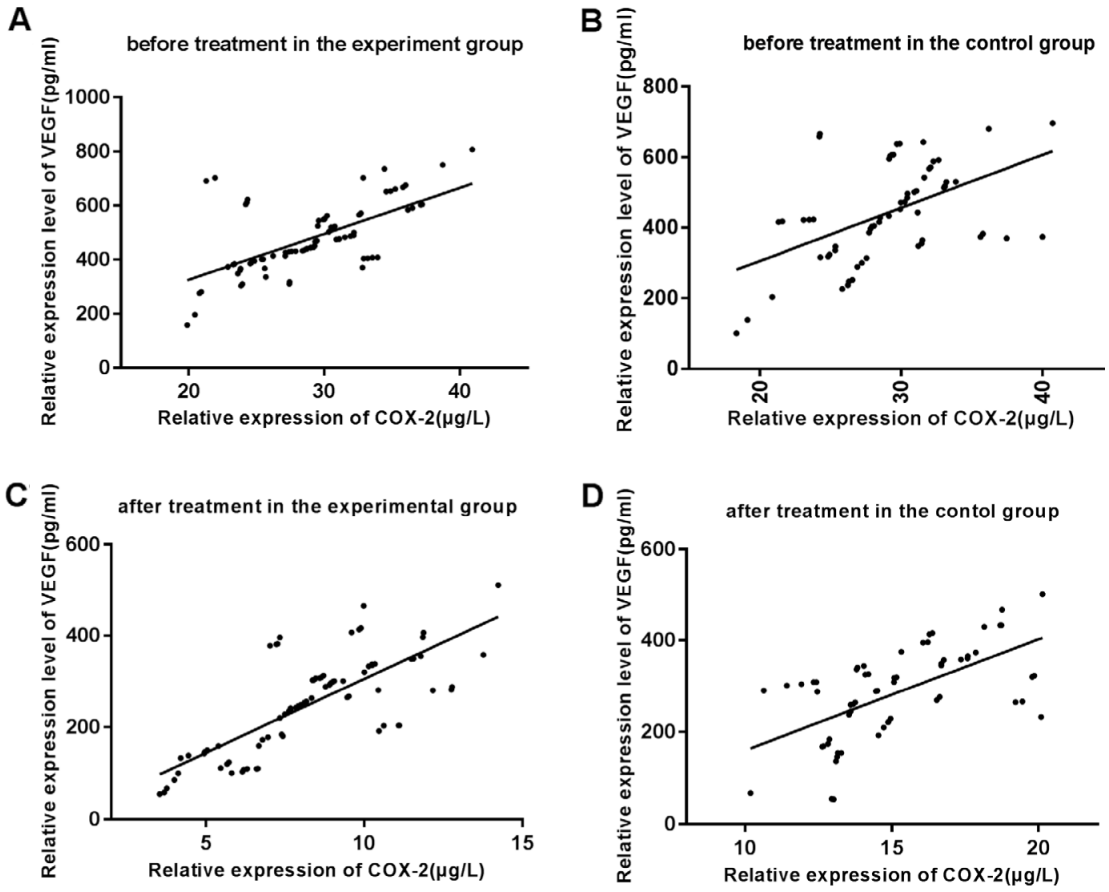

Figure 2. Correlation between COX-2 and VEGF expression before and after treatment. Pearson correlation analysis showed that **A:** There was a significant positive correlation between COX-2 and VEGF in the experimental group before treatment (r=0.6218, p<0.05). **B:** There was a significant positive correlation between COX-2 and VEGF before treatment (r=0.5038, p<0.05). **C:** There was a significant positive correlation between COX-2 and VEGF in the experimental group after treatment (r=0.7554, p<0.05). **D:** There was a significant positive correlation between COX-2 and VEGF in the control group after treatment (r=0.6118, p<0.05).

months. The survival rate of the control group at 12 and 24 months was 39.06% and 14.06%, respectively, and the median survival time was 9 months. The survival rate of the experimental group at 12 months and 24 months was significantly higher than that of the control group after treatment (x^2=5.138, p<0.05). There was no significant difference in median survival time between the two groups (p>0.05).

Relationship between expression of COX-2 and VEGF and survival rate in patients in the experimental group

1. Relationship between COX-2 expression and survival rate

According to the expression level of COX-2, there were 43 subjects (≥8.12) μg/L in the high expression group and 39 subjects (<8.12) μg/L

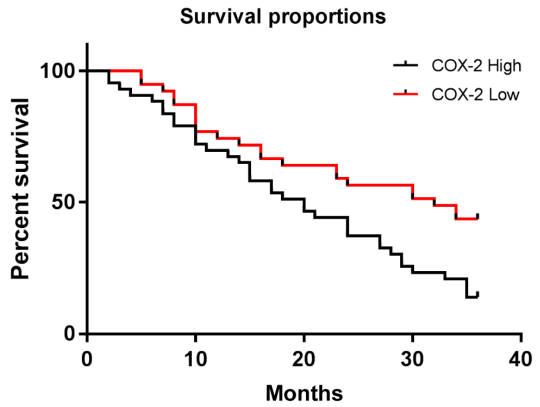

Figure 3. The relationship between COX-2 expression and survival rate in the experimental group. The survival rate in the high expression group was 13.95%, and the survival rate in the low expression group was 43.59%. The survival rate of COX-2 high expression group was significantly lower than that of low expression group (x^2=8.900, p<0.05).

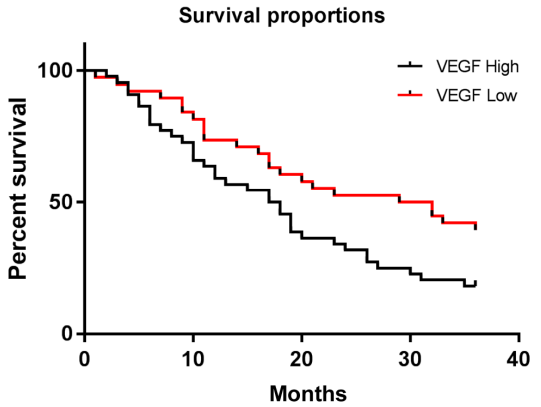

Figure 4. The relationship between VEGF expression and survival rate in the experimental group after treatment. The survival rate of the high expression group was 18.18%, and the survival rate of the low expression group was 39.47%. The survival rate of the VEGF high expression group was significantly lower than that of the low expression group (x^2=4.580, p<0.05).

Table 4. Univariate analysis

	Death group (n=59) *n (%)*	*Survival group (n=23)* *n (%)*	x^2/t	*P*
Gender			0.006	0.940
Male	39 (66.10)	15 (65.22)		
Female	20 (33.90)	8 (34.78)		
Age (years)			0.105	0.746
≤60	31 (52.54)	13 (56.52)		
>60	28 (47.46)	10 (43.48)		
Weight (kg)			0.631	0.427
<50	18 (30.51)	5 (21.74)		
≥50	41 (69.49)	18 (78.26)		
Smoking status			2.660	0.103
Smoking	42 (71.19)	12 (52.17)		
Non-smoking	17 (28.81)	11 (47.83)		
ECOG score			20.860	<0.001
≤2	7 (11.86)	14 (60.87)		
>2	52 (88.14)	9 (39.13)		
Incidence types			4.677	0.031
Single	27 (45.76)	17 (73.91)		
Multiple	32 (54.24)	6 (26.09)		
COX-2 (μg/L)	8.92±1.68	7.32±1.94	3.708	0.000
VEGF (pg/mL)	242.23±107.22	185.31±97.68	2.212	0.030

in the low expression group. After three years of follow-up, the survival rate of the high expression group was 13.95%, and the survival rate of the low expression group was 43.59% (Figure 3). The survival rate of the COX-2 high expression group was significantly lower than that of the low expression group (x^2=8.900, p<0.05).

2. Relationship between VEGF expression and survival rate

According to the expression level of VEGF, there were 44 subjects (≥213.77) pg/ml in the high expression group and 38 subjects (<213.77) pg/ml in the low expression group. After three years of follow-up, the survival rate of high expression group was 18.18%, and the survival rate of low expression group was 39.47% (Figure 4). The survival rate of the VEGF high expression group was significantly lower than that of the low expression group (x^2=4.580, p<0.05).

Influencing factors of poor prognosis in the experimental group

After follow-up, according to the survival of the experimental group, the patients were divided into the death group (n=59) and the survival group (n=23). Univariate analysis was used to analyze the data (Table 4). There was difference in the ECOG score, pathological type, COX-2 and VEGF levels between the death group and the survival group (p<0.05). The indicators were assigned values (Table 5). The results of multivariate Cox regression analysis of risk factors showed that ECOG score, pathological type, COX-2 and VEGF levels were independent risk factors for death in the experimental group (Table 6).

Table 5. Assignment

ECOG score	≤2:1, >2:2
Incidence types	Single:1, Multiple:2
COX-2 (μg/L)	Continuous data using raw data analysis
VEGF (pg/mL)	Continuous data using raw data analysis

Discussion

Lung cancer promotes excessive maturation and activation of osteoclasts during bone metastases. The balance of normal bone resorption and reconstruction is destroyed, resulting in an increase in bone resorption and bone destruction [17]. The occurrence of bone metastasis in lung cancer seriously reduces the quality of life of patients, and the quality of life can be significantly improved through orthopedic surgery, chemotherapy, radiotherapy, gamma knife intervention, zoledronic acid and gefitinib [18].

With the development of anticancer drugs and research on cancer cell signaling pathways, molecular targeted therapies are increasingly chosen as effective treatments for bone metastasis of lung cancer. Gefitinib, one of the targeted therapy drugs, is also very common in clinical practice, the action mechanism of which is as follows: it inhibits EGFR-TKI and terminates phosphorylation, inhibits the proliferation and metastasis of cancer cells, induces apoptosis of cancer cells, interferes with vascular development, and exerts antitumor effects [19-21]. Some studies have shown [22,23] that the radiosensitivity of various tumor cells was negatively correlated with the expression of EGFR in tumor tissues. Radiotherapy combined with EGFR-TKI treatment may prolong the survival of patients with advanced NSCLC. Whether molecular targeted therapy combined with radiotherapy have the same effect in bone metastasis of lung cancer remains to be further studied.

Some information has shown that COX-2 plays a very important role in the development of lung cancer, and can evaluate the prognosis of squamous cell carcinoma (SCC), adenocarcinoma (ADC) and stage I non-small cell lung cancer [24]. COX-2 is a key enzyme in the synthesis of prostaglandin E2 (PGE2). Studies have shown that COX-2 is highly expressed in tumors, resulting in increased PGE2 content in tumor cells, which promotes tumor cell growth and proliferation, and cell invasion can also be promoted by increasing the expression of β1-integrin in NSCLC, which is an important cytokine involved in tumorigenesis and progression [25,26].

Table 6. Multivariate analysis

	β	*SD*	x^2	*P*	*HR (95% CI)*
ECOG score	-2.612	0.830	9.911	0.002	0.073 (0.014-0.373)
Incidence types	-1.812	0.818	4.911	0.027	0.163 (0.033-0.811)
COX-2 (μg/L)	-0.696	0.259	7.208	0.007	0.499 (0.300-0.829)
VEGF (pg/mL)	-0.016	0.005	8.459	0.004	0.984 (0.974-0.995)

In lung cancer, VEGF plays an important role in vascular supply in tumors [27]. The VEGF/VEGF receptor axis consists of multiple ligands and receptors; there were overlap and difference between the ligand and receptor in binding specificity, cell type expression and function; targeted inhibition of VEGF signaling pathway can partially inhibit tumor angiogenesis and growth [28,29].

This study mainly explored the expressions of COX-2 and VEGF in serum and their clinical significance in patients with bone metastases of lung cancer. The results have shown that the levels of COX-2 and VEGF in the serum of the two groups were significantly lower than those before treatment ($p<0.05$). The content of COX-2 and VEGF in the experimental group was significantly lower than in the control group ($p<0.05$), suggesting that molecular targeted therapy combined with radiotherapy can significantly reduce the contents of COX-2 and VEGF, and has a good therapeutic effect. A positive correlation has been reported between VEGF and COX-2 expressions in patients with oral squamous cell carcinoma ($r=0.462$, $p<0.001$) [30]. In this study, before and after treatment, there was a significant positive correlation between COX-2 and VEGF in the serum of the experimental and the control group ($p<0.05$). This suggests that COX-2 and VEGF may have synergistic effects in tumorigenesis and disease development. Also studies have found that the inhibition of COX-2 gene expression by shRNA in tongue cancer cells can significantly reduce the synthesis of VEGF-C mRNA and affect its protein level [31]. Moreover, in cervical cancer cells, COX-2 inhibitors can affect cell invasion and metastasis by inhibiting the expression of VEGF-C [32]. Therefore, COX-2 and VEGF are expected to be good indicators of bone metastasis of lung cancer.

All the patients in the two groups completed all treatments and follow-ups. The effective rate and local tumor efficiecny of the two groups were compared and found that the effective rate and local tumor efficiency of the experimental group were higher than those of the control group ($p<0.05$). Herbst et al [33] found that gefitinib often had side effects such as diarrhea and rash less than II degrees, with incidence rates of 55 and 46%, respectively. In this study, there were fewer adverse reactions in the treatment in the two groups. Diarrhea, asthenia and vomit in the experimental group were significantly lower than those in the control group ($p<0.05$), but they were mild and could be relieved spontaneously. Therefore, it is believed that gefitinib can significantly reduce the incidence of adverse reactions. Results of D'Antonio et al [23] showed that radiotherapy combined with EGFR-TKI has a synergistic effect, it can prolong the survival of patients with advanced lung cancer, and reduce the radiation resistance of tumors in the late stage and the secondary drug resistance of EGFR-TKI, and the adverse reactions were lighter than simultaneous radiotherapy and chemotherapy, which is consistent with the results of this study. Some studies have found that EGFR-TKI treatment can improve the quality of life, reduce the pain and prolong the progression-free survival of patients with advanced NSCLC with newly diagnosed bone metastases [34]. It has been reported that in patients with NSCLC who received platinum-based chemotherapy, the disease-free survival of patients with COX-2 expression was significantly lower than that of patients without COX-2 expression ($p=0.017$) [35]. An et al [36] have shown that the survival rate of patients with advanced NSCLC with lower plasma VEGF levels after treatment with bevacizumab plus chemotherapy was improved. The study found that the survival rate of COX-2 and VEGF high expression group was significantly lower than that of low expression group. It is suggested that the expression levels of COX-2 and VEGF are correlated with poor prognosis of patients with bone metastasis of lung cancer. Pathological types, number of bone metastases, clinical stage, ECOG score and serum alkaline phosphatase (ALP) levels are prognostic factors for bone metastasis in lung cancer [37]. In this study, ECOG score, pathological type, COX-2, and VEGF levels were independent risk factors for death in the experimental group.

This study found that the mechanism of molecular targeting drug gefitinib combined with radiotherapy in the treatment of bone metastases in lung cancer is related to their respective mechanisms of action, and gefitbib with radiation therapy may also have synergistic effects. However, the specific mechanism is still unclear, which requires further studies. The combined use of the two also has a significant effect on patients with bone metastases of lung cancer. However, due to the retrospective analysis and the small number of samples, it is necessary to expand the number of samples in the subsequent research to get a more reliable conclusion.

In summary, targeted therapy has a strong inhibitory effect on the expression of COX-2 and VEGF in bone metastasis of lung cancer, and the expression of COX-2 and VEGF is significantly positively correlated. The use of targeted therapy combined with radiotherapy can significantly improve the efficacy and quality of life, and prolong survival.

Conflict of interests

The authors declare no conflict of interests.

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