



Effect of radiotherapy on serum SCC, CEA, CRFRA21-1, TAG72, CA199 and lymphocyte subsets in patients with esophageal squamous cell carcinoma

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ABSTRACT

Objective: To study the effect of radiotherapy on serum SCC, CEA, CRFRA21-1, TAG72, CA199 and lymphocyte subsets in patients with esophageal squamous cell carcinoma. **Methods:** A total of 60 patients with esophageal squamous cell carcinoma in our hospital from January 2013 to January 2016 were selected as experiment group and 40 healthy subjects were selected as control group. Patients in experiment group were treated with 6MV X-ray radiation therapy. Serum SCC, CEA, CRFRA21-1, TAG72, CA199 and the cell percentage of peripheral blood CD4⁺, CD8⁺ were compared in control group and the experimental group before and after 1 month radiotherapy. **Results:** Before treatment, the levels of serum SCC, CEA and CRFRA21-1 in the experimental group were significantly higher than those in the control group ($P < 0.05$); After treatment, the levels of serum SCC, CEA and CRFRA21-1 in the experimental group were significantly lower than those before treatment, but the experimental group patients were significantly higher than those in the control group ($P < 0.05$); There was no significant difference between the experimental group and the control group in the level of serum TAG72 and CA199 before treatment, and there was no significant difference in the serum levels of TAG72 and CA199 before and after radiotherapy in the experimental group ($P > 0.05$). Before treatment, the cell percentage of peripheral blood CD4⁺, CD8⁺ and the ratio of CD4⁺/CD8⁺ in experimental group was significantly lower than that of the control group, the percentage of peripheral blood CD8⁺ in the experimental group was significantly higher than that in the control group ($P < 0.05$); Compared with before treatment, there was no statistically significant difference after treatment in the cell percentage of peripheral blood CD4⁺, CD8⁺ and the ratio of CD4⁺/CD8⁺ in experimental group ($P > 0.05$), and in the experimental group, the proportion of CD4⁺ cells and the ratio of CD4⁺/CD8⁺ in peripheral blood was significantly lower than that of the control group, the proportion of CD8⁺ was significantly higher than that of the control group ($P < 0.05$). **Conclusions:** Radiotherapy can significantly reduce the serum SCC, CEA, CRFRA21-1, TAG72 and CA199 levels of the patients with esophageal squamous cell carcinoma, but have less influence on the T lymphocyte subsets.

1. Introduction

Esophageal squamous cell carcinoma is a malignant tumor with high incidence in our country. Its mortality accounts for fourth of all malignant tumors, and the 5-year survival rate of it remains

only about 30%, which is a serious threat to people's lives[1]. There is no obvious clinical symptom in the early stage of the disease, which is often ignored by patients. It is often diagnosed in the late stage of pathology[2,3]. At present, the clinical treatment of esophageal squamous cell carcinoma is often used in surgery and radiotherapy measures[4]. Some studies have reported that patients with esophageal squamous cell carcinoma have large individual differences in radiotherapy, and often lead to a large difference in the efficacy of radiotherapy in patients with similar pathological symptoms[5]. Therefore, it is of great significance to select the sensitive index of esophageal squamous cell carcinoma. Squamous

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cell carcinoma antigen (SCC), carcinoembryonic antigen (CEA), cytotokerantin-19-fragment antigen 21-1 (CRFRA21-1), tumor associated glycoprotein (TAG72) and cancer antigen 199 (CA199) are the common tumor markers in clinic[6,7]. Most of the studies have found that patients with malignant tumor have low cellular immune function, mainly manifested as a disordered proportion of T lymphocyte subsets in different cells. Suppression of immune function can decrease the body's ability to resist tumor, but there exists different views about whether radiotherapy will further suppress the immune function of patients. This research examines the effect of radiotherapy on serum SCC, CEA, CRFRA21-1, TAG72, CA199 and lymphocyte subsets in patients with esophageal squamous cell carcinoma. The results are as follows.

2. Materials and methods

2.1. General information

A total of 60 patients with esophageal squamous cell carcinoma in our hospital from January 2013 to January 2016 were selected as experiment group. Case inclusion criteria were as follows: (1) Patients diagnosed as esophageal squamous cell carcinoma by endoscopic and pathology; (2) No operation pointer or reject an operation; (3) Measurable lesion; (4) Did not receive radiotherapy. Case exclusion criteria were as follows: (1) Without distant metastasis; (2) Patients with other malignant tumors; (3) With radiotherapy contraindications; (4) Women in pregnancy or lactation; (5) Poor radiotherapy dependence. A total of 40 healthy subjects at the same period were selected as control group.

There were 38 males and 22 females in the experimental group, they were aged from 32 to 70 years old, mean age (50.27±15.18) years old; Weight 48-71 kg, mean weight (55.67±7.19) kg; Pathological stage: 3 cases of stage I, 35 cases of stage II, 22 cases of stage III. There were 26 males and 14 females in the control group, they were aged from 30 to 69 years old, mean age (49.34±13.11) years old; Weight 49-72 kg, mean weight (57.73±8.36) kg. There were no significant differences in gender, age, weight and other general data between the two groups ($P>0.05$).

2.2. Experimental method

The patients in the experimental group were given three-dimensional conformal external irradiation. Firstly, the esophageal barium meal and CT were used to determine the location of the lesion, then body plate or head and neck shoulder frame was used to fix position. CT scan was simulated; the scanning image was transmitted to the three-dimensional treatment planning system through the image acquisition and transmission system. Outline of target area was drawn, including primary lesion to decide whether to pack and lymphatic drainage area according to the patient's tumor stage and physical condition. Swedish Medical Elekta synergy linear

accelerator 6MV X-ray irradiation was used, the primary tumor and metastatic lymph node was given 60-66 Gy/30-33 f/5-6 w and corresponding lymph drainage area was give 45-50 Gy /25 f/5 w.

2.3. Detection of indexes

Fasting elbow venous blood 5 mL was collected, with the period of 1 months before and after radiotherapy in experimental group, while the control group was in physical examination. Then serum separation was performed for 15 min with a speed of 3 000 rpm. The level of serum SCC, CEA, CRFRA21-1, TAG72, CA199 and the ratio of peripheral blood CD4⁺, CD8⁺, CD4⁺/CD8⁺ cells was detected and compared in control group and in the experimental group before and after treatment.

The serum SCC and CEA level was analyzed by chemiluminescence immunoassay. Abbott Architecti2000 chemiluminescence analyzer detection was used, reagent was from Abbott Company supporting products. The level of serum CRFRA21-1, TAG72, CA199 was detected by luminescence immunoassay, using Cobas2000 full automatic immune analyzer, and all operations were carried out strictly in accordance with the kit instructions. Peripheral blood CD4⁺ and CD8⁺ cells were detected by FACSCalibur BD automatic multi color analysis flow cytometry system. The positive criteria of tumor markers SCC, CEA, CRFRA21-1, TAG72, CA199 were as follows: SCC>1.5 ng/mL, CEA>5.0 ng/mL, CRFRA21-1>3.3 ng/mL, TAG72>4.0 U/mL, CA199>37.0 U/mL[8].

2.4. Statistical analysis

SPSS19.0 software package was used, measurement data were expressed as mean ± standard deviation. *t* test was used to compare measurement data and count data between groups, with $P<0.05$ as statistically significant difference.

3. Results

3.1. Comparison of serum SCC, CEA and CRFRA21-1 levels before and after treatment

Before treatment, the levels of serum SCC, CEA and CRFRA21-1 in the experimental group were significantly higher than those in the control group ($P<0.05$); After treatment, the levels of serum SCC, CEA and CRFRA21-1 in the experimental group were significantly lower than those before treatment, but the experimental group patients were significantly higher than those in the control group ($P<0.05$) (Table 1).

3.2. Comparison of serum TAG72 and CA199 levels before and after treatment

Before and after treatment, there was no significant difference

Table 1

Comparison of serum SCC, CEA and CRFRA21-1 levels before and after treatment (ng/mL).

Groups	<i>n</i>		SCC	CEA	CRFRA21-1
Experimental group	60	Before treatment	2.24±1.22 [#]	4.52±2.38 [#]	4.62±1.11 [#]
		After treatment	0.77±0.41 ^{*#}	2.35±1.01 ^{*#}	1.95±0.66 ^{*#}
Control group	40		0.18±0.05	1.02±0.87	1.04±0.29

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, [#] $P<0.05$.

between the experimental group patients and the control group in the level of serum TAG72 and CA199. After treatment, there was no significant difference in the serum levels of TAG72 and CA199 before and after radiotherapy in the experimental group ($P>0.05$) (Table 2).

Table 2

Comparison of serum TAG72 and CA199 levels before and after treatment (μmL).

Groups	n		TAG72	CA199
Experimental group	60	Before treatment	1.67±1.13	15.74±7.67
		After treatment	1.43±0.92	13.56±5.81
Control group	40		1.32±0.97	12.85±6.82

3.3. Comparison of peripheral blood lymphocyte subsets levels before and after treatment

Before treatment, the cell percentage of peripheral blood CD4⁺, CD8⁺ and the ratio of CD4⁺/CD8⁺ in experimental group was significantly lower than that of the control group, the percentage of peripheral blood CD8⁺ in the experimental group was significantly higher than that in the control group ($P<0.05$); Compared with before treatment, there was no statistically significant difference after treatment in the cell percentage of peripheral blood CD4⁺, CD8⁺ and the ratio of CD4⁺/CD8⁺ in experimental group ($P>0.05$), and in the experimental group, the proportion of CD4⁺ cells and the ratio of CD4⁺/CD8⁺ in peripheral blood was significantly lower than that of the control group, the proportion of CD8⁺ was significantly higher than that of the control group ($P<0.05$) (Table 3).

4. Discussion

At present, the treatment methods of esophageal squamous cell carcinoma including surgery, radiotherapy and chemotherapy, but because of different sensitivity to radiotherapy in patients with esophageal squamous cell, however, because of the different sensitivity of esophageal squamous cell carcinoma patients to radiotherapy, there exists different radiation effects[9]. Clinical often use the enhanced CT, PET-CT or barium meal examination results to determine the effect of radiotherapy in patients with esophageal squamous cell carcinoma, but the first two methods are complex and expensive, and often difficult to bear, while the latter has the shortcoming that some patients with small lesions and other metastasis sites may not be detected early. So to find effective tumor markers to predict the efficacy of radiotherapy in patients with esophageal squamous cell carcinoma has important clinical significance[10]. So far, different tumors have hundreds of different tumor markers, but still lack of ideal tumor marker for esophageal squamous cell carcinoma patients to determine

the effect of radiotherapy[11]. SCC is a kind of tumor associated glycoprotein, which is closely related to the activity of esophageal squamous cell carcinoma cells. It is commonly used in diagnosis and prognosis of esophageal squamous cell carcinoma[12]. CEA is a broad spectrum tumor marker in the immunoglobulin superfamily. It has a high serum level in a variety of tumor patients[13]. CRFRA21-1 is a protein antigen which is composed of 19 segments of cells in tumor epithelial cells. With the increase of cell proliferation and cell volume in esophageal squamous cell carcinoma, the positive detection rate in serum is significantly increased[14]. TAG72 is a kind of high molecular viscosity protein, has high expression in the digestive tract tumor, ovarian cancer and other malignant tumors, and has close relation with tumor metastasis, malignancy degree and prognosis[15]. CA199 is a kind of related gastrointestinal tumors in tumor cell membrane lipid sugar, with higher levels in the serum of patients with esophageal squamous cell carcinoma, and with the degree of malignancy increased, the expression increased[16]. Cancer patients often have low immunity, especially cell immune function, radiotherapy can aggravate the patient's immune function[17]. T lymphocyte subsets are important indicators of the immune function of the body, and have two primary cells: helper CD4⁺ and inhibitory CD8⁺. The former has the effect of regulating the immune response and the latter plays the role of immune inhibition and cytotoxicity. This research examines the effect of radiotherapy on serum SCC, CEA, CRFRA21-1, TAG72, CA199 and lymphocyte subsets in patients with esophageal squamous cell carcinoma, so that we can provide a certain clinical basis for the selection of reasonable tumor markers in the treatment of to judge the effect of radiotherapy in patients with esophageal squamous cell carcinoma and observe the effect of radiotherapy on the immune function in patients with esophageal cancer.

Before treatment, the levels of serum SCC, CEA and CRFRA21-1 in the experimental group were significantly higher than those in the control group, the difference was statistically significant ($P<0.05$); After treatment, the levels of serum SCC, CEA and CRFRA21-1 in the experimental group were significantly lower than those before treatment, but the experimental group patients were significantly higher than those in the control group, the difference was statistically significant ($P<0.05$). However, there was no significant difference between the experimental group and the control group in the level of serum TAG72 and CA199 before treatment, after treatment, and there was no significant difference in the serum levels of TAG72 and CA199 before and after radiotherapy in the experimental group ($P>0.05$). This suggests that radiotherapy can significantly reduce the level of serum SCC, CEA and CRFRA21-1 in patients with esophageal squamous cell carcinoma, but it has no effect on the level of serum TAG72 and CA199. And this can also predicts that CEA, CRFRA21-1 and SCC can be used to determine the effect of radiotherapy in patients with esophageal squamous cell carcinoma.

Table 3

Comparison of peripheral blood lymphocyte subsets levels before and after treatment (%).

Groups	n		CD4 ⁺	CD8 ⁺	CD4 ⁺ /CD8 ⁺
Experimental group	60	Before treatment	24.19±2.57 [*]	29.41±2.18 [*]	0.82±0.15 [*]
		After treatment	23.12±1.16 [*]	31.09±1.82 [*]	0.74±0.12 [*]
Control group	40		30.29±5.47	25.70±3.75	1.18±0.17

Note: compared with the control group, ^{*} $P<0.05$.

This may be because that radiotherapy can quickly kill esophageal squamous cell carcinoma tumor cells, inhibit the proliferation and metastasis of tumor cells, resulting in serum SCC, CEA, CRFRA21-1 and other tumor markers significantly reduced[18]. In addition, the results of this study show that before treatment, the cell percentage of peripheral blood CD4⁺, CD8⁺ and the ratio of CD4⁺/CD8⁺ in experimental group was significantly lower than that of the control group, the percentage of peripheral blood CD8⁺ in the experimental group was significantly higher than that in the control group ($P < 0.05$); Compared with before treatment, there was no statistically significant difference after treatment in the cell percentage of peripheral blood CD4⁺, CD8⁺ and the ratio of CD4⁺/CD8⁺ in experimental group ($P > 0.05$), and in the experimental group, the proportion of CD4⁺ cells and the ratio of CD4⁺/CD8⁺ in peripheral blood was significantly lower than that of the control group, the proportion of CD8⁺ was significantly higher than that of the control group ($P < 0.05$). This suggests that the immune function of patients with esophageal squamous cell carcinoma was lower than that of healthy persons, and the effect of radiotherapy on cellular immune function in patients with esophageal squamous cell carcinoma was small. The cellular immune function decreased in most of the cancer patients after radiotherapy, but the experimental results showed that there was no significant change in the cellular immune function after radiotherapy in patients with esophageal squamous cell carcinoma, this may be due to the main effect of radiotherapy on the humoral immunity of patients with esophageal squamous cell carcinoma, so that it has little effect on the level of T lymphocyte subpopulation[19,20]. And because the sample size is small, the sample size should be further studied.

In summary, radiotherapy can significantly reduce the level of serum SCC, CEA and CRFRA21-1 in patients with esophageal squamous cell carcinoma, has no significant effect on the level of TAG72 and CA199, suggesting that the tumor markers SCC, CEA and CRFRA21-1 can be used to determine the efficacy of radiotherapy in patients with esophageal squamous cell carcinoma, so it is worth popularizing in clinic. The study found that the effect of radiotherapy on the immune function of patients with esophageal carcinoma is not obvious, and the effect of radiotherapy on the immune function of patients with esophageal cancer is controversial, so the verification needs to be further clinical and basic experiments.

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