

Original Article

Changes of serum levels of tumor necrosis factor (TNF- α) and soluble interleukin-2 receptor (SIL 2R) in patients with cervical cancer and their clinical significance

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Abstract: Objective: The goal of the current trial was to investigate the expression levels of tumor necrosis factor- α (TNF- α) and soluble interleukin-2 receptor (SIL-2R) in serum of patients with cervical cancer and analyze their clinical significance. Methods: We randomly selected 50 cases of cervical cancer patients who came to our hospital from March 2018 to March 2020 as the experimental group and 50 cases of healthy adult women during the same period as the control group. The experimental group received laparoscopic radical hysterectomy. We compared two groups of patients' serum level of TNF- α and SIL-2R expression. The receiver operating characteristic (ROC) curve was used to determine the diagnostic efficacy of serum TNF- α and SIL-2R in cervical cancer. Results: The expression levels of serum TNF- α and SIL-2R in the experimental group before radical hysterectomy were significantly higher than that one week after surgery; the preoperative serum TNF- α and SIL-2R expression levels of the experimental group were notably higher than those of the control group; and no marked difference in the expression levels of serum TNF- α and SIL-2R was observed between the control group and the experimental group one week after operation. The area under the curve of TNF- α was 0.846 (95% CI: 0.605~0.978), the diagnostic sensitivity was 81.54%, and the specificity was 70.12%; The area under the curve of SIL-2R is 0.813 (95% CI: 0.601~0.943), the diagnostic sensitivity was 80.13%, and the specificity was 69.97%. Conclusion: Serum levels of TNF- α and SIL-2R expression in patients with cervical cancer are usually noticeably elevated. After surgical treatment, the serum levels of TNF- α and SIL-2R expression will gradually become normal. It is of significant clinical relevance to detect the serum levels of TNF- α and SIL-2R expression for early diagnosis of intervention of cervical cancer.

Keywords: Cervical cancer, TNF- α , SIL-2R, expression level, clinical significance

Introduction

Cervical cancer is a common and life-threatening malignant tumor in adult women [1-3]. Due to the fact that the incidence of cervical cancer has been increasing among younger women, the treatment and diagnosis of cervical cancer need to be addressed urgently. At present, radical hysterectomy is the major treatment for cervical cancer [4-6]. Tumor necrosis factor- α (TNF- α) is a regulator of immune response and a tumor cell killing factor. Soluble interleukin-2 receptor (SIL-2R) is one of the components in the tumor necrosis factor cell network. It has anti-tumor and regulation immunity and other effects. It was reported that the expression levels of serum TNF- α and SIL-2R increased

significantly in patients with malignant tumors, and their expression levels decreased after treatment [7-9]. In this study, we investigated the significance of the changes in the expression levels of TNF- α and SIL-2R in patients with cervical cancer by comparing to those before surgery. The medical records obtained from 50 patients with cervical cancer admitted to our hospital from March of 2018 to March of 2020 were also reviewed.

Materials and methods

Subjects

We randomly selected 50 cases of cervical cancer patients admitted to our hospital from

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Table 1. General Data ($\bar{x}\pm s$, n)

Group	Experimental Group	Control Group	t/X ²	P
Age (Year)	59.37 \pm 6.44	60.08 \pm 6.71	0.54	0.59
Height (cm)	163.32 \pm 5.80	162.59 \pm 4.99	0.67	0.50
Weight (kg)	67.08 \pm 10.12	66.71 \pm 10.85	0.18	0.86
High blood pressure	13	15	0.20	0.66
Diabetes	5	4	0.12	0.72
Hyperlipemia	3	4	0.15	0.70
Smoke	11	10	0.06	0.81
Drinking	23	20	0.37	0.55

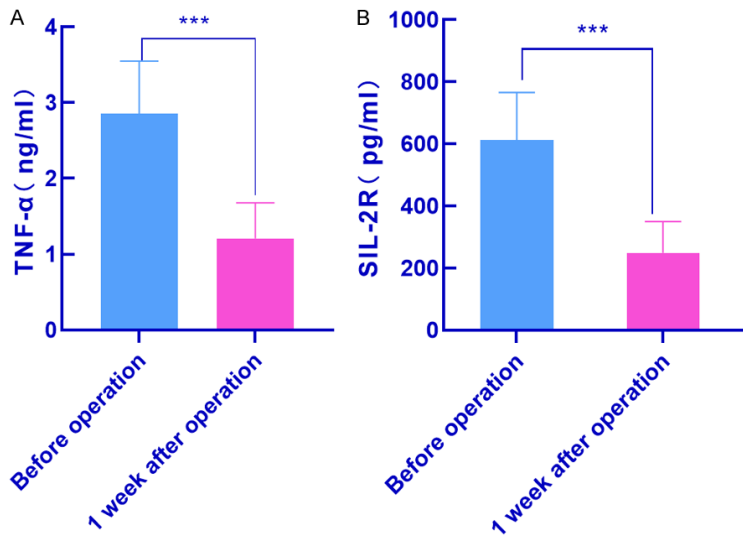


Figure 1. Comparison of serum TNF- α and SIL-2R expression levels in the experimental group before and one week after surgery. Note: The abscissa of (A) represents before and after operation in the experimental group from left to right, and the ordinate represents the expression level of TNF- α (ng/ml); the abscissa of (B) represents before and after operation of the experimental group from left to right, and the ordinate represents the 2R (pg/ml) expression level value. The expression level of TNF- α (ng/ml) before laparotomy radical hysterectomy was (2.86 \pm 0.69) ng/ml, and one week after operation (1.21 \pm 0.47) ng/ml; The expression level of SIL-2R (pg/ml) before laparotomy radical hysterectomy was (610.84 \pm 154.32) pg/ml, and one week after operation (249.08 \pm 100.30) pg/ml. Comparison of serum TNF- α (ng/ml) expression levels in the experimental group before and one week after surgery (t=13.98, ***P<0.001); Comparison of serum SIL-2R (pg/ml) expression level of experimental group patients before and one week after surgery (t=13.90, ***P<0.001).

March 2018 to March 2020 and 50 healthy adult women confirmed by the healthy examination results during the same period as the experimental group and the control group, respectively. The patients in the experimental group were 38 to 75 years old. The age of the control group was 40-78 years old. They were of comparability with respect to age and other data (P>0.05). See **Table 1**.

Inclusion/exclusion criteria

Inclusion criteria: ① Met the clinical signs of cervical cancer [9]; ② Aged ≥ 18 years old; ③ No history of drug abuse, no history of drug allergy, no bad habits; ④ Normal mental state, clear consciousness, able to cooperate with research; ⑤ This study was reviewed by the hospital ethics committee, and informed consent form was obtained.

Exclusion criteria: ① Treated with anticoagulant drugs recently and presented with coagulopathy; ② With other organic diseases or malignant tumors; ③ Recently used anesthetics or received other surgical operations; ④ Lack of clinical data.

Methods

Surgical methods: Patients in the experimental group underwent laparotomy radical hysterectomy. First, it is required to fully prepare for the operation, for instance cleaning the patient's vagina, performing general anesthesia for the patient, and keeping the head lower than the lower limbs. Then, we should choose the abdomen for the incision position, remove the peripheral lymphatic tissues of the common iliac, external iliac, internal iliac and groin, open the uterine rectum and reflexed the peritoneum, cut off the bladder side ligament, main ligament and other parts. Finally the corresponding vaginal tissue should be removed and then the incision be sutured [10-13].

TNF- α , SIL-2R expression level detection method: 5 ml of fasting venous blood from patients in the control group was collected, and 5 ml of venous blood before radical hysterectomy in the experimental group and 5 ml of fasting

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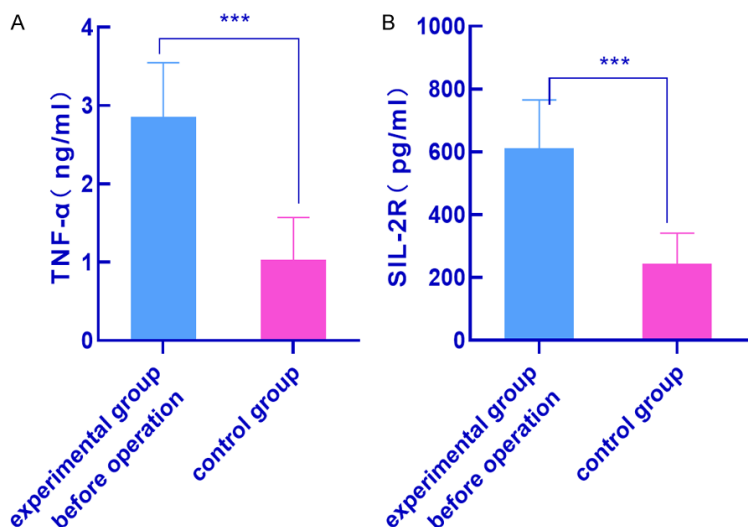


Figure 2. Comparison of serum TNF- α and SIL-2R expression levels between the experimental group before operation and the control group. Note: The abscissa of (A) indicates the experimental group and the control group from left to right, and the ordinate indicates the expression level of TNF- α (ng/ml). In (B), the abscissa indicates the experimental group and the control group from left to right, and the ordinate indicates the expression level of SIL-2R (pg/ml). The expression level of TNF- α (ng/ml) before laparotomy radical hysterectomy was (2.86±0.69) ng/ml, and the expression level of serum TNF- α (ng/ml) in the control group was (1.03±0.54) ng/ml; The expression level of SIL-2R (pg/ml) before laparotomy radical hysterectomy was (610.84±154.32) pg/ml, and the expression level of serum SIL-2R (pg/ml) in the control group was (243.51±97.61) pg/ml. Expression level of TNF- α (ng/ml) between the experimental group before operation and the control group was significantly different ($t=14.77$, $***P<0.001$). Comparison of the expression level of SIL-2R (pg/ml) between the experimental group before operation and the control group was statistically significant ($t=14.22$, $***P<0.001$).

venous blood one week after surgery were collected. They were centrifuged at 3500 r/min for 10 min to obtain the supernatant for use, and stored at -20°C. The enzyme-linked immunosorbent assay was used to detect the concentration of TNF- α and SIL-2R.

Observation indicators

We compared serum TNF- α and SIL-2R expression levels in the experimental group before and one week after operation. Moreover, we compared serum TNF- α and SIL-2R expression levels in the experimental group and the control group. And we explored the changes in the expression levels of serum TNF- α and SIL-2R in patients after radical hysterectomy.

Statistical analysis

All data were analyzed with SPSS ver. 21.0. Clinical data were presented as mean \pm standard deviation, number, and percentage, and

were compared using the t test and X^2 test, respectively. The receiver operating characteristic (ROC) curve was used to determine the diagnostic efficacy of serum TNF- α and SIL-2R in cervical cancer. A P value of <0.05 was defined as statistical significance.

Results

Serum TNF- α and SIL-2R expression levels in the experimental group before and one week after surgery

The expression levels of serum TNF- α and SIL-2R in the experimental group before laparotomy radical hysterectomy were elevated substantially as compared to those one week after surgery ($P<0.05$). It demonstrated that laparotomy radical hysterectomy can effectively reduce the serum TNF- α and SIL-2R expression levels (**Figure 1**).

Comparison of serum TNF- α and SIL-2R expression levels between the experimental group before surgery and the control group

The preoperative serum TNF- α and SIL-2R expression levels of the experimental group were found to be notably higher when compared to the control group ($P<0.05$), indicating that serum TNF- α and SIL-2R expression levels in patients with cervical cancer will be significantly elevated. See **Figure 2**.

Comparison of serum TNF- α and SIL-2R expression levels between the experimental group one week after surgery and the control group

We found no marked difference in the expression levels of serum TNF- α and SIL-2R between the control group and the experimental group one week after operation ($P>0.05$), suggesting that the serum TNF- α and SIL-2R expression levels in patients with cervical cancer after laparotomy radical hysterectomy gradually become normal. See **Figure 3**.

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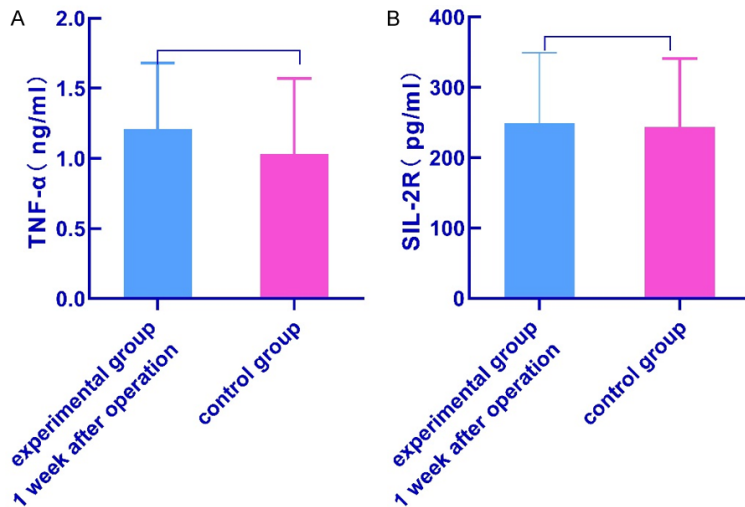


Figure 3. Comparison of serum TNF- α and SIL-2R expression levels between the experimental group one week after surgery and the control group. Note: The abscissa of (A) represents the expression level of TNF- α (ng/ml) in the experimental group one week after surgery and the control group, and the ordinate represents the expression level value. In (B), the abscissa indicates the expression level of SIL-2R (pg/ml) in the experimental group one week after surgery and the control group from left to right, and the ordinate indicates the expression level. The expression level of TNF- α (ng/ml) one week after laparotomy radical hysterectomy was (1.21±0.47) ng/ml, and the expression level of serum TNF- α (ng/ml) in the control group was (1.03±0.54) ng/ml; SIL-2R (pg/ml) expression level was (249.08±100.30) pg/ml one week after laparotomy radical hysterectomy, serum SIL-2R (pg/ml) expression level was (243.51±97.61) pg/ml in the control group. Expression level of TNF- α (ng/ml) between the experimental group one week after operation and the control group was not statistically different ($t=1.78$, $P=0.08$); Expression level of SIL-2R (pg/ml) in the experimental group one week after surgery and the control group was not statistically different ($t=0.28$, $P=0.78$).

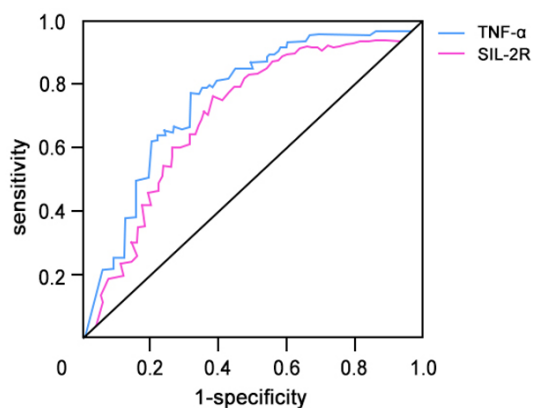


Figure 4. ROC curve analysis. Note: The area under the curve of TNF- α was 0.846 (95% CI: 0.605~0.978), the diagnostic sensitivity was 81.54%, and the specificity was 70.12%; The area under the curve of SIL-2R is 0.813 (95% CI: 0.601~0.943), with the sensitivity and specificity being 80.13% and 69.97% respectively.

ROC curve analysis

The ROC curve was plotted to determine the diagnostic efficacy of serum TNF- α and SIL-2R in cervical cancer. The area under the curve of TNF- α was 0.846 (95% CI: 0.605~0.978), the diagnostic sensitivity was 81.54%, and the specificity was 70.12%; The area under the curve of SIL-2R is 0.813 (95% CI: 0.601~0.943), with the sensitivity and specificity being 80.13% and 69.97% respectively. See **Figure 4**.

Discussion

The burden owing to cervical cancer prevalence, incidence and mortality is substantial [14-19]. Multiple trials have been conducted on tumor resection and clinical treatment with an attempt to reduce the mortality of cervical cancer patients and to improve the clinical efficacy [20-23]. In this regard, we investigated and compared the expression levels of TNF- α and SIL-2R in cervical cancer patients after tumor resection and before surgery and those in healthy adult women.

The occurrence and development of tumors are closely related to a variety of cytokines. TNF- α is a polypeptide cytokine with a two-way regulatory function. It is not only an immune protective medium, but also an important substance for immune pathological damage [16-18]. Under normal circumstances, TNF- α has an anti-tumor effect, but abnormally increased TNF- α has a counterproductive effect, which can cause the body's pathological immune damage. SIL-2R is a protein shed from the surface of lymphocytes and a marker of lymphocyte activation. SIL-2R can regulate inflammatory factors and inhibit autocrine effects, thereby inhibiting T cell proliferation. SIL-2R exists in soluble form in the blood, and its

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expression level is closely related to the immune response mediated by T cells. TNF- α and SIL-2R are closely related to the occurrence and development of a variety of malignant tumors, and also important predictors [19, 20]. We found in this study that the expression levels of serum TNF- α and SIL-2R in the experimental group before radical hysterectomy were significantly higher than that one week after surgery; the preoperative serum TNF- α and SIL-2R expression levels of the experimental group were notably higher than those of the control group; and no marked difference in the expression levels of these two indexes between the control group and the experimental group one week after operation was observed. This is similar to the study conducted by Wang Xueqing et al. [24] wherein they proposed that neoadjuvant chemotherapy can effectively reduce the serum TNF- α expression in patients with cervical cancer. It can be seen that both expression levels in patients with cervical cancer before laparotomy radical hysterectomy were significantly higher than those in healthy adult women in the control group and in patients one week after surgery. And there is no significant difference between the serum levels of TNF- α and SIL-2R expression in cervical cancer patients one week after surgery and healthy adult women. We can speculate that the changes of serum levels of TNF- α and SIL-2R expression in patients with cervical cancer can predict the onset of cervical cancer to a certain extent. In addition, the treatment of radical hysterectomy can also be evaluated by detecting the serum TNF- α and SIL-2R expression levels in patients. Therefore, the detection of the above two indicators in patients can be used for early diagnosis as well as evaluation of cervical cancer. This result is consistent with the findings from Emilia Lubowicka et al. [25] who pointed out that the detection of M-CSF expression level can be used as the evidence for early diagnosis of cervical cancer. The ROC curve was further used to evaluate the diagnostic efficacy of serum TNF- α and SIL-2R in cervical cancer. The area under the curve of TNF- α was 0.846, the diagnostic sensitivity was 81.54%, and the specificity was 70.12%; under the curve of SIL-2R, the area was 0.813, the diagnostic sensitivity was 80.13%, and the specificity was 69.97%, suggesting that serum TNF- α and SIL-2R have higher diagnostic efficiency for cervical cancer. However, due to the

size of sample included in this study is small, and long-term follow-up has not been performed. In the future, long-term trials with larger sample size are needed to garner refined data.

To sum up, serum TNF- α and SIL-2R expression levels in patients with cervical cancer will elevate noticeably. After surgical treatment, the serum TNF- α and SIL-2R expression levels will gradually become normal. Therefore, serum TNF- α and SIL-2R expression detection is a promising technique for early diagnosis and possible treatment of cervical cancer.

Disclosure of conflict of interest

None.

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