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Application of Circulating Tumor Cells in Peripheral Blood in Judging the Prognosis of Patients with Renal Cancer and Related Indexes of Blood Coagulation

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Abstract

Objective: To investigate the value of the number of circulating tumor cells (CTC) in peripheral blood in the prognosis and coagulation-related indicators of patients with renal cancer. **Methods:** 65 patients with renal cell carcinoma (RCC) confirmed pathologically were divided into CTC positive group and CTC negative group according to the CTC count (5 pcs/3.5 ml). Compare the age, gender, tumor location, TNM (clinical stage), pathological grade, tissue type, lymph node metastasis, distant metastasis, prognosis and prothrombin time (PT), fibrinogen (FIB), partial coagulation of the two groups of patients The correlation between the results of zymogen time (APTT) and D-dimer (DD) and the number of CTC. **Results:** There were significant differences in TNM, lymph node metastasis, and distant metastasis between the two groups ($P < 0.05$). The number of CTC in patients was correlated with FIB and D-D levels ($P < 0.05$). **Conclusion:** The number of CTC in patients with renal cell carcinoma is correlated with some clinical phenotypes (TNM, lymph node metastasis, distant metastasis) and some coagulation indexes (FIB, D-D), and can jointly predict the prognosis of renal cancer.

Keywords

Peripheral Blood Circulating Tumor Cells, Renal Cancer, Clinical Phenotype, Coagulation Index

1. Introduction

Renal cell carcinoma (RCC) accounts for about 2% - 3% of adult malignant tumors, and it is increasing at a rate of more than 200,000 new cases and more

than 100,000 deaths worldwide each year. Among RCC patients, 30% of patients had metastasis when the tumor was discovered, and it was also found that the postoperative recurrence rate of patients with localized RCC reached about 30% [1]. Therefore, the current important problem facing RCC is how to prevent tumor recurrence and metastasis.

Circulating tumor cells (CTC) are a type of tumor cells in the circulatory system. Previous studies have shown that, compared with the primary tumor, CTC has greater potential in predicting tumor recurrence, metastasis and prognosis [2]. In recent years, the value of CTC as a malignant biomarker and prognostic evaluation index has received more and more attention [3]. At present, CTC quantification has been used to assess tumor staging [4] [5]. The updated knowledge indicates that CTC plays a potentially key role in the prognosis or diagnosis of RCC. In this study, the number of CTCs in peripheral blood of patients with renal cancer was detected, combined with various clinical phenotypes and coagulation-related test indicators, to provide clinical data support for the prognosis of CTC-based RCC.

2. Materials and Methods

2.1. General Information

This study conducted a retrospective study of 65 RCC patients who visited the Department of Urology from May 2018 to February 2020 in the Affiliated Hospital of Chengde Medical College (hereinafter referred to as our hospital).

2.2. Inclusion Criteria

1) All patients were diagnosed pathologically, through hand gestures or renal tumor biopsy. 2) All patients have complete clinical data. 3) All patients signed an informed consent form.

2.3. Exclusion Criteria

1) Patients with other tumors; 2) Patients with blood system related diseases (including thrombotic diseases and drugs that affect blood coagulation); 3) Patients who cannot tolerate surgery or biopsy; 4) Within 1 week Patients undergoing dialysis and blood transfusion; 5) Patients participating in other clinical studies within one month; 6) Children, pregnant women, breastfeeding women, and mentally ill patients.

2.4. Judgment Criteria

The criteria for the positive grouping of patients with CTC are based on domestic and foreign literature [6], the criteria for the positive group is CTC ≥ 5/3.5 mL, and the negative group is CTC < 5/3.5 mL.

2.5. Detection Method

The peripheral blood of 65 patients with renal cancer in our hospital was taken

early in the morning to detect the number of CTCs. At the same time, the age, gender, tumor location, TNM (clinical stage), pathological grade, tissue type, and lymph node metastasis of the two groups were recorded. Distant metastasis, prognosis and the values of prothrombin time (PT), fibrinogen (FIB), partial prothrombin time (APTT) and D-dimer (DD).

2.6. Statistics

Use SPSS 22.0 to perform statistical analysis on the data. The measurement data are expressed as mean ± standard deviation, which conforms to the t-test of homogeneity of variance and normal distribution. The comparison of count data adopts the chi-square test. $P < 0.05$ means the difference is statistically significant.

3. Results

1) There was no difference in general information between the CTC-positive group and the CTC-negative group (see Table 1).

2) The two groups of patients have differences in TNM, lymph node metastasis, and distant metastasis ($P < 0.05$) (see Table 2).

3) CTC count is correlated with some coagulation indexes in patients with renal cell carcinoma ($P < 0.05$) (see Table 3).

4. Discussion

At present, the early diagnosis of RCC is still an important factor affecting the prognosis, and the benefit of patients with advanced RCC is still limited [7]. CTC detection can detect the primary tumor earlier, reflect the metastasis of the primary tumor in time, and assist in judging the progress of the disease [8]. As a type of tumor cells free from the circulatory system, the number of CTC has been shown to be related to the prognosis of the tumor [9]. Related studies have found that CTC also plays a certain role in guiding tumor treatment [10]. It has also been confirmed as a tumor biomarker that can predict the outcome of

Table 1. Comparison of general information of patients.

Group	Number of cases	Gender (example)		age	Onset location (case)	
		Female	male		Left	Right
CTC positive group	33	15	18	54.9 ± 1.2	19	14
CTC negative group	32	15	17	52.1 ± 0.8	17	15
χ^2 value		0.406			6.079	
t value				−2.311		
P value		0.273		0.09	0.30	

Note: All P values are >0.05, the difference is not statistically significant.

Table 2. Comparison of the clinical phenotypes of the two groups of patients.

	CTC positive group	CTC negative group	statistics	P value
TNM (T1/≥T2)	12/21	25/7	z = 4.105	<0.0001
Pathological grade (≤II/≥III)	16/3	9/1	z = 0.7569	0.3615
Tissue type (clear cell carcinoma/papillary carcinoma)	22/2	14/1	z = 0.274	0.8083
Lymph node metastasis (positive/negative)	11/20	0/20	z = 3.005	0.0036
CTC	11.25 ± 0.9070	1.950 ± 0.3362	t = 9.415	<0.0001
Distant transfer (yes/no)	15/15	1/19	z = 3.345	0.0008
Prognosis (survival/death)	25/4	17/0	z = 1.759	0.073

Table 3. The relationship between CTCs and PT, APTT, FIB, D-D in patients with renal cancer (x ± s).

Group	Number of cases	PT (s)	APTT (s)	FIB (g/L)	D-D (ug/L)
CTC positive group	33	21.80 ± 6.20	33.50 ± 1.50	5.06 ± 0.25	316.10 ± 22.50
CTC negative group	32	15.50 ± 0.70	29.80 ± 1.20	3.87 ± 1.21	232.20 ± 13.10
Z value		4.155	4.183	3.113	3.068
P value		0.366	0.317	0.043	0.045

treatment [11]. Although the survival and metastasis mechanism of CTC in peripheral blood has not been fully revealed, previous studies have confirmed that the mortality of most RCC patients is related to CTC-induced tumor metastasis [12]. In this study, we also found that there are significant differences in some clinical phenotypes of patients with different numbers of CTC renal cell carcinoma, such as TNM staging, lymph node metastasis, etc., indicating that CTC levels will affect the clinical phenotype of renal cell carcinoma patients, so we infer that, the number of CTC will also have a significant impact on the prognosis of renal cancer patients, and has the potential to predict the prognosis of RCC patients.

Previous studies have found that the occurrence and metastasis of tumor cells are related to the increase of D-D and FIB [13] [14]. The main reason is that D-D is related to the occurrence of tumors, which can increase fibrinolytic response and help tumor cell colonization and aggregation. Second, when tumor metastasis or micrometastasis occurs, FIB in the body will increase, indicating that FIB is related to tumor metastasis. In this study, the D-D and FIB of the CTC positive group were significantly higher than those of the negative group,

suggesting that patients in the CTC positive group are beneficial to tumor occurrence and metastasis. Therefore, observing the changes in CTC counts can reflect the changes in the body's environment and help determine whether the tumor has metastasized.

The number of CTCs in renal cancer patients combined with TNM staging, lymph node metastasis, distant metastasis and FIB, D-D values can assist renal cancer patients in judging their curative effect and prognosis, and provide clinical data support for patients with CTC-based RCC. This study is a single-center study with a limited amount of data. Future studies will further expand the sample size.

Funded Project

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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