



## The clinical significance of serum SCC–Ag combined with CD105 in patients with cervical cancer during the early stage diagnosis

Ru–Chan Ma<sup>1</sup>, Hong Bi<sup>2</sup>, Sen–Yang Cao<sup>2</sup>✉

<sup>1</sup>Department of Gynecologic Oncology, Yancheng Maternal and Child Health–Care Center, Jiangsu, Yancheng 224002, China

<sup>2</sup>Department of Reproductive Technology, Yancheng Maternal and Child Health–Care Center, Jiangsu, Yancheng 224002, China

### ARTICLE INFO

#### Article history:

Received 8 Aug 2016

Received in revised form 17 Aug 2016

Accepted 11 Aug 2016

Available online 24 Aug 2016

#### Keywords:

SCC–Ag

CD105

Cervical cancer

Early stage diagnosis

Clinical significance

### ABSTRACT

**Objective:** To invest the clinical significance of serum SCC–Ag combined with CD105 in early diagnosis of cervical cancer to provide new ideas for early diagnosis and clinical treatment of cervical cancer. **Methods:** A total of 74 cases cervical cancer patients were selected as cervical cancer group, and 52 cases uterine fibroids patients were selected as normal cervical group, serum samples were collected in the early morning fasting condition, SCC–Ag and CD105 were checked by ELISA method, SCC–Ag and CD105 of two groups were analyzed by t-test, and to compare SCC–Ag and CD105 in different TMN staging, lymph gland metastasis and non-lymph gland metastasis in patients with cervical cancer, the correlation analysis was used by Pearson correlation analysis method. **Results:** These results came from ELISA method, comparing with normal cervical group, the SCC–Ag and CD105 of cervical cancer group increased, the difference was statistically significant. Comparing with I period of TMN staging, SCC–Ag and CD105 of II period increased, III, IV period increased, the difference was statistically significant. Comparing with II period, SCC–Ag and CD105 of III, IV period increased, the difference was statistically significant. Comparing with non-lymph gland metastasis, SCC–Ag and CD105 of lymph gland metastasis increased in cervical cancer with surgical treatment, the difference was statistically significant. According to Pearson correlation analysis, SCC–Ag and CD105 were positively correlated. **Conclusion:** SCC–Ag and CD105 in patients with cervical cancer increase highly, it has important clinical value that of serum SCC–Ag combined with CD105 in the early diagnosis of cervical cancer, especially it has clinical guiding significance to staging and lymph gland metastasis of cervical cancer, and it is worthy of clinical reference.

## 1. Introduction

Cervical cancer is one of the common malignant tumors in women, and the incidence of cervical cancer is rising with the change of social environment and life style. The incidence of cervical intraepithelial neoplasia (CIN) increased gradually among young women, resulting in the younger trend of cervical cancer[1,2]. At present, cervical cancer mainly treated by surgery, radiotherapy and chemotherapy, but most patients have been in the late stage

of cervical cancer, tumor metastasis and poor prognosis seriously restricted the clinical efficacy of the treatment[3]. Therefore, early diagnosis of cervical cancer has important significance for its treatment and prognosis, our study aims to investigate the significance of serum squamous cell carcinoma antigen (SCC–Ag) combined vascular endothelial growth factor (CD105) detection in early diagnosis of cervical cancer, and to provide new ideas for the diagnosis of cervical cancer.

## 2. Materials and methods

### 2.1. General information

✉Corresponding author: Sen–Yang Cao, Department of Reproductive Technology, Yancheng Maternal and Child Health–Care Center, Jiangsu, Yancheng 224002, China. Tel: 15950206599. Email: maruchan97@163.com. Fund: Fund was supported by health department of Jiangsu provincial (201389622).

A total of 74 cases of cervical cancer who were admitted in the department of gynaecology in our hospital from June 2012 to February 2016 were selected as cervical cancer group. All patients met the following criteria: (1) Age from 27 to 68 years old; (2) All patients were confirmed by pathological examination for cervical cancer; (3) Excluded the SCC-Ag increase caused by non-neoplastic lesions and other tumors; (4) Excluded patients with serious infectious diseases and liver and kidney dysfunction; (5) No drug, surgery, radiotherapy or chemotherapy for all patients before treatment. Patients in the cervical cancer group aged from 27 to 66 years old with an average (43.84±13.96) years; Squamous cell carcinoma in 64 cases, adenocarcinoma in 10 cases; FIGO stage (2009): stage I in 30 cases, stage II a in 13 cases, stage II b in 10 cases, stage III in 14 cases and stage IV in 7 cases; 43 cases patients were treated by surgery and 16 cases patients were found to have lymph node metastasis. In the same period, 52 cases hospitalized patients with uterine fibroids who were treated by total hysterectomy were selected as normal cervical group. All were confirmed by pathological examination after surgery, age from 28 to 68 years old with an average (44.91±13.27) years. The average age of the two groups was not statistically significant ( $P>0.05$ ), and was comparable.

## 2.2. Detection indexes

Collected 5ml venous blood in the fasting state and placed in sterile coagulation tube for all selected cases, 3 000 r/min centrifugal separation of serum and put the serum in -20 °C refrigerator. Enzyme linked immunosorbent assay (ELISA) was used to detect the levels of serum SCC-Ag and CD105, the kits were purchased from US R & D company, operation strictly according to the specification, measured the OD value at the wavelength of 450nm, sample concentration was calculated according to the standard curve.

## 2.3. Statistical methods

The data were statistically analyzed by SPSS 19 software, the measurement data were represented by mean plus or minus standard deviation, T test was used to compare the data between the two groups, using Pearson correlation analysis,  $P<0.05$  was indicated the difference was statistically significant.

## 3. Results

### 3.1. Comparison the levels of SCC-Ag and CD105 in two groups patients

ELISA results showed that SCC-Ag in cervical cancer group (74 cases patients) was from 0.87 µg/L to 5.68 µg/L with an average (2.04±0.47) µg/L; SCC-Ag in normal cervical group (52 cases patients) was from 0.11 µg/L to 0.73 µg/L with an average (0.35±0.08) µg/L; T test results found that SCC-Ag in cervical cancer group was significantly higher than that in the normal cervical group, and the difference was statistically significant ( $t=25.640$ ,  $P<0.05$ ). CD105 in cervical cancer group was from 54.79 µg/L to 238.09 µg/L with an average (117.50±21.74) µg/L; CD105 in normal cervical group was from 17.32 µg/L to 42.68 µg/L with an average (31.26±7.68) µg/L; T test results found that CD105 in cervical cancer group was significantly higher than that in the normal cervical group, and the difference was statistically significant ( $t=27.402$ ,  $P<0.05$ ). See table 1.

**Table 1.**

Comparison the levels of SCC-Ag and CD105 in two groups patients.

Group	n	SCC-Ag (µg/L)	CD105 (µg/L)
Normal cervical	52	0.35±0.08	31.26±7.68
Cervical cancer	74	2.04±0.47	117.50±21.74
T value		25.640	27.402
P value		$P<0.05$	$P<0.05$

Ps: Compared with the control group, \* $P<0.05$ ; Compared with the CIN group, # $P<0.05$ .

### 3.2. Comparison the levels of SCC-Ag and CD105 in cervical cancer patients with different TMN stages

ELISA results showed that SCC-Ag in cervical cancer TMN stage I patients was from 0.87 µg/L to 1.39 µg/L with an average (1.25±0.38) µg/L; SCC-Ag in stage II patients was from 1.67 µg/L to 2.40 µg/L with an average (2.14±0.49) µg/L; SCC-Ag in stage III and IV patients was from 3.89 µg/L to 5.68 µg/L with an average (4.78±0.68) µg/L; The results of t test showed that SCC-Ag in stage II, stage III and IV was increased compared with that in stage I, and the differences were statistically significant ( $P<0.05$ ); SCC-Ag in stage III and IV was increased compared with that in stage II, and the difference was statistically significant ( $P<0.05$ ). CD105 in cervical cancer TMN stage I patients was from 54.79 µg/L to 86.32 µg/L with an average (72.30±9.51) µg/L; CD105 in stage II patients was from 119.08 µg/L to 160.95 µg/L with an average (147.48±19.75) µg/L; CD105 in stage III and IV patients was from 178.54 µg/L to 238.09 µg/L with an average (216.05±35.82) µg/L; The results of t test showed that CD105 in stage II, stage III and IV was increased compared with that in stage I, and the differences were statistically significant ( $P<0.05$ ); CD105 in stage III and IV was increased compared with that in stage II, and the difference was statistically significant ( $P<0.05$ ). See table 2.

**Table 2.**

Comparison the levels of SCC-Ag and CD105 in cervical cancer patients with different TMN stages.

TMN stage	n	SCC-Ag (μg/L)	CD105 (μg/L)
Stage I	30	1.25±0.38	72.30±9.51
Stage II	23	2.14±0.49 *	147.48±19.75 *
Stage III, IV	21	4.78±0.68 *#	216.05±35.82 *#

Ps: Compared with Stage I, \* $P<0.05$ ; Compared with Stage II, # $P<0.05$ .

### 3.3. Comparison the levels of SCC-Ag and CD105 in cervical cancer patients with and without lymph node metastasis

ELISA results showed that SCC-Ag in patients without lymph node metastasis was from 0.87 μg/L to 2.35 μg/L with an average (1.70±0.29) μg/L; SCC-Ag in patients with lymph node metastasis was from 2.78 μg/L to 3.17 μg/L with an average (2.98±0.53) μg/L; T test results showed that SCC-Ag in patients with lymph node metastasis was significantly higher than that in patients without lymph node metastasis, and the difference was statistically significant ( $t=10.109$ ,  $P<0.05$ ). CD105 in patients without lymph node metastasis was from 54.79 μg/L to 102.21 μg/L with an average (81.41±13.70) μg/L; CD105 in patients with lymph node metastasis was from 136.54 μg/L to 175.08 μg/L with an average (158.35±28.06) μg/L; T test results showed that CD105 in patients with lymph node metastasis was significantly higher than that in patients without lymph node metastasis, and the difference was statistically significant ( $t=11.720$ ,  $P<0.05$ ). See table 3.

**Table 3.**

Comparison the levels of SCC-Ag and CD105 in cervical cancer patients with and without lymph node metastasis.

Group	n	SCC-Ag (μg/L)	CD105 (μg/L)
Non lymphatic metastasis	27	1.70±0.29	81.41±13.70
Lymph node metastasis	16	2.98±0.53	158.35±28.06
T value		10.109	11.720
P value		$P<0.05$	$P<0.05$

### 3.4. Correlation analysis of SCC-Ag and CD105 in cervical cancer

Pearson correlation analysis showed that SCC-Ag was significantly positively correlated with CD105 ( $r=0.547$ ,  $P<0.05$ ).

## 4. Discussion

The morbidity of cervical cancer was the first place in the malignant tumor of female reproductive system, which seriously threaten women's health and life, and its occurrence and development was a complex process under multiple factors [4]. Oncogene activation, tumor suppressor genes inactivation, tumor angiogenesis, and

interstitial degradation play important roles in the pathogenesis of cervical cancer, cancer invasion through formation of neovascularization in the surrounding tissue penetration[5,6]. In order to ensure the efficacy of surgical treatment, extensive hysterectomy combined with pelvic lymph node resection is the first choice for the treatment of early stage cervical cancer. But it was hard to determine whether there has lymph node metastasis, which leads to most patients without lymph node metastasis underwent lymph node excision, caused serious postoperative complications and serious damage to the patient's immune system and increased the risk of surgical treatment of the patients[7–9]. Therefore, early diagnosis of cervical cancer and finding lymph node metastasis indexes has important clinical significance for the treatment and prognosis of cervical cancer.

SCC-Ag is an endogenous serine protease inhibitor, which belongs to tumor TA-4 antigen and participates in tumor invasion and metastasis[10]. As one of the biomarkers of tumor, the expression of SCC-Ag was positively correlated with the volume of tumor[11]. Studies found the detection rate of SCC-Ag in the early diagnosis of cervical cancer was up to 87.7%, its increase rate was closely related to the postoperative recurrence of the patients[12]. However, SCC-Ag was not specific in cervical cancer, its expression was elevated in other squamous carcinoma, even expressed in pemphigus, renal failure and other non-neoplastic lesions[13,14]. SCC-Ag has been widely used in the assisted diagnosis of cervical cancer, but there were no reports on the relationship between SCC-Ag combined CD105 and cervical cancer, we aims to detect the expression of SCC-Ag and CD105 in the serum of patients with cervical cancer, and to explore its value in early cervical cancer diagnosis. CD105 is a glycoprotein with 2 monomers connected by two sulfur bonds, it plays an important role in signal transduction, endothelial cell proliferation and angiogenesis[15]. CD105, as a new biomarker, it highly expressed in tumor tissue and vascular endothelial cells while did not expressed in the normal tissue of vascular endothelial cells[16,17]. It was found that the expression of CD105 was closely related to tumor differentiation and invasion. It was involved in tumor tissue invasion of vascular lymphatic vessels, and related to tumor stage and lymph node metastasis[18]. Therefore, CD105 plays an important role in the diagnosis, treatment and prognosis of malignant tumors. CD105 was highly expressed in the tumor tissue of cervical cancer patients, by blocking TGF-β 1/ALK5 signal transduction, CD105 induces the proliferation and migration of tumor vascular endothelial cells to increase the number of new blood vessels, further promoting the proliferation, invasion and metastasis of tumor cells[19,20]. Our results showed that compared with the normal cervical group, SCC-Ag and CD105 increased in the cervical cancer group; With the progress of TMN staging, SCC-Ag and CD105 showed a gradual increase trend; Among patients

with cervical cancer, compared with non-lymphatic metastasis, SCC-Ag and CD105 increased in lymph node metastasis; Serum SCC-Ag was positively correlated with CD105, this showed that SCC-Ag combined CD105 detection has important reference value in the early diagnosis, pathological typing and clinical treatment of cervical cancer.

In summary, serum SCC-Ag and CD105 levels were significantly increased in patients with cervical cancer, combined detection of the two has important clinical application value in the early diagnosis of cervical cancer, especially for cervical cancer stage and lymph node metastasis, it has clinical significance and worthy clinical reference.

## References

- [1] Jiang Y, Hu SY, Hernandez Donoso L. A systematic literature review on risk factors for cervical cancer in chinese population. *Value Health* 2014; 17(7): 733-734.
- [2] Bai Caiyun, Wang Yanming. The relationship between high risk HPV infection and potential malignant biological behavior in patients with cervical intraepithelial neoplasia. *J Hainan Med Univ* 2015; 21(9): 1290-1293.
- [3] Zhu Tao, Zhu Jianqing, Gao Yongliang. Current status and progress of diagnosis and treatment of cervical cancer. *Chin J Oncol* 2013; 22(12): 970-974.
- [4] Mega Tiber P, Baloglu L, Ozden S. The association of apoptotic protein expressions sensitive to apoptosis gene, p73 and p53 with the prognosis of cervical carcinoma. *Onco Targets Ther* 2014; 26(7): 2161-2168.
- [5] Tung WC, Lu M, Smith-Gagen J. Latina women and cervical cancer screening: decisional balance and self-efficacy. *Clin J Oncol Nurs* 2016; 20(3): 71-76.
- [6] Zhao Yi, Yang Yijun, Tu Haijian. Expression of PCNA and Ki-67 in cervical lesions and its correlation with high risk HPV infection. *J Hainan Med Univ* 2015; 21(04): 523-526.
- [7] Kessler TA. Journey of a woman with terminal cervical cancer. *Clin J Oncol Nurs* 2016; 20(3): 340-342.
- [8] Yang Wenjing, Wang Lu. Expression and clinical significance of VEGF and its receptor KDR in the elderly patients with cervical cancer. *Pract Geriatric Med* 2015; 29(11): 929-932.
- [9] Luo Min, Tan Shisheng, Ni Tingting. Dosimetric study of pelvic irradiation therapy after cervical cancer surgery. *Guizhou Med* 2014; 38(6): 498-501.
- [10] Salvatici M, Achilarré MT, Sandri MT. Squamous cell carcinoma antigen (SCC-Ag) during follow-up of cervical cancer patients: Role in the early diagnosis of recurrence. *Gynecol Oncol* 2016; 8258(16): 30162-30167.
- [11] Ou Yanghua, Jia Xibiao, Chen Cen. Diagnostic value of serum squamous cell carcinoma antigen in cervical squamous cell carcinoma. *J Pract Gynecol Obstetr* 2013; 29(5): 345-347.
- [12] Farzaneh F, Shahghasempour S, Noshine B. Application of tumor markers SCC-Ag, CEA, and TPA in patients with cervical precancerous lesions. *Asian Pac J Cancer Prev* 2014; 15(9): 3911-3914.
- [13] Wang Hongxia, Ding Xiaoping, Hou Qingxiang. Changes and clinical significance of SCC-Ag in cervical cancer before and after neoadjuvant chemotherapy. *Chin J Clin Obstetr Gynecol* 2015; 16(3): 229-232.
- [14] Feng Chuncui. Detection of serum TSGF and SCC levels in patients with cervical cancer and evaluation of the biological behavior of tumor. *J Hainan Med Univ* 2015; 21(01): 105-107+110.
- [15] Dubinski W, Gabriel M, Iakovlev VV. Assessment of the prognostic significance of endoglin (CD105) in clear cell renal cell carcinoma using automated image analysis. *Hum Pathol* 2012; 43(7): 1037-1043.
- [16] Bu Lan, Ma Yumei, Shi Shufen. Expression of CD31, CD105 and PTEN in cervical carcinoma and its clinical pathological significance. *China Mater Child Health Care* 2015; 9(30): 1446-1449.
- [17] Martinez LM, Labovsky V, Calcagno Mde L. Comparative prognostic relevance of breast intra-tumoral microvessel density evaluated by CD105 and CD146: A pilot study of 42 cases. *Pathol Res Pract* 2016; 212(4): 350-355.
- [18] Huang Xiaojuan, Qi Wenhui, Wang Li. Expression of CD31 and CD105 in epithelial ovarian tumor and its clinical and pathological significance. *Chin J Histochem Cell Chem* 2012; 21(6): 544-550.
- [19] Qu Changping, Xu Zonglan, Wang Qu Yuan. The level and clinical significance of serum CD105 in cervical cancer. *Chin J Clin* 2012; 6(13): 3747-3748.
- [20] Barbu I, Craitoiu S, Simionescu CE. CD105 microvessels density, VEGF, EGFR-1 and c-erbB-2 and their prognostic correlation in different subtypes of cervical adenocarcinoma. *Rom J Morphol Embryol* 2013; 54(3): 519-530.