Expression of SATB1 and E-cad in tissues of patients with endometrial carcinoma and the relationship with clinicopathological features

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Abstract. The expression of special AT-rich sequence binding protein 1 (SATB1) and E-cadherin (E-cad) in tissues of patients with endometrial carcinoma and the relationships with clinicopathological features were investigated. One hundred and four cases of carcinoma tissues and 104 cases of para-carcinoma tissues of patients pathologically diagnosed as endometrial carcinoma in Affiliated Hospital of Jining Medical University (Jining, China) from August 2015 to August 2016 were selected. The expressions of SATB1 and E-cad in tissues was detected via streptavidin peroxidase biotin (SP) immunohistochemical method, and the relationship with clinicopathological features of patients was analyzed. SATB1 was positively expressed in 71 out of 104 cases of endometrial carcinoma tissues (the expression rate was 68.27%) and in 25 out of 104 cases of para-carcinoma tissues (the expression rate was 24.03%). The expression of SATB1 in endometrial carcinoma tissues was significantly higher than that in para-carcinoma tissues ($P<0.05$). E-cad was positively expressed in 60 out of 104 cases of carcinoma tissues (the expression rate was 57.6%) and 95 out of 104 cases of para-carcinoma tissues (the positive expression rate was 91.3%) ($P<0.05$). The expression of SATB1 and E-cad in endometrial carcinoma tissues was not associated with the menopausal status or age of patients ($P>0.05$), but correlated with the histological grade of endometrial carcinoma, depth of tumor invasion, lymph node metastasis and tumor lymph node metastasis (TNM) staging ($P<0.05$). In conclusion, SATB1 and E-cad play important roles in the occurrence and development of endometrial carcinoma, which are of great significance to the potential therapeutic target and prognosis estimation of endometrial carcinoma.

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Introduction

Endometrial carcinoma (EC) is one of the most common malignant tumors in the female reproductive system. It often occurs in perimenopausal women, mainly those aged 50 years. Recent studies have shown that its incidence rate has an increasing trend (1). Special AT-rich sequence binding protein 1 (SATB1) is a binding protein that can bind to AT-rich bases and regulate the downstream gene expression (2). Previous studies showed that SATB1 plays an important role in the differentiation of T cells; at the same time, SATB1 is highly expressed in a variety of tumors and can regulate the expression of genes and promote the cell proliferation, invasion and metastasis (3). Studies have shown that SATB1 is expressed abnormally in gastric cancer, esophageal cancer (4), liver cancer (5) and other malignant tumors, which is closely related to the tumor growth, development and prognosis, but there has been no research on the expression of SATB1 in tissues of EC patients. E-cadherin (E-cad) is a key gene in epithelial-mesenchymal transition (EMT). Studies have shown that the downregulation of E-cad in tissues promotes the invasion and metastasis of malignant tumors. Therefore, the expressions of SATB1 and E-cad in 104 cases of EC tissues and 104 cases of para-carcinoma tissues were detected using the immunohistochemical method in this study, the relationship of their expression with clinicopathological features of EC patients was analyzed, and then the influence on the occurrence and metastasis of EC were investigated.

Materials and methods

General materials. One hundred and four cases of carcinoma tissues of patients pathologically diagnosed as EC in Affiliated Hospital of Jining Medical University (Jining, China) from from August 2015 to August 2016 were selected. All patients underwent panhysterectomy, bilateral adnexectomy and pelvic lymph node dissection. Patients did not receive chemotherapy, radiotherapy and biological targeted therapy, before operation. Patients were aged from 31 to 67 years with an average of 47.56±15.49 years. According to the degree of pathological differentiation, there were 38 cases

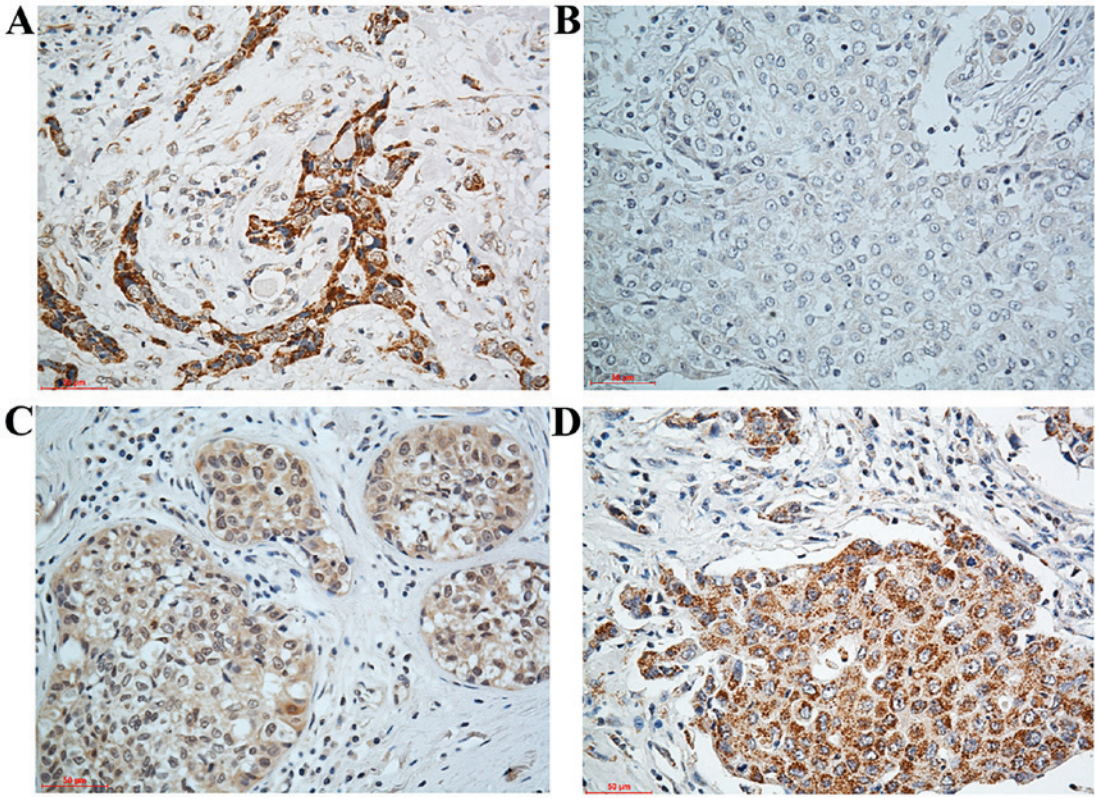

Figure 1. Expression of special AT-rich sequence binding protein 1 (SATB1) and E-cadherin (E-cad) in para-carcinoma tissues and carcinoma tissues. The immunohistochemical results show that the positive expression of SATB1 in carcinoma tissues is significantly higher than that in para-carcinoma tissues (P<0.05); the positive expression of TLR4 in para-cancerous tissues is significantly higher than that in carcinoma tissues (P<0.05). (A) Expression of SATB1 in para-carcinoma tissues; (B) expression of SATB1 in carcinoma tissues; (C) expression of E-cad in para-carcinoma tissues; (D) expression of E-cad in carcinoma tissues (x200).

of high differentiation, 34 cases of moderate differentiation and 32 cases of low differentiation. According to the staging criteria of the International Federation of Gynecology and Obstetrics (IFGO) in 2009, there were 26 cases of stage I, 31 cases of stage II, 29 cases of stage III and 18 cases of stage IV. In terms of pathological type, there were 59 cases of endometrioid adenocarcinoma, 23 cases of clear cell carcinoma and 22 cases of papillary serous carcinoma and 104 para-carcinoma tissues of EC patients during the same period were selected. The patients were aged from 29 to 70 years with an average of 48.39±16.21 years. The study was approved by the Ethics Committee of the Affiliated Hospital of Jining Medical University and written informed consents were signed by the patients and/or guardians.

Materials and methods

Major reagents. Rabbit anti-human SATB1 monoclonal antibody (cat. no. ab92307) and rabbit anti-human E-cad monoclonal antibody (cat. no. 1ab40772) were purchased from Abcam (Cambridge, MA, USA); immunohistochemical SP kit, diaminobenzidine (DAB) developing kit and hematoxylin were purchased from Beijing Zhongshan Golden Bridge Biological Technology Co., Ltd. (Beijing, China).

Immunohistochemistry. The tissue paraffin block of EC patients was continuously sliced into 4 μm-thick sections and heated at 65˚C for 2 h, followed by dewaxing and hydration using the immunohistochemical SP method in strict accordance with the instructions of kit. Primary antibody SATB1 (1:500) or E-cad (1:400) was added at 4˚C overnight, and then goat anti-rabbit secondary polyclonal antibody (dilution 1:2,000; cat. no. ab150077; Abcam Cambridge, MA, USA) was used, instead of the primary antibody, as the negative control in the experiment, and the known positive sections were used as positive controls.

Determination of results. The positive expression of both SATB1 and E-cad showed the brown yellow or yellow particles. The positive expression of SATB1 was located in the nucleus, while that of E-cad was located in the cytoplasm or membrane. Six visual fields were randomly selected under the microscope (x400), and the results were determined according to the percentage of positive cells and the staining depth. i) According to the cell staining depth: Negative, 0 point; pale yellow, 1 point; brown yellow, 2 points; dark brown, 3 points. ii) According to the percentage of positive cells in total cells: 0-30%, 1 point; 30-70%, 2 points; 70-100%, 3 points. The product of both scores greater than or equal to 3 points indicated positive expression; otherwise, it indicated negative expression (6).

Statistical analysis. SPSS 22.0 (version X; IBM, Armonk, NY, USA) software was used for statistical analysis of data, and Chi-square test was used for enumeration data. P<0.05 suggested that the difference was statistically significant.

Table I. Expression of SATB1 and E-cad in breast cancer tissues.

		SATB1			E-cad		
Group	Case (n)	-	+	Positive rate (%)	-	+	Positive rate (%)
Breast cancer tissue	104	33	71	68.27	44	60	57.6
Para-carcinoma tissue	104	79	25	24.03	9	95	91.3

SATB1, special AT-rich sequence binding protein 1; E-cad, E-cadherin.

Table II. Relationship of the expression of SATB1 and E-cad with the clinicopathological features of EC.

		SATB1 positive expression				E-cad positive expression			
Pathological feature	Total case	n	Percentage	χ^2	P-value	n	Percentage	χ^2	P-value
Menopausal status									
Yes	64	46	71.88	0.142	>0.05	49	76.56	0.172	>0.05
No	40	26	65.00			30	75.00		
Age (years)									
≥50	80	56	70.00	0.473	>0.05	44	55.00	0.382	>0.05
<50	24	16	66.67			13	66.67		
Histological grade									
I	42	30	71.43	13.287	<0.05	34	80.95	15.382	<0.05
II	30	22	73.33			21	70.00		
III	32	19	59.38			11	34.38		
Depth of invasion									
Shallow	38	24	63.16	5.692	<0.05	32	84.21	7.482	<0.05
Deep	66	47	71.21			49	74.24		
Lymph node metastasis									
No	58	38	65.52	8.472	<0.05	31	53.45	10.372	<0.05
Yes	46	33	71.74			35	76.09		
TNM staging									
I, II	42	28	66.67	6.489	<0.05	30	71.43	7.386	<0.05
III, IV	62	45	72.58			51	82.26		

SATB1, special AT-rich sequence binding protein 1; E-cad, E-cadherin.

Results

Expression of SATB1 in tissues of EC patients. Microscopic observation revealed that the positive expression of SATB1 was located in the nucleus, showing dark brown or yellow particles. In this study, immunohistochemical results showed that SATB1 was positively expressed in 71 out of 104 cases of EC tissues (the expression rate was 68.27%) and in 25 out of 104 cases of para-carcinoma tissues (the expression rate was 24.03%). The expression of SATB1 in EC tissues was significantly higher than that in para-carcinoma tissues (χ^2=27.849, P<0.05). Besides, microscopic observation also revealed that the positive expression of E-cad was located in the cytoplasm and membrane, showing dark brown or yellow particles. E-cad was positively expressed in 60 out of 104 cases of carcinoma tissues (the expression rate was 57.6%) and 95 out of 104 cases of para-carcinoma tissues (the positive expression rate was 91.3%) (χ^2=7.516, P<0.05) (Fig. 1 and Table I).

Relationship of SATB1 and E-cad expression in tissues of EC patients with clinicopathological features. The expression of SATB1 and E-cad in EC tissues were not associated with the menopausal status and age of patients (P>0.05), but correlated with the histological grade of EC, depth of tumor invasion, lymph node metastasis and TNM staging (P<0.05) (Table II).

Discussion

SATB1 is a binding protein of tissue-specific expression in matrix attachment region, located in 3p23 region of

chromosome 3 and a total of 763 amino acids in length (7,8). SATB1 contains an AT-rich MAR sequence with a high base pairing region. It has been found that SATB1 can promote the stable binding of SATB1 and MAR sequence through anchoring the chromosome ring, thus participating in the structural remodeling, methylation and histone acetylation of chromosomes (9,10). SATB1 is basically not expressed in normal tissues and abnormally expressed in a variety of malignant tumor tissues. Alvarez *et al* (11) established an animal model with SATB1 gene knockout, and randomly observed the expression of 597 genes. The results showed that 10 genes were upregulated, while 1 gene was downregulated. The analysis of expression profile of SATB1 gene knockout found that SATB1 regulates the expression of genes with poor prognosis, such as genes that control cell cycle, signal transduction pathways and apoptosis. Through upregulating the expression of CDK4, SATB1 can induce cell proliferation, promote the cell cycle, inhibit the Fas-related protein-mediated apoptosis pathway and inhibit cell apoptosis (12). Han *et al* (13) found that the mRNA and protein in SATB1 are highly expressed in breast cancer cell lines, and showed that SATB1 is closely related to the prognosis of patients combined with 1,318 cases of tissue samples of breast cancer patients, and the survival of patients with high expression of SATB1 is short. At the same time, it was found that the SATB1 can upregulate the expression of genes related to invasion and metastasis of breast cancer cells, and inhibit the expression of tumor suppressor genes, thus promoting the tumor growth and metastasis. Zheng *et al* (14) reported that SATB1 is highly expressed in invasive breast cancer tissues. Zhang *et al* (15) found that SATB1 is not expressed in para-breast carcinoma tissues, the positive expression rate in breast cancer tissues is 67.9%, and the expression difference between the para-carcinoma tissues and carcinoma tissues was statistically significant. In addition, it was also found that the expression of SATB1 is closely related to the histological grade and clinicopathological staging of breast cancer patients. The higher the clinicopathological staging is the poorer the differentiation of tumor cells is, the higher the positive expression rate of SATB1 in tissues will be, suggesting that SATB1 is involved in the proliferation and metastasis of breast cancer. The COX regression model revealed that SATB1 can also be used as an independent factor for the prognosis of breast cancer patients. However, there are different results in studies during the same period. It was found (15) that the expression of SATB1 is not correlated with the prognosis of patients. The gene chip analysis showed that there is no significant relationship between the survival time of breast cancer patients and the expression of SATB1; and the expression of SATB1 does not significantly affect the proliferation and metastasis of breast cancer cells, so it is thought that SATB1 is not involved in the proliferation and metastasis of breast cancer, and it will not affect the prognosis of patients. In this study, the expressions of SATB1 in 104 cases of EC tissues and 104 cases of para-carcinoma tissues were detected using the immunohistochemical method, and the correlation of expression with clinicopathological features of EC patients was also analyzed. The research results revealed that the positive expression rate of SATB1 in EC tissues was 68.27%, and its expression is related to the histological grade, depth of tumor invasion, lymph node metastasis and TNM staging, and the differences were statistically significant ($P<0.05$). The results suggested that SATB1 may be associated with the occurrence of EC, but its specific mechanism remains unclear and needs further study.

E-cad is a key protein in EMT, whose main function is to maintain the normal cellular morphology, and it also plays an important role in continuing the tissue integrity and reducing the cell dispersion (16). The expression of E-cad is different in cytoplasm and membrane of various normal epithelial cells in the body; at the same time, the downregulation of E-cad expression in cells will promote the invasion and metastasis of tumor cells (17,18). The results of this study showed that E-cad was positively expressed in 60 out of 104 cases of carcinoma tissues (the expression rate was 57.6%) and 95 out of 104 cases of para-carcinoma tissues (the positive expression rate was 91.3%) ($\chi^2=7.516$, $P<0.05$), which was consistent with the research of scholars world-wide.

In conclusion, the above results suggested that the downregulation of E-cad expression leads to the tumor invasion and metastasis, which is consistent with the results reported by Yu *et al* (19). In conclusion, SATB1 and E-cad are involved in the occurrence and development of EC, which are of great significance to the potential therapeutic target and prognosis estimation of EC.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

YF wrote the manuscript. YF and XW performed immunohistochemistry and made substantial contributions to analysis and interpretation of data. QW conceived and designed the study, and gave final approval of the version to be published. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Affiliated Hospital of Jining Medical University (Jining, China). Signed written informed consents were obtained from the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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