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Original Article

Study on the expression of S100A4 and HMGA1 in endometrial carcinoma and their correlation with metastasis

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Abstract: Objectives: To investigate the relationship between the expression of S100 calcium-binding protein A4 (S100A4), high mobility group protein A1 (HMGA1) and clinicopathological features, as well as postoperative recurrence and metastasis in endometrial cancer patients. Methods: Sixty endometrial cancer patients (observation group) were selected for this study, along with 40 patients who underwent hysterectomy for benign diseases (control group) during the same period. Surgically resected endometrial cancer tissues and normal endometrial tissues were collected. The expression levels of HMGA1 and S100A4 mRNA were detected using real-time fluorescence quantitative polymerase chain reaction (qPCR), while the HMGA1 and S100A4 protein expression was detected by immunohistochemistry and Western blot. Clinical data including tumor diameter, histological grading, distant metastasis, lymph node metastasis, depth of infiltration, lymphovascular infiltration, and International Federation of Gynecology and Obstetrics (FIGO) staging were collected. Patients with endometrial cancer were categorized into a non-recurrent-metastasis group and a recurrent-metastasis group based on their one-year postoperative follow-up results. Results: The mRNA and protein expression levels of HMGA1 and S100A4 were significantly higher in endometrial cancer tissues compared to normal endometrial tissues (all $P<0.05$). Protein expression of HMGA1 and S100A4 was significantly associated with tumor diameters, distant metastases, lymph node metastases, depth of infiltration and lymphovascular infiltration. Specifically, endometrial cancer patients with tumor diameters >2 cm, distant metastases, lymph node metastases, infiltration depths beyond ½ myometrium, and higher lymphovascular infiltration rates, exhibited significantly higher positive expression of HMGA1 and S100A4 (all $P<0.05$). In the recurrent-metastasis group, HMGA1 and S100A4 protein expression levels were significantly higher than those in the no recurrent-metastasis group (all $P<0.05$). Significant differences were found between the two groups in terms of tumor diameter, histological grading, infiltration depth, lymphovascular infiltration and FIGO stage (all $P<0.01$). Multifactorial logistic regression analysis identified HMGA1 and S100A4 protein expression, infiltration depth, lymphovascular infiltration and FIGO stage as independent risk factors for postoperative recurrence and metastasis in endometrial cancer patients after surgery. Receiver operator characteristic (ROC) curves showed that HMGA1 and S100A4 protein expression had high predictive value for postoperative recurrence and metastasis in endometrial cancer patients (all $P<0.05$). Conclusion: The increased positive expression of HMGA1 and S100A4 in the endometrial cancer tissues is closely related to the clinicopathological features and postoperative recurrence and metastasis. HMGA1 and S100A4 have significant predictive value for assessing the likelihood of postoperative recurrence and metastasis in endometrial cancer patients.

Keywords: Endometrial carcinoma, HMGA1, S100A4, recurrence, metastasis

Introduction

Endometrial carcinoma (EC) is a common estrogen-dependent epithelial malignancy of the female reproductive system, predominantly affecting postmenopausal women [1]. In recent years, the incidence of EC is on the rising, and the age of onset has been getting younger. Patients diagnosed under 40 years of age are characterized by well-differentiated tumors,

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limited or no infiltration into the muscularis propria [2]. Currently, surgical resection of tumor lesions is the primary choice for EC patients without demand for retaining reproductive function [3]. However, there is still a lack of reliable indicators to predict postoperative recurrence and metastasis. Several studies have showed that tumor stage and metastasis are significant risk factors for disease progression and prognosis in EC patients [4]. At present, clinical assessment of patients' condition and prognosis are primarily based on pathological and imaging findings, but there is a lack of efficient and specific tumor markers.

High mobility group protein A1 (HMGA1) is a member of the high mobility group superfamily found in eukaryotic cells. It is a non-histone chromosome-binding protein, localized in the clustered region of chromosome breaks in a variety of tumor cells, and is specifically expressed in gynecological tumors [5]. Studies have reported that HMGA1 is highly expressed in epithelial malignant tumors and is closely related to cancer progression and prognosis [6]. However, there were fewer clinical studies on its expression in endometrial cancers. S100 calcium-binding protein A4 (S100A4) is a member of the calcium-binding family and is involved in the processes such as cell proliferation and differentiation [7]. It has been found that S100A4 plays a role in the development of multiple tumors, such as breast cancer [8]. Additionally, research has demonstrated that S100A4 is highly expressed in various tumor types, such as bladder and pancreatic cancers, making it a potential prognostic marker for these malignancies [9, 10]. Despite these findings, there are few studies, both domestically and internationally, on the expression of S100A4 protein in endometrial cancer and its relationship with patient prognosis. Based on this, this study analyzed the protein expression of S100A4 and HMGA1 in endometrial cancer tissues and explored their correlation with clinicopathological features, recurrence and metastasis in endometrial cancer. The results of this study could provide references for early diagnosis, treatment evaluation, and improved prognosis in endometrial cancer patients.

Methods

General information

This retrospective study involved a total of 60 patients with endometrial carcinoma that were treated at the Second Affiliated Hospital of Shandong First Medical University from July 2020 to January 2022, serving as the observation group. Additionally, another 40 patients with benign uterine diseases treated during the same period were selected as the control group. This study was approved by the Ethics Committee of The Second Affiliated Hospital of Shandong First Medical University (No. 2020-109).

Inclusion criteria: A diagnosis of endometrial cancer based on previously reported criteria [11], which was confirmed by pathological examination, or a diagnosis of benign uterine diseases; No contraindications to the surgery; Regular follow-up after operation; Initial diagnosis; No previous radiotherapy or chemotherapy; Complete medical records. Exclusion criteria: Patients with metastasized endometrial carcinoma; Presence of heart, liver, kidney or other organ diseases; Presence with other malignant tumors, hematopoietic dysfunction or mental diseases.

At one year after surgery, according to the follow-up results, these endometrial carcinoma patients were divided into a no recurrent metastasis group (N = 23) and a recurrent metastasis group (N = 37).

Data collection and criteria for determining postoperative recurrence and metastases

The demographic and clinical data, including age, tumor diameter, histological grade, distant metastasis, lymph node metastasis, depth of infiltration, lymphovascular infiltration and International Federation of Gynecology and Obstetrics (FIGO) staging, were collected. Criteria for determining postoperative recurrence and metastasis were as follows: Physical examination findings suggestive of recurrence, such as enlarged lymph nodes or abdominal mass; Elevated levels of serum tumor markers; Confirmation of metastasis through imaging examinations, such as magnetic resonance imaging (MRI) and computed tomography (CT) scans; Detection of tumor cells from recurrent or metastatic sites through tissue biopsy or fine-needle aspiration for pathological examination. According to 1-year postoperative outpatient follow-up, patients were divided into a non-recurrence-metastasis group and a recurrence-metastasis group.

RT-PCR detection

Fasting venous blood was collected, and RNA was extracted from peripheral blood after anticoagulation. cDNA was obtained using reverse transcription kit (Takara Company, USA), and the products were verified by electrophoresis. The expression levels of HMGA1 and S100A4 were detected by RT-PCR. The reaction system consisted of 6.5 μL PCR buffer, 2 μL each of upstream and downstream primers (HMGA1 forward primer: 5'-CCTGGACAAGGCTAACATCC-3', reverse primer: 5'-GTGACTGCATCTCCATCAC-C-3'; S100A4 forward primer: 5'-TCAGAACTAA-AGGA GCTGCTGACC-3', reverse primer: 5'-TTT-CTTCCTGGGCTGCTTAT CTGG-3'; GAPDH forward primer: 5'-AATC-CCATCACCATCTTCCA-3', reverse primer: 5'-TTTCTTCCTGGGC TGCTTAT-CTGG-3'), 1 μL fluorescent probe, 9.5 μL Taq polymerase, and 5 μL cDNA. The reaction conditions were as follows: pre-denaturation at 94°C for 5 min, denaturation at 94°C for 10 s, annealing at 64°C for 25 s, extension at 72°C for 45 s, for a total of 40 cycles.

Immunohistochemistry

Surgically resected endometrial cancer tissues and normal endometrial tissues were collected, fixed in formaldehyde, and embedded in paraffin. The sections were deparaffinized, hydrated, and prepared for staining. Antigen retrieval was performed by boiling the formaldehyde-fixed tissues at 95°C to restore protein antigenicity. To block non-specific staining, the sections were treated with a methanol solution containing 3% H_2O_2 to eliminate endogenous peroxidase activity. The sections were incubated in a humid chamber overnight at 4°C with primary antibodies against HMGA1 and S100A4 proteins. Then, the sections were incubated with a biotin-labelled secondary antibody, followed by the addition of horseradish peroxidase-labelled streptavidin. The sections were placed in a substrate-containing incubation solution for the chromogenic reaction, and counterstained with hematoxylin to visualize the nuclei. After dehydration with gradient alcohol, vitrification and sealing, the sections were observed under a light microscope to assess the expression of S100A4 and HMGA1 proteins. The expression of these proteins was scored according to the intensity of staining and the proportion of positive cells, using a 4-point scale (0, 1, 2, 3), with higher scores indicating stronger expression. The final classification was either negative (0-2 points) or positive (≥3 points), based on the intensity of staining and proportion of positive cells.

Western blot analysis

The expression levels of HMGA1 and S100A4 proteins in chondrocytes from different groups were detected using Western blot analysis. Cells were lysed in Radio Immunoprecipitation Assay (RIPA) buffer containing protease inhibitors and centrifuged at 12,000 rpm for 10 min at 4°C. The cell supernatant was harvested, and proteins were separated by SDS/polyacrylamide gel electrophoresis and transferred onto Polyvinylidene Fluoride (PVDF) membranes, which were blocked in TBS-T buffer containing 5% skim milk for 1 hour. After washing with Tris Buffered Saline-T (TBS-T) buffer, the membranes were incubated overnight at 4°C with primary antibodies, including HMGA1 (Dilution: 1:1000, No. ab252930, Abcam Company, USA), S100A4 (Dilution: 1:1000, No. ab197896, Abcam Company, USA), and GAPDH (Dilution: 1:1000, No. ab9485, Abcam Company, USA). After rinsing, HRP-labeled Goat Anti-Rabbit IgG (Dilution: 1:1500, No. A0208, Beyotime Biotech. Inc., China) was added and incubated for 2 hours at room temperature. Finally, the PVDF membrane was visualized using an enhanced chemiluminescence reagent, and images were captured using the Bio-rad Gel Imaging System (Bio-Rad Laboratories, Inc., USA). The expressional levels of proteins associated with the Wnt signaling pathway were normalized to GAPDH levels.

Statistical methods

All clinical data collected in this study were analyzed using Statistic Package for Social Science (SPSS) version 23.0. The measurement data were expressed as Mean ± Standard deviation, and the comparison was conducted by independent t test. The count data was presented as percentages/cases, with comparisons between groups performed using χ^2 test. Variables including HMGA1, S100A4, tumor diameter, histological grading, depth of infiltration, lymph-pulvinar infiltration and FIGO stage were further analyzed using multiple Logistic regression models with the forward LR method to identify

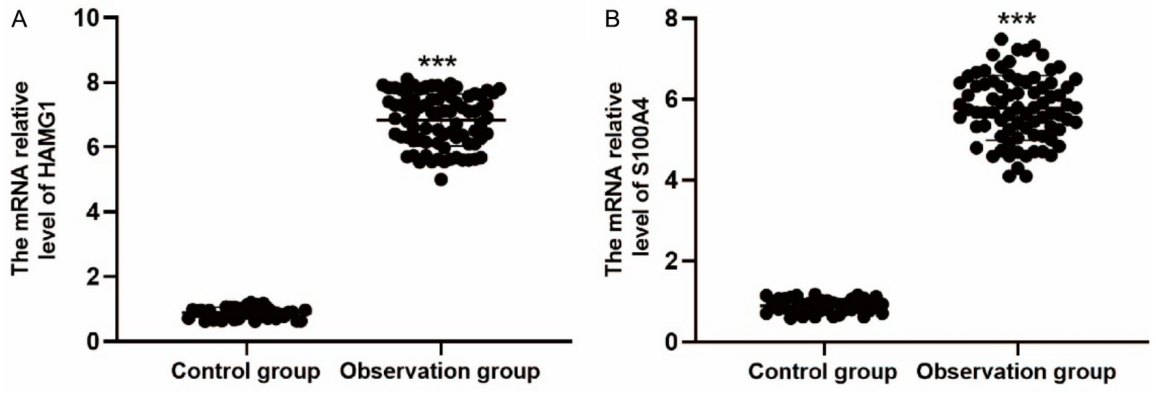

Figure 1. Comparison of HMGA1 and S100A4 mRNA expression between the control (n = 40) and observation (n = 60) groups. A: HMGA1 expression; B: S100A4 expression. Notes: HMGA1: High mobility group protein A1; S100A4: S100 calcium-binding protein A4. ***P<0.001 vs. control group.

Table 1. Comparison of positive expression rates in HMGA1 and S100A4 between the two groups

Group	HMGA1	S100A4
Control group (n = 40)	8/40 (20%)	7/40 (17.5%)
Observation group (n = 60)	40/60 (66.67%)	42/60 (70%)
χ^2 value	20.940	7.127
P value	<0.001	0.008

Notes: HMGA1: High mobility group protein A1; S100A4: S100 calcium-binding protein A4.

the risk factors for postoperative recurrence and metastasis in patients with endometrial cancer. The Logistic regression analysis was performed according to the previous reported [12]. The predictive value of HMGA1 and S100A4 for postoperative recurrence and metastasis in patients with endometrial cancer, including specificity and sensitivity, was assessed using the receiver operating characteristic (ROC) curve [13]. The Delong test was applied to compare different areas under the curves (AUCs). A P<0.05 was considered statistically significant.

Results

Comparison of general information between the two groups

The observation group consisted of 60 endometrial cancer patients, while the control group included 40 patients with benign uterine diseases. There was no significant difference between the two groups in terms of age, body mass index (BMI), course of disease, or underlying disease such as hypertension, diabetes and hyperlipidemia (all P>0.05), indicating that the two groups were comparable.

Comparison of HMGA1 and S100A4 expression between the two groups

As shown in **Figure 1**, RT-PCR results showed that the mRNA levels of HMGA1 and S100A4 were significantly higher in the observation group than those in the control group (all P<0.001).

Immunohistochemistry results (**Table 1** and **Figure 2**) showed that the positive expression rates of HMGA1 and S100A4 in the control group were 20% (8/40) and 17.5% (7/40), respectively, which were significantly lower than those in the observation group [HMGA1: 66.67% (40/60), P<0.001; S100A4: 70% (42/60), P = 0.008].

Comparison of HMGA1 and S100A4 expression between the no recurrent metastasis group and the recurrent metastasis group

As shown in **Figure 3**, Western blot results showed that the protein levels of HMGA1 and S100A4 were significantly higher in the recurrent-metastasis group compared to the non-recurrent-metastasis group (all P<0.001).

Comparison of HMGA1 and S100A4 expression among endometrial carcinoma patients with different clinicopathological parameters

As shown in **Table 2**, significant differences were observed in the positive expression of

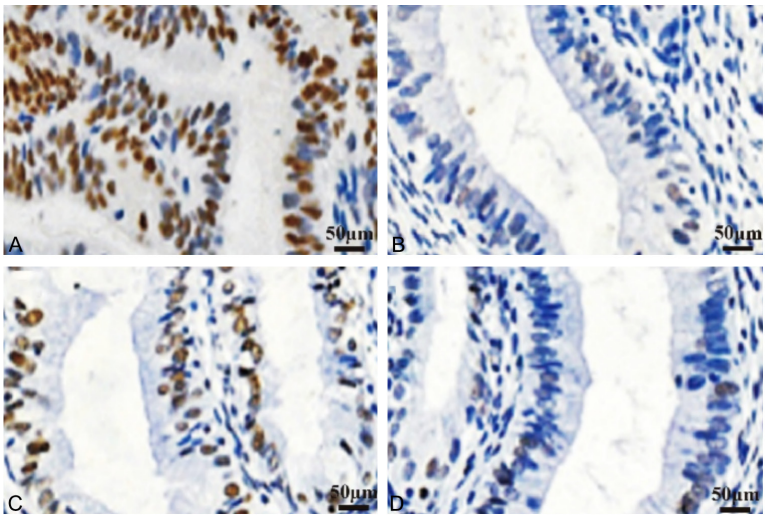

Figure 2. Immunohistochemistry results of HMGA1 and S100A4 proteins in the control (N = 40) and observation (N = 60) groups. A: HMGA1 expression in the observation group; B: HMGA1 expression in the control group; C: S100A4 expression in the observation group; D: S100A4 expression in the control group. Notes: HMGA1: High mobility group protein A1; S100A4: S100 calcium-binding protein A4.

HMGA1 and S100A4 among endometrial carcinoma patients with different tumor diameters, distant metastasis, lymph node metastasis, depth of infiltration and lymph-vascular infiltration (all $P<0.05$), while no significant differences were observed in the expression of HMGA1 and S100A4 among patients with different histological grading and FIGO stage (all $P>0.05$).

Comparison of clinicopathological parameters between non-recurrent-metastasis and recurrent-metastasis groups

As shown in **Table 3**, significant differences were observed in tumor diameter, histological grade, depth of infiltration, lymph-vascular infiltration, and FIGO stage between the non-recurrent-metastasis group and the recurrent-metastasis group (all $P<0.001$).

Multifactorial logistic regression analysis of risk factors influencing postoperative recurrence and metastasis in endometrial cancer

In the multifactorial logistic regression analysis, postoperative recurrence and metastasis in endometrial cancer patients was used as the dependent variable (no recurrence-metastasis = 0, recurrence-metastasis = 1). The independent variables included HGMA1 and S100A4 expression (negative expression = 0, positive expression = 1), tumor diameter (≤2 cm = 0, >2 cm = 1), histological grading (grade I = 0, grade II = 1), depth of infiltration (≤1/2 muscular layer = 0, >1/2 muscular layer = 1), lymphovascular infiltration (Yes = 0, No = 1), and FIGO stage (Ia = 0, Ib = 1). Multifactorial logistic regression analysis results showed that HGMA1, S100A4 protein expression, infiltration depth, lymphovascular infiltration and FIGO stage were independent influencing factors for the recurrence and metastasis in endometrial cancer patients, as shown in **Table 4**.

Predictive value of HGAM1 and S100A4 protein expression for postoperative recurrence and metastasis in endometrial cancer patients

As shown in **Figure 4** and **Table 5**, the sensitivity of HGAM1 and S100A4 protein expression in predicting postoperative recurrence and metastasis in endometrial cancer patients was plotted as the vertical coordinate, with 1-specificity as the horizontal coordinate. The area under the ROC curve (AUC) was calculated. The results showed that the protein expression of HGAM1 and S100A4 had a high predictive value for postoperative recurrence and metastasis in endometrial cancer patients, among which their combined detection showed the highest predictive value (AUC = 0.858).

Discussion

Endometrial cancer is a malignant tumor that arises from the endometrial tissue, and its pathogenesis remains unclear. Some studies have suggested that endometrial cancer is related to the abnormal expression of proto-oncogenes, oncogenes, and other factors [14]. While most patients have a good prognosis after early-stage surgical treatment, those with late-stage disease often have a poor prognosis and a high recurrence rate due to lymph node metastasis [15]. The treatment of endometrial cancer patients with recurrent metastasis after surgery is more complex, requiring additional surgery, radiotherapy, chemotherapy or targeted therapy. Currently, the risk of recurrence and

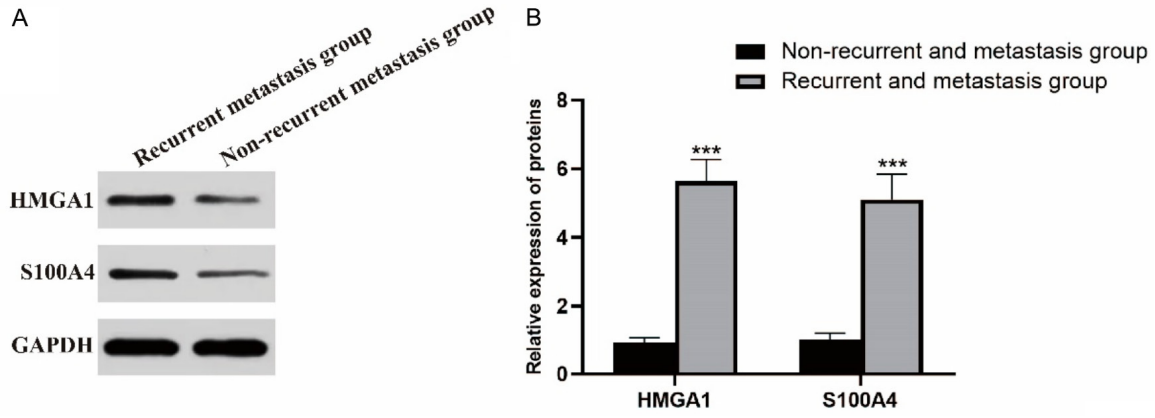

Figure 3. Comparison of protein expression of HMGA1 and S100A4 between the non-recurrent-metastasis group (n = 23) and recurrent-metastasis group (n = 37). A: The representing images of Western blot; B: Comparison of HMGA1 and S100A4 expression between the non-recurrent-metastasis group and recurrent-metastasis group. ***P<0.001 vs. no recurrent-metastasis group.

Table 2. Comparison of positive expression rates in HMGA1 and S100A4 across endometrial carcinoma patients with different clinicopathological parameters

Clinicopathological parameters		Cases (n)	HMGA1 [n (%)]	χ^2/*P* value	S100A4 [n (%)]	χ^2/*P* value
Tumor diameter	≤2 cm	37	20 (54.05)	19.538/<0.001	20 (54.05)	23.876/<0.001
	>2 cm	23	20 (86.96)		22 (95.65)	
Histological grading	Class I	46	30 (65.21)	1.792/0.105	30 (65.21)	3.509/0.058
	Class II	14	10 (71.43)		12 (85.71)	
Distant metastasis	Yes	24	19 (79.17)	17.183/<0.001	19 (79.17)	12.195/<0.001
	No	36	21 (58.33)		23 (63.89)	
Lymph node metastasis	Yes	28	22 (78.57)	18.629/<0.001	22 (78.57)	15.279/<0.001
	No	32	18 (56.25)		20 (62.50)	
Depth of infiltration	≤1/2 muscular layer	32	16 (50.00)	26.712/<0.001	18 (56.25)	20.187/<0.001
	>1/2 muscular layer	28	24 (85.71)		24 (85.71)	
Lymph-Vascular infiltration	Yes	23	20 (86.96)	29.868/<0.001	20 (86.96)	27.185/<0.001
	No	37	20 (54.05)		22 (59.46)	
FIGO stage	Ia	46	31 (67.39)	1.560/0.098	33 (71.74)	1.483/0.135
	Ib	14	9 (64.29)		9 (64.29)	

Notes: HMGA1: High mobility group protein A1; S100A4: S100 calcium-binding protein A4; FIGO: International federation of gynecology and obstetrics.

Table 3. Comparison of clinicopathological parameters between the no recurrent-metastasis and recurrent-metastasis groups

		Non-recurrent-metastasis group (N = 23)	Recurrent-metastasis group (N = 37)	χ^2/*P* value
Tumor diameter	≤2 cm	17 (73.91)	20 (54.05)	21.509/<0.001
	>2 cm	6 (26.09)	17 (45.95)	
Histological grading	Class I	20 (86.96)	26 (70.27)	18.915/<0.001
	Class II	3 (13.04)	11 (29.73)	
Depth of infiltration	≤1/2 muscular layer	19 (82.61)	13 (35.14)	27.465/<0.001
	>1/2 muscular layer	4 (17.39)	24 (64.86)	
Lymph-Vascular infiltration	Yes	2 (8.70)	21 (56.76)	31.573/<0.001
	No	21 (91.30)	16 (43.24)	
FIGO stage	Ia	18 (78.26)	27 (72.97)	16.916/<0.001
	Ib	5 (21.74)	10 (27.03)	

Note: FIGO: International federation of gynecology and obstetrics.

Table 4. Multifactorial logistic regression analysis of risk factors for postoperative recurrent metastasis in endometrial cancer patients

The dependent variable and assignment	B	SE	Wald χ^2 value	*P* value	OR value	95% CI
HGAM1	1.894	0.249	16.874	<0.001	1.687	1.215-6.264
S100A4	2.301	0.317	19.116	<0.001	2.049	1.439-7.194
Tumor diameter	0.275	0.162	2.760	0.097	1.292	0.986-1.775
Histological grading	0.185	0.129	1.586	0.203	1.206	0.973-1.892
Depth of infiltration	1.770	0.211	13.305	0.002	1.615	1.112-5.696
Lymph-pulvinar infiltration	2.103	0.282	17.431	<0.001	1.811	1.253-6.615
FIGO stage	1.690	0.205	11.825	0.007	1.494	1.096-5.318

Notes: HMGA1: High mobility group protein A1; S100A4: S100 calcium-binding protein A4; FIGO: International federation of gynecology and obstetrics.

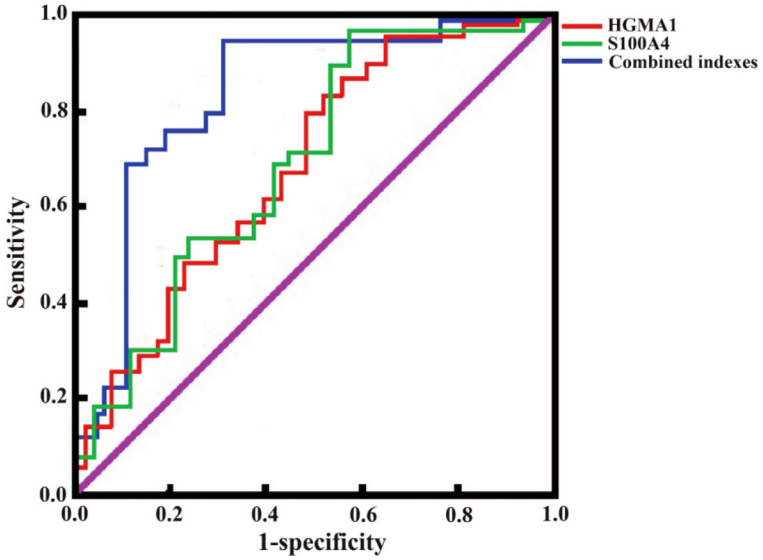

Figure 4. ROC curves for HGMA1 and S100A4 in predicting postoperative recurrence and metastasis in endometrial cancer patients.

metastasis in endometrial cancer is considered to be closely related to factors such as the degree of tumor infiltration, differentiation, FIGO stage, lymph node metastasis, which can provide a reference for the prognosis of endometrial cancer [16]. Identifying biomarkers closely related to the degree of tumor infiltration, differentiation, FIGO stage, lymph node metastasis, and other risk factors is essential for the early diagnosis and prognosis evaluation of endometrial cancer in clinical practice.

S100A4 is a calcium-binding protein primarily located in the cytoplasm and nucleus and is an important protein involved in the cytoskeletal architecture of actin and myosin. Some studies have shown that when S100A4 binds to calcium ions, it is involved in regulating key processes such as cell proliferation, differentiation, adhesion, migration, and apoptosis by regulating relevant cell signaling pathways and gene expression pathways [17]. Another study reported that the expression of S100A4 protein was elevated in colon cancer and had a close relationship with its pathological features and prognosis [18]. In this study, the results showed that the mRNA and protein expression levels of S100A4 in endometrial cancer tissues were significantly higher than normal endometrial tissues, aligning with previous reports [19]. Additionally, HMGA1 is a non-histone nuclear protein widely present in eukaryotic cells. It regulates the expression of tumor-related genes through various pathways and participates in the occurrence and development of gynecological tumors [20]. Some studies reported that HMGA1 was highly expressed in cervical cancer, and the serum HMGA1 levels increased significantly with the severity of cervical lesions, suggesting its potential clinical value in assessing the progression of cervical cancer [21]. The results of this study showed that HMGA1 expression in endometrial cancer lesions was significantly higher than that from the control group. Furthermore, another study showed that the expression of HMGA1 in lesions and serum of breast cancer patients was higher than in those with benign breast tumors [22], consistent with the findings of this study. Additional research showed that HMGA1

Table 5. The predictive value of HGMA1 and S100A4 for postoperative recurrence and metastasis in endometrial cancer patients

Indexes	AUC value	95% CI	Cut-off value	*P* value	Sensitivity (%)	Specificity (%)
HGMA1	0.703	0.651-0.764	61.82%	0.012	75.21	86.24
S100A4	0.742	0.697-0.802	65.24%	0.005	81.15	78.95
Combined indexes	0.858	0.794-0.911	-	<0.001	94.18	83.04

Notes: HMGA1: High mobility group protein A1; S100A4: S100 calcium-binding protein A4.

may be involved in the nuclear translocation of β-catenin protein and the invasion of endometrial cancer by binding to the matrix metalloproteinase-2 promoter [23].

The results of this study showed that HMGA1 and S100A4 expression levels in the recurrent-metastasis group were significantly higher than those in the non-recurrent-metastasis group. Moreover, significant differences in HMGA1 and S100A4 positive expression were observed in relation to myometrial infiltration, tumor diameter, lymph node metastasis status, distant metastasis, depth of infiltration, and lymph-vascular infiltration. These findings suggest that HMGA1 and S100A4 proteins are involved in the progression of endometrial cancer, playing an important role in tumor invasion and metastasis. The higher positive expression rates of S100A4 and HMGA1 in endometrial cancer tissues with deeper myofibrillar infiltration, earlier lymph nodes metastasis, and a higher likelihood of vascular cancer embolism indicate that these patients are at higher risk of poor prognosis. ROC curves showed that the AUC of HMGA1 was similar to that of S100A4, and the joined evaluation provided a higher predictive value than either marker alone. Logistic regression analysis identified HMGA1 and S100A4 as independent risk factors for predicting postoperative recurrence and metastasis in endometrial cancer patients. These results suggest that HMGA1 and S100A4 can serve as predictive factors for the recurrence and metastasis of endometrial cancer and can be used to assess patient prognosis. In clinical practices, quantitative assessments of HMGA1 and S100A4 can be used to stratify the risk of recurrence and metastasis in EC patients. This information can guide the design of clinical drug trials, inform prognosis evaluations, and facilitate early interventions, ultimately improving the quality of life and reducing mortality in endometrial cancer patients. These findings are consistent with previous studies [24, 25].

In summary, the individual detection of HMGA1 and S100A4 can be considered useful for predicting recurrence and metastasis in endometrial cancer patients. Both HMGA1 and S100A4 have been identified as independent risk factors for the recurrence and metastasis of endometrial cancer that are worth promoting and applying in clinical practices. However, this study has several limitations: it is a single-center study with a small sample size, lacks long-term follow-up data, does not include subgroup comparisons, and does not explore the underlying mechanisms. Future research should involve multicenter, long-term follow-up studies with larger sample sizes to further validate these findings.

Disclosure of conflict of interest

None.

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