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ABOUT COVER

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Retrospective Study

Efficacy and prognosis of adjuvant treatment of endometrial cancer with medroxyprogesterone acetate COX regression analysis

Ding-Ran Wang

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Abstract

BACKGROUND

Endometrial cancer is one of the most commonly diagnosed gynecological cancers worldwide, and early-stage high-risk endometrial cancer has a poor prognosis. Adjuvant treatments after surgery, such as chemotherapy and radiotherapy, have been widely used in clinical practice to improve patient survival. Medroxyprogesterone acetate is a synthetic progestogen that has been reported to have potential anticancer effects in endometrial cancer. However, its efficacy, safety, and long-term prognostic benefits as an adjuvant treatment for endometrial cancer remain controversial. Therefore, this study aimed to observe the efficacy and prognostic impact of adjuvant medroxyprogesterone acetate treatment in patients with early-stage high-risk endometrial cancer and evaluate its safety.

AIM

To observe the efficacy and prognosis of adjuvant treatment of endometrial cancer with medroxyprogesterone acetate and to evaluate its safety.

METHODS

We collected the clinical data of 200 patients with early-stage high-risk endometrial cancer who were admitted to the Department of Obstetrics and Gynecology of our hospital from January 2018 to December 2022. The control group (100 patients) underwent conventional surgical treatment, and the study group (100 patients) was administered adjuvant medroxyprogesterone acetate tablets on top of the control group. The Kaplan-Meier curve analysis and log-rank test were performed to determine the possible factors influencing the 5-year cumulative survival rate in the patients. The Cox regression analysis was performed to identify the factors influencing the survival prognosis of endometrial cancer.

RESULTS

According to the Cox regression analysis, age [hazard ratio (HR) = 4.636, 95%

confidence interval (95%CI): 1.411-15.237], pathological type (HR = 6.943, 95%CI: 2.299-20.977), molecular typing (HR = 5.789, 95%CI: 3.305-10.141), and myometrial infiltration (HR = 5.768, 95%CI: 1.898-17.520) were factors influencing the prognosis of patients with early-stage high-risk endometrial cancer.

CONCLUSION

Age, pathological type, molecular typing, and myometrial infiltration were all relevant factors affecting the prognosis of early-stage high-risk endometrial cancer. The potential long-term prognostic benefit of adjuvant postoperative radiotherapy in patients with early-stage high-risk endometrial cancer is worthy of clinical consideration.

Key Words: Endometrial cancer; Independent risk factors; Postoperative adjuvant therapy; Clinical analysis; Prognostic analysis

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Core Tip: Adjuvant treatment with medroxyprogesterone acetate may have potential long-term prognostic benefits for patients with early-stage high-risk endometrial cancer. Age, pathological type, molecular typing, and myometrial infiltration were identified as relevant factors affecting patient prognosis.

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INTRODUCTION

Patients with endometrial cancer develop clinical symptoms early. Although the prognosis of patients with early adjuvant postoperative treatment is generally good, patients who are not treated promptly may continue to develop postoperative recurrence or metastasis, which is associated with a poor prognosis and a high mortality rate. Therefore, these patients require adjuvant postoperative treatment depending on their pathology[1-5]. The present study suggests that there are other factors associated with adjuvant postoperative treatment that highly influence patient prognosis, but whether they are independent risk factors remains uncertain[6-10].

Progestins include natural, synthetic, and semi-synthetic progestins that effectively prevent abnormal endometrial hyperplasia caused by single estrogen stimulation. These progestins exert a protective effect on the endometrium[11-14]. The structure of progestins is similar to that of natural progesterone. Progestins act on the pituitary-gonadal axis to regulate gonadotropin secretion and reduce the levels of the luteinizing hormone and follicle-stimulating hormone. In addition, medroxyprogesterone acetate acts directly on the endometrium to inhibit its persistent hyperplasia and induce its shrinkage, thereby reducing endometrial thickness[15-25]. We here investigated the clinical value of postoperative adjuvant treatment with medroxyprogesterone acetate through a prognostic analysis of endometrial cancer patients. Moreover, the independent risk factors affecting patient prognosis were determined to provide clinical guidance for endometrial cancer treatment.

MATERIALS AND METHODS

Case selection and general information

We collected the clinical data of 200 patients with early-stage high-risk endometrial cancer who were admitted to the Department of Obstetrics and Gynaecology of our hospital from January 2018 to December 2022.

We included the data of patients with complete surgical pathological staging, those diagnosed with endometrial cancer on the basis of surgical pathology, all of those who were followed up, and those for whom complete clinicopathological data were available. Data of patients treated first with non-surgical treatment (e.g., preoperative chemotherapy), who died postoperatively because of severe comorbidities, and who postoperatively developed other malignant tumors were excluded.

Methodology

Conventional surgery was performed in the control group (100 cases), while adjuvant treatment with 4 mg medroxyprogesterone acetate tablets (Shanghai Xinyi Tianping Pharmaceutical Co., Ltd., State Pharmacopoeia H31020976) was administered to the study group (100 cases) once daily for 3 mo. The tablets were swallowed with warm water.

Statistical analysis

Statistical analysis was completed using SPSS 23.0. The statistical data were described as relative numbers. The survival analysis was conducted by plotting Kaplan-Meier curves. The parallel log-rank test was conducted for factors that affected survival, as indicated in a one-way test. The multiple factors affecting survival were analyzed using the Cox regression model analysis and evaluated by hazard ratio (HR) and 95% confidence interval (CI). The test-level α was 0.05 (two-tailed).

RESULTS

Cumulative survival rate

The cumulative survival rates of endometrial cancer patients with or without pregnancy history, or combined polycystic ovary syndrome, hypertension, and obesity exhibited no statistical significance, all $P > 0.05$. The cumulative survival rates of patients aged < 50 years and with non-menopausal endometrial cancer were higher than those of patients aged ≥ 50 years and with menopausal endometrial cancer, all $P < 0.05$ (Table 1).

Effect of postoperative adjuvant therapy on cumulative survival

The cumulative survival rate of patients with endometrial cancer with or without postoperative adjuvant therapy exhibited no statistical significance, $P > 0.05$. The cumulative survival rate of patients treated with medroxyprogesterone acetate after surgery was higher than that of those treated without medroxyprogesterone acetate, $P < 0.05$ (Table 1).

Survival analysis of patients with different pathological features

The cumulative survival rates of patients with early-stage high-risk endometrial cancer of different stages, pathological stages, and histological grades exhibited no statistical significance, all $P > 0.05$. The cumulative survival rates of patients with the molecular staging of high-copy type, with choroidal infiltration, N3 grade lymph node metastasis, and myometrial infiltration $\geq 1/2$ were lower than those of patients with other molecular stagings, without choroidal infiltration, N0-N2 grade lymph node metastasis, and myometrial infiltration $< 1/2$. The differences were statistically significant, all at $P < 0.05$ (Table 1).

Analysis of prognostic independent risk factors

Univariate variables were included in the multifactor Cox independent regression analysis for assignment (Table 2). The analysis revealed that age, type of pathology, molecular typing, and myometrial infiltration were factors influencing the prognosis of patients with early-stage high-risk endometrial cancer, all at $P < 0.05$ (Table 3).

DISCUSSION

Endometrial cancer is among the most common malignant tumors of the reproductive system. It poses a severe threat to women's health, and the number of endometrial cancer cases is increasing every year[26-30]. The mechanism underlying endometrial cancer development remains unclear. Delayed menopause, polycystic ovary syndrome, hypertension, and diabetes mellitus may act as risk factors for endometrial cancer[31,32]. The former type occurs commonly in perimenopausal women and is mostly endometrial adenocarcinoma. Patients with this type of endometrial cancer exhibit a high-risk clinical presentation of endometrial hyperplasia without shedding, which is closely related to persistently high estrogen levels. The latter type is more common in older menopausal patients, and the pathological type is mostly plasmacytotic endometrial cancer. This type of endometrial cancer is highly malignant and has a relatively poor prognosis[33]. Traditional staging is a crucial clinical reference for the postoperative adjuvant treatment of endometrial cancer patients; however, the clinical evaluation of this treatment is variable[34-39]. In this study, no statistically significant difference was observed in the cumulative survival rate between the two types of early-stage high-risk endometrial cancer patients. This may be because the study included data from patients with early-stage endometrial cancer with good pathological differentiation and therefore a better prognosis. Although postoperative adjuvant treatment and prognostic analysis of early-stage high-risk patients were generally good, patients who received no treatment in time continued to experience postoperative recurrence or metastasis. Therefore, postoperative adjuvant treatment was administered depending on the pathological findings of the patients. The present study suggests that not only postoperative adjuvant therapy but also other associated factors affect patient prognosis, but whether they are independent risk factors remains uncertain[40].

In this study, the cumulative survival rates of patients treated with and without postoperative adjuvant medroxyprogesterone acetate were similar, but those of patients treated with combined medroxyprogesterone acetate were higher than those of patients without combined medroxyprogesterone. This suggests that postoperative adjuvant therapy improves the clinical outcome and prognosis of early-stage high-risk endometrial cancer, especially in combination with radiotherapy. This may be because postoperative radiotherapy can inhibit the infiltration and metastasis of residual cancer cells in the blood and improve the radicality of surgical treatment.

The multifactor Cox regression analysis revealed that age, pathological type, molecular staging, and myometrial infiltration were factors influencing the prognosis of patients with early-stage high-risk endometrial cancer. The cumulative survival rates of patients with early-stage high-risk endometrial cancer who were aged ≥ 50 years, pathological type of

Table 1 Comparison of cumulative survival rates of 200 patients with endometrial cancer based on clinical characteristics

Clinical features	n	Cumulative survival rate (%)	χ^2 value	P value
Age (yr)				
< 50	84	97.4	5.897	0.002
≥ 50	116	81.5		
Non-menopausal	81	96.8	6.793	0.008
Menopausal	119	87.5		
Pregnancy history				
Yes	155	90.4	0.634	0.269
None	45	100.0		
Comorbidities				
Polycystic ovary syndrome				
Yes	33	100.0	0.310	0.454
None	168	90.6		
High blood pressure				
Yes	81	88.1	0.600	0.358
None	119	92.1		
Obesity				
Post-operative adjuvant radiotherapy	79	85.7	1.062	0.280
	121	92.1		
Post-operative medroxyprogesterone acetate treatment	72	85.7	0.673	0.195
	128	80.0		
Co-Medroxyprogesterone Acetate	61	96.6	4.552	0.047
Not combined with medroxyprogesterone acetate	139	81.0		
Type of pathology				
Adenocarcinoma	144	95.6		
Adenosquamous carcinoma	10	37.5	32.321	< 0.001
	7	77.8		

Table 2 Assignment of factors influencing prognosis at the early-stage high-risk endometrial cancer

Factors	Assignment
Age	< 50 yr = 0, ≥ 50 yr = 1
Menopause	Not menopausal = 0, Menopausal = 1

Postoperative adjuvant therapy combined medroxyprogesterone acetate = 0, uncombined medroxyprogesterone acetate = 1 pathological type adenocarcinoma = 0, non-adenocarcinoma = 1, adenosquamous carcinoma = 2; molecular typing DNA polymerase gene (POLE) mutation = 0, microsatellite highly unstable type (MSI-H) type = 1, low copy type = 2, high copy type = 3; vascular infiltration None = 0, Yes = 1.

adenosquamous carcinoma, molecular staging of high-copy type, with choroidal infiltration, grade N3 lymph node metastasis, and myometrial infiltration extent $\geq 1/2$ were lower ($P < 0.05$). This indicated that the survival prognosis of early-stage high-risk endometrial cancer was closely associated with age and pathological factors. Age factors affect the prognosis of endometrial cancer patients and may be associated with multiple comorbidities, poor physical function, high incidence of specific histopathological types, adverse prognostic factors, and poor tolerance to surgical trauma and postoperative radiotherapy. and performing full-staged surgery and adequate cycles of adjuvant radiotherapy is often difficult. In this study, data showed that patients with early-stage, high-risk endometrial cancer tend to be younger, and the death risk increases with age. Thus, increasing awareness and screening for endometrial cancer in young women is necessary.

Table 3 Factors influencing the prognosis of patients with early-stage high-risk endometrial cancer

Factors	Assignment
Lymph node metastasis	N0 = 0, N1 = 1, N2 = 2, N3 = 3
Myofilament infiltration	< 1/2 = 0, ≥ 1/2 = 1

The main pathological types of endometrial cancer include plasmacytoma, clear cell carcinoma, and endometrial adenocarcinoma. The survival rate of study patients with adenosquamous carcinoma was lower than that of those with other pathological types. Therefore, in the specific clinical management of endometrial cancer, the pathological type of the patient and the early treatment of patients with adenosquamous endometrial cancer must be considered to improve their prognosis. In this study, no significant difference in survival prognosis was observed between stage I and II patients, which may be because most study patients had early-stage endometrial cancer, which was highly curative and was associated with a good prognosis after surgical treatment. The univariate analysis also exhibited a higher survival rate for patients treated with postoperative adjuvant radiotherapy, but the Cox regression analysis did not reveal that it was an independent factor for prognosis. This suggests that chemotherapy has some therapeutic effect on high-risk early-stage endometrial cancer, but it has a limited effect on its long-term prognosis.

CONCLUSION

In conclusion, many factors influence the adjuvant postoperative treatment of early-stage high-risk endometrial cancer, including age, pathological type, molecular typing, and myometrial infiltration. Postoperative adjuvant medroxyprogesterone acetate is beneficial in patients with early-stage high-risk endometrial cancer and deserves clinical consideration.

ARTICLE HIGHLIGHTS

Research background

Patients with endometrial cancer have an early onset of clinical symptoms, and although the prognosis for patients with early adjuvant postoperative treatment is generally good, patients who do not receive timely treatment may develop postoperative recurrence or metastasis, which has been associated with a poor prognosis and a high mortality rate, therefore requiring adjuvant postoperative treatment depending on the patient's pathology.

Research motivation

To determine the efficacy and prognosis of adjuvant treatment of endometrial cancer with medroxyprogesterone acetate and medroxyprogesterone acetate and to evaluate their safety.

Research objectives

To provide a reference for the prognosis and anesthesia of clinical operations.

Research methods

Kaplan-Meier curve analysis and log-rank test were performed to determine the potential influencing factors on the 5-year cumulative survival rate of the study patients, while Cox regression analysis was performed to identify the factors influencing the survival prognosis of endometrial cancer.

Research results

The Cox regression analysis revealed that age [hazard ratio (HR) = 4.636, 95% confidence interval (95%CI): 1.411-15.237], pathological type (HR = 6.943, 95%CI: 2.299-20.977), molecular typing (HR = 5.789, 95%CI: 3.305-10.141), myometrial infiltration (HR = 5.768, 95%CI: 1.898-17.520) were influential factors in the prognosis of patients with early-stage high-risk endometrial cancer.

Research conclusions

The possibility of the long-term prognostic benefit of adjuvant postoperative radiotherapy in patients with early-stage high-risk endometrium is worthy of clinical consideration.

Research perspectives

Future research may investigate optimal medroxyprogesterone acetate dosage and duration for early endometrial cancer. Can explore combining medroxyprogesterone acetate with other therapies. Also, include patient-reported outcomes to understand treatment impact.

FOOTNOTES

Author contributions: Wang DR designed the research study, performed the research, analyzed the data, wrote the manuscript, and read and approved the final manuscript.

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