

High-risk endometrial cancer may benefit from adjuvant radiotherapy plus chemotherapy

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Objective: To present patterns of practice and outcomes in the adjuvant treatment of intermediate- and high-risk endometrial cancer.

Methods: Retrospective data on 224 women with intermediate-risk and high-risk endometrial cancer from 1999 to 2006 were reviewed. All patients underwent surgical staging. Patterns of adjuvant treatment, consisting of pelvic radiotherapy, chemotherapy, and radiotherapy plus chemotherapy, were assessed. The 3- and 5-year disease-specific survival (DSS) rates were calculated using the Kaplan-Meier method.

Results: The difference in 5-year DSS rate was statistically significant between adjuvant group and non-adjuvant group (80.65% vs. 63.80%, $P=0.040$). In 110 high-risk patients who underwent adjuvant treatment, both 5-year DSS rate and recurrent rate were significantly different in combined radiotherapy and chemotherapy group compared with radiotherapy alone and chemotherapy alone groups (DSS rate, $P=0.049$; recurrent rate, $P=0.047$). In 83 intermediate-risk women who underwent adjuvant treatment, there was no significant difference in 5-year DSS rate and recurrence rate among the combined radiotherapy and chemotherapy, radiotherapy alone and chemotherapy alone groups (DSS rate, $P=0.776$; recurrent rate, $P=0.937$).

Conclusions: Adjuvant radiotherapy plus chemotherapy is associated with a higher 5-year DSS rate and lower recurrence rate compared with radiotherapy alone and chemotherapy alone in high-risk endometrial cancer patients. Patients with intermediate-risk endometrial cancer may be not likely to benefit from adjuvant combined radiotherapy and chemotherapy.

Key Words: Adjuvant treatment; chemotherapy; endometrial cancer; radiotherapy; recurrence



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Introduction

Endometrial cancer is one of the most common gynecologic malignancies, with an ever-increasing incidence (1). Although consensus on surgical staging has been reached, postoperative adjuvant treatment remains controversial. Major prognostic factors are stage, histological type, grade, depth of myometrial invasion, and lymph-vascular space invasion (LVSI). Adjuvant treatment has been tailored to these risk factors.

Radiation therapy (RT) is the conventional postoperative adjuvant treatment for patients with intermediate- and

high-risk endometrial cancer. However, a number of studies have indicated that postoperative adjuvant pelvic external beam radiotherapy (EBRT) or vaginal brachytherapy (VBT) reduced the local recurrence rate without increasing the overall survival (OS) rate (2,3). In the past 20 years, much attention has been paid to postoperative chemotherapy (CHEMO), concurrent RT and CHEMO, as well as combined RT and CHEMO (RT&CHEMO). However, relatively little is known regarding regimen selection and efficacy of chemotherapy-containing adjuvant treatments.

The aim of this study was to explore the feasibility,

effectivity and toxicity of adjuvant treatment for intermediate- and high-risk endometrial cancer.

Materials and methods

General information

This study included 224 patients with intermediate-risk and high-risk factors treated from January 1999 to December 2006 in Beijing Obstetrics and Gynecology Hospital, of which, 193 cases received postsurgical treatment (adjuvant treatment group) and 31 patients did not undergo any adjuvant treatment (non-adjuvant treatment group). Surgical staging [International Federation of Gynaecology and Obstetrics (FIGO) 2009], including extrafascial total abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymphadenectomy (PLN)/para-aortic lymph node dissection, was administered in all patients. The intermediate-risk group (105 cases) included patients with stage IA G3 or other non-endometrial adenocarcinoma pathological type; stage IB, G1 and G2, with endometrioid type histology (4). The high-risk group (119 cases) are stage IB of grade 3 or of non-endometrioid histology; or stage II or III (4).

Adjuvant treatment: postoperative pelvic EBRT with or without VBT (RT group)

A total of 162 patients (including 109 RT alone and 53 RT+CHEMO cases) were treated with EBRT, of which 148 (91.36%) had pelvic standard rectangular field RT and 14 (8.64%) received BOX field RT, with a dose range of 40-45 Gy. Four Patients (2.47%) with positive common iliac lymph nodes or para-aortic lymph nodes were assigned to concurrent pelvic irradiation and para-abdominal aortic extended field irradiation with a dose range of 40-45 Gy, and 7 patients (4.32%) with parametrial metastasis or local pelvic lymph node metastasis were given the above pelvic EBRT and subsequent reduced field irradiation covering the parametrial region or lymph node metastatic region with the dose range of 5-10 Gy. Ten patients (6.17%) including 6 intermediate-risk patients and 4 high-risk patients consented to receive EBRT followed by immediate VBT with a dose range of 10-20 Gy. None of the patients in this study underwent postoperative VBT alone.

Postoperative CHEMO

Among 84 patients (45.52%, including 31 CHEMO

alone and 53 RT+CHEMO cases) who were assigned to postoperative systemic CHEMO, 31 (36.90%) adopted 4-6 cycles of CHEMO, 32 (38.10%) underwent 2-3 cycles of CHEMO followed by RT (CHEMO-RT); 3 (3.57%) received RT followed by 2-3 cycles of CHEMO (RT-CHEMO); 9 (10.71%) had 2-3 cycles of CHEMO first and then RT followed by same regimen CHEMO for 2-3 cycles (CHEMO-RT-CHEMO); 3 (3.57%) received RT plus 2-3 cycles of CHEMO at the same time (RT+CHEMO); and 6 (7.14%) underwent 2-3 cycles of CHEMO first followed by RT plus the same CHEMO regimen at the same time for 2-3 cycles (CHEMO-CHEMO+RT). CHEMO was delivered at 21-d intervals. The regimens were: cisplatin, doxorubicin plus cyclophosphamide (PAC) for 36 patients (42.86%); cisplatin plus paclitaxel (PT) for 33 patients (39.29%); cisplatin plus doxorubicin (PA) for 10 patients (11.90%); cisplatin, vincristine plus doxorubicin (PVA) for 1 patient (1.19%); cisplatin, ifosfamide plus doxorubicin (PIA) for 1 patient (1.19%); cisplatin, etoposide plus cyclophosphamide (PEC) for 1 patient (1.19%); cisplatin plus cyclophosphamide (PC) for 1 patient (1.19%); and cyclophosphamide, doxorubicin plus 5-fluorouracil (CAF) for 1 patient (1.19%).

Follow up

The median follow-up time was 49 months (range, 3-130 months). Fifty-nine (26.34%) of the 224 patients were lost during the follow-up period. Survival time was calculated as the time from diagnosis to death or the last follow up. Disease-specific survival (DSS) time was calculated under the following situations: patients were died of diseases, or patients' death was caused by treatment-induced complications directly or indirectly.

Statistical analysis

SPSS 17.0 statistical software package (SPSS Inc., Chicago, IL, USA) was adopted for the statistical analysis. The Kaplan-Meier method was used to estimate the survival rates and log-rank test was used to analyze the significance. Comparison of rates including recurrence rates and toxicity rates was performed by Pearson Chi-square and continuity correction test.

Results

General characteristics

The study included 224 patients with a median age of 57 years