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Original Research

Analysis of endometrial carcinoma in young women at a high-volume cancer center

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HIGHLIGHTS

- Endometrial cancer is uncommon in patients 40 years of age and younger.
- The prognosis for EC among younger patients tends to be more favorable than that for older patients.
- CA 125 level ≥35 is the most significant factor affecting survival in patients with aged ≤40 years with endometrial cancer.

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ABSTRACT

Objective: To investigate the clinicopathological characteristics, treatment, survival, and prognosis of endometrial cancer in women aged ≤40 years.
Methods: Women who underwent surgery for endometrial cancer at a single high-volume cancer center between January 1995 and December 2014 were retrospectively reviewed. Women aged >40, patients with missing data, and those who did not undergo surgical staging were excluded. Univariate and multivariate regression models were used to identify the risk factors for overall survival and progression-free survival.
Results: A total of 40 patients with endometrial cancer were assessed. The median age at diagnosis was 38 (range, 21–40) years, and most of the uterine tumors found were early-stage (85%), low-grade (67.5%), and endometrioid carcinomas (97.5%). The median serum cancer antigen 125 level was 10.9 IU/mL (range, 3–1284 IU/mL). Optimal cytoreductive surgery was achieved in 35 patients (87.5%). All patients underwent total abdominal hysterectomy, and 97.5% of the patients underwent hysterectomy plus bilateral salpingo-oophorectomy. Among the total group of 40 patients, 21 (52.5%) underwent pelvic and para-aortic lymph node dissection, and 15 (37.5%) underwent only pelvic lymph node dissection. Multivariate analysis confirmed that a cancer antigen 125 level ≥35 was the only independent prognostic factor for both progression-free survival (hazard ratio, 22.997; 95% confidence interval, 1.783–296.536; p = 0.016) and overall survival (hazard ratio, 22.541; 95% confidence interval, 1.75–290.364; p = 0,017).
Conclusions: Our study demonstrated that a cancer antigen 125 level ≥ 35 is the only independent prognostic factor for both progression-free survival and overall survival in patients aged ≤40 years with endometrial cancer.

1. Introduction

Endometrial cancer (EC) is the most frequent malignant tumor of the female reproductive system [1]. Most women are diagnosed at an early stage owing to abnormal vaginal bleeding [2]. Although the prognosis of EC tends to be favorable, it can range from an excellent prognosis to aggressive disease. The standard treatment for EC is a total hysterectomy with bilateral salpingo-oophorectomy (BSO). Although lymphadenectomy in women with EC is a greatly controversial subject, it is performed in most centers on both localized and advanced disease [3,4].

EC commonly occur in postmenopausal, women and the median

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age of patients is 61 years [5]. The incidence of EC in women aged ≤40 years is approximately 5% [6]. Most patients in this age group have a history of recognizable estrogen- or hormone-related disorders, such as obesity, nulliparity, chronic anovulation, and polycystic ovary syndrome [7]. The prognosis for EC among younger patients tends to be more favorable than that for older patients. Among these patients, early stage diagnosis and well-differentiated tumors are reported more frequently, which may explain the higher survival rate [8,9]. In a broad population-based study investigating the prognostic factors affecting the survival of younger women with uterine cancer, the overall 5-year disease-specific survival was 93% in women under 40 years [8].

Although the classic treatment for EC requires at least a hysterectomy with BSO regardless of the patient's age and the stage of the tumor, the management of women aged ≤40 years with EC is more difficult than that for older patients. The standard treatment options for this age group are not clearly defined. Most patients have the desire to become pregnant at some stage. Hysterectomy results in the loss of fertility; thus, it is not often accepted by women desiring pregnancy. However, regarding uterine preservation, increasing evidence suggests that fertility-sparing management is feasible for women aged ≤40 years with early stage, low-grade EC [10–14].

Another highly controversial issue that requires further research in young patients with EC is ovarian preservation. Routine oophorectomy is performed at the time of surgery to eliminate concurrent ovarian malignancy and occult ovarian metastases. Concurrent ovarian cancer with EC occurs in approximately 5% of stage I EC and 10% of stage II EC cases [15,16]. In younger patients, the incidence of concomitant ovarian cancer with EC in younger patients is 2–7 times greater than that of ovarian metastasis [17,18]. However, oophorectomy leads to premature menopause, resulting in a reduced quality of life, increased risk of cardiovascular disease, and osteoporosis in the future [19,20]. Although earlier studies have revealed the risk of concurrent ovarian malignancy in patients with early stage EC [21–23], only a few have presented the long-term oncological results of ovarian preservation. However, current studies have shown that ovarian preservation does not affect the survival of early stage EC patients unfavorably [5,10,24]. Thus, the safety of young patients desiring ovarian preservation is controversial and needs further consideration.

Currently, the management of young patients, especially early stage, low-grade EC, is a contentious issue. In the present study, we analyzed the clinicopathological characteristics, treatment, survival, and prognosis related to EC in women aged ≤40 years.

2. Materials and methods

The medical records of all women aged ≤40 years who underwent surgery for EC at a single high-volume cancer center between January 1995 and December 2014 were retrospectively reviewed. This study was conducted according with the ethical standards of the Declaration of Helsinki and received institutional review board approval. Women aged >40, patients with missing data, or patients who did not undergo surgical staging were excluded. Consequently, 40 women with EC aged ≤40 years were recognized.

Demographic data, including age at surgery, parity, comorbid diseases, body mass index (BMI), and preoperative cancer antigen 125 (CA 125) levels, as well as surgical details and follow-up information, were attained from the medical records. The histopathological findings, comprising the primary tumor diameter (PTD), depth of myometrial invasion (MI), lymphovascular space invasion (LVSI), International Federation of Gynecology and Obstetrics (FIGO) grade, tumor-free distance (TFD) from the uterine serosa, cervical stromal invasion (CSI), and pelvic (P) and/or paraaortic (PA) lymph node (LN) metastasis, were obtained from the surgical pathology reports. All pathology slides were analyzed by an experienced gynecological pathologists.

All patients underwent peritoneal washing, cytology, omentectomy or omental biopsy, hysterectomy, and BSO. However, the decision to perform a P and/or PA LND was made according to the surgeon's discretion. No LNs were sampled in some patients; complete staging with bilateral P LND was performed in some patients; and some patients underwent complete staging with bilateral P and PA LND. Staging was defined postoperatively according to the 2009 FIGO staging system.

The PTD was described as the largest field in each of the three dimensions of the tumor. If more than one tumor was present, the tumor with the largest diameter was taken into consideration. Depth of MI was classified into two groups, as follows: 1) invasion of half or fewer than half of the myometrium and 2) invasion of more than half of the myometrium. LVSI was described as the presence of tumor cells in a vascular space lined by endothelium and/or the attachment of tumor cells to the vascular wall, irrespective of the number of LVSI foci.

Adjuvant therapy, including radiotherapy (RT) alone, chemotherapy (CT) alone, or a combination of the two, was administered to patients depending on stage, nodal metastasis status, performance status, and the presence/absence of medical comorbidities. The patients returned for follow-up examinations every 3 months for the first 2 years, every 6 months for the next 3 years, and annually after that. Follow-up examinations involved physical and vaginal examinations, vaginal cytology, ultrasound scanning, and measurement of serum CA 125 levels. Computed tomography or magnetic resonance imaging was applied annually. Progression-free survival (PFS) was calculated as the time from the date of primary surgery to the determination of recurrence or the latest observation. Overall survival (OS) was calculated as the number of months from the date of surgery to the date of death or last contact.

Statistical analyses were carried out using IBM SPSS Statistics 22 (SPSS Inc., Chicago, IL). The variables were evaluated using visual (histograms, probability plots) and analytical (Shapiro–Wilk test) methods to determine whether they were normally distributed. Continuous data were examined using the Mann–Whitney *U* test for non-normal data. To compare the proportions between groups, the chi-square test was used. Univariate and multivariate logistic regression models were employed to identify risk factors. Kaplan–Meier curves were generated to examine the survival curve, and comparisons were calculated with the log rank test. A p-value < 0.05 was considered statistically significant.

3. Results

A total of 40 patients with EC who were treated surgically and fulfilled the inclusion criteria were included in the study. Table 1 shows the baseline characteristics and pathological features of these patients. The median age at diagnosis was 38 (range, 21–40) years, and most uterine tumors found were early stage (85%), low-grade (67.5%), and endometrioid carcinomas (97.5%). The median serum CA 125 level was 10.9 IU/mL (range, 3–1284 IU/mL).

Among the 40 study participants, 29 (72.5%) displayed ≤ 50% MI, while 11 (27.5%) had > 50% MI. Half of the patients had a PTD of >2 cm. LVSI was detected in nine (22.5%) patients. Optimal cytoreductive surgery was achieved in 35 patients (87.5%). Most patients who were optimally cytoreduced had stage I disease (75%). All patients underwent total abdominal hysterectomy; in 97.5% of the patients, hysterectomy plus BSO was performed. Among the 40 patients, 21 (52.5%) underwent P/PA LND, and 15 (37.5%) underwent only P LND. The various types of surgeries performed are shown in Table 2.