European Journal of Obstetrics & Gynecology and Reproductive Biology 222 (2018) 151–154

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Risk factors for ovarian involvement in young and premenopausal endometrioid endometrial cancer patients

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ARTICLE INFO

Article history:
Received 21 May 2017
Received in revised form 21 January 2018
Accepted 25 January 2018

Keywords:
Endometrioid endometrial cancer
Ovarian involvement
Ovarian preservation
Risk factors

ABSTRACT

Objective: This study aimed to investigate the incidence of ovarian malignant involvement in young and premenopausal endometrioid endometrial cancer and study the possible risk factors.
Methods: Premenopausal patients 45 years of age or younger with endometrioid endometrial cancer treated at the OB/GYN Hospital of Fudan University between 2009 and 2013 were identified. The incidence of ovarian malignant involvement in young and premenopausal endometrioid endometrial cancer patients were calculated and the possible risk factors were investigated.
Results: A total of 144 younger (age $\leq$ 45, premenopausal) patients with endometrioid endometrial cancer were identified and coexisting malignant ovarian neoplasms were detected in 6 patients. Univariate analysis revealed that deeper myometrial invasion, positive lymphonode metastasis, positive LVSI, and high histologic grade (G2-G3) were associated with ovarian involvement in younger endometrial cancer patients. However, multivariate analysis revealed that only deep myometrial invasion was an independent risk factors for ovarian involvement (OR = 12.81, P = 0.046).
Conclusion: In conclusions, the incidence of coexisting ovarian malignant neoplasms in young and premenopausal patients with endometrioid endometrial cancer is low, and these findings may facilitate preoperative counseling of patients and decision making at the time of surgery.

Introduction

Endometrial cancer is one of the most common gynecological malignancies, of which the incidence is increasing in young women. The standard surgical approach for endometrial cancer includes total hysterectomy and bilateral salpingo-oophorectomy (BSO) with or without pelvic and para-aortic lymph node dissection [1–3]. Oophorectomy is indicated even in young patients with low grade early stage endometrioid cancer because the disease is regarded as estrogen dependent and co-existing malignant ovarian neoplasms are occasionally found. However, this traditional surgical treatment has been challenged due to the low incidence of ovarian involvement in endometrial cancer and the short- and long-term adverse sequelae associated with oophorectomy in premenopausal women [4,5]. Indeed, several studies have demonstrated that ovarian preservation in premenopausal women with low risk endometrial cancer does not negatively impact the survival [1,6–11]. These make us raise the question whether we should preserve ovary in low risk endometrial cancer or not; and if yes, which kind of patients are appropriate for ovarian preservation. Knowledge of the incidence of ovarian involvement in patients with endometrial cancer and the risk factors for ovarian malignant involvement might give us some help to answer these questions.

In this study, we retrospectively analyzed young and premenopausal endometrioid endometrial cancer cases in our hospital. We calculated the rate of ovarian malignant involvement in these patients and further analyzed possible risk factors for ovarian involvement.

Materials and methods

Ethics statement

This study complied with the tenets of the Helsinki Declaration, and was approved by the Medical Ethics Committee of the

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https://doi.org/10.1016/j.ejogrb.2018.01.030
0301-2115/

Obstetrics and Gynecology Hospital of Fudan University (hereafter referred to as "OB&GYN Hospital"). All patients signed an informed consent form before participating in the study.

Patient cohorts and study design

Patients with endometrioid endometrial cancer who received operation at the OB/GYN Hospital of Fudan University between 2009 and 2013 were retrospectively analyzed. All patients received total hysterectomy and bilateral salpingo-oophorectomy (BSO) with or without pelvic and para-aortic lymph node dissection. Pathological diagnosis was confirmed by at least two pathologists in OB/GYN Hospital. The original pathological reports after operation were reviewed. A total of 1264 endometrial cancer patients were identified and 206 patients with non-endometrioid histology were excluded. Among the remaining cases, 144 premenopausal patients 45 years of age or younger with endometrioid endometrial cancer were obtained through hospital paper charts and the electronic medical records system.

Statistical analysis

The differences between groups were evaluated using Chi-square test or Fisher's exact test for categorical variables. Multivariate regression models were developed to identify the risk factors for predicting ovarian involvements in endometrial cancer. Statistical analysis was performed using SPSS version 16.0. ROC curves were plotted with MedCalc software.

Results

General characteristics of the endometrioid endometrial cancer patients

A total of 144 young and premenopausal patients with endometrioid endometrial cancer were included in this study. Of these patients, six patients (4.2%) had coexisting ovarian malignancies. Metastatic ovaries were suspect during surgery in five patients, and were only diagnosed by the pathological examination in one patient. The general characteristics of these patients was shown in Table 1. The details of the 6 patients with ovarian involvement were listed in Table 2.

Identification of risk factors for ovarian involvement

Univariate analysis revealed that deeper myometrial invasion, positive lymph node metastasis, positive LVSI, and high histologic grade (G2-G3) were associated with ovarian involvement (Table 3). By multivariate analysis, only deep myometrial invasion was independent risk factors for ovarian involvement (Table 4). Consistently, the method using deep myometrial invasion alone was not significantly inferior to the method using combination of deep myometrial invasion, lymph node metastasis, LVSI, and histologic grade in identifying younger endometrial cancer patients with ovarian involvement (Fig. 1). The AUC were 0.85 (95% confidence interval [CI], 0.79–0.91) and 0.93 (95% confidence interval [CI], 0.88–0.97) for "deep myometiral invasion alone group" and "combination group" respectively.

Discussion

The incidence of endometrial cancer in young patients is increasing. Previous studies have indicated that approximately 14% of patients with endometrial cancer are premenopausal, and about 5% of cases are diagnosed before the age of 40 years [8,12,13]. In Korea, this incidence is higher. Namely, approximately 37% of patients diagnosed with endometrial cancer were premenopausal women and 10.4% of disease occurred in women aged 40 years or younger [6].

There are two major concerns with ovarian preservation in endometrial cancer. First, estrogen production from the ovaries may facilitate the growth of residual microscopic endometrial cancer, given that in vitro data have demonstrated that exogenous estrogen stimulation could increase endometrial cancer cell viability [14,15]. To date, this theoretical risk has not been observed clinically. Several studies have revealed that estrogen replacement therapy has little impact on recurrence or survival in patients with endometrial cancer [16–20]. Moreover, ovarian preservation reportedly does not adversely impact clinical outcomes in young patients with early-stage endometrial cancer [1,6–8]. The second concern of ovarian preservation is the presence of occult ovarian metastasis and synchronous primary ovarian tumors [21,22]. In a recent study of endometrioid endometrial cancer clinically confined to the uterus, 38 patients (5%) had either ovarian metastases or synchronous primary ovarian malignanr tumors [4]. Previous studies of a Chinese population have reported that the incidence of coexisting ovarian tumors in young patients with endometrial cancer ranged from 2.05% to 5.4% [1,23]. In our dataset, the incidence of ovarian involvement in younger premenopausal women with endometrioid endometrial cancer

Table 1
General characteristics of the 144 younger endometrioid endometrial cancer patients.

Characteristics	No. of patients	%
Age		
≤35	28	19.4%
>35	116	80.6%
Stage		
I	114	79.2%
II	14	9.7%
III	14	9.7%
IV	2	1.4%
Myometrial invasion		
<1/2	122	84.7%
≥1/2	22	15.3%
Longest tumor diameter		
<2 cm	100	69.4%
≥2 cm	44	30.6%
Lymphadenectomy		
Yes	99	68.8%
No	45	31.2%
Lymph node metastasis		
Yes	9	9.1%
No	90	90.9%
Cervical extension		
Yes	30	20.8%
No	114	79.2%
Histologic grade		
G1	109	75.7%
G2-G3	34	23.6%
N/A	1	0.7%
Lymph-vascular space invasion		
Yes	20	13.9%
No	123	85.4%
N/A	1	0.7%
Ovarian involvement		
Yes	6	4.2%
No	138	95.8%