European Journal of Obstetrics & Gynecology and Reproductive Biology 200 (2016) 113–116

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

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

Does synchronous endometrioid endometrial cancer have any prognostic effect on Stage I endometrioid ovarian cancer?

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ARTICLE INFO

Article history:
Received 1 December 2015
Received in revised form 7 January 2016
Accepted 10 March 2016

Keywords:
Ovarian cancer
Endometrial cancer
Synchronous cancers
Survival

ABSTRACT

Objective: To determine the effect of synchronous endometrial endometrioid cancer (SEEC) on the prognosis of patients with Stage 1 endometrioid ovarian cancer (EOC).
Study design: Clinicopathological data of cases with Stage 1 EOC from January 2000 to November 2013 were retrieved from the computerized database of Etlik Zubeyde Hanim Women's Health and Research Hospital. Of the 31 patients included in the study, 15 patients had primary synchronous endometrial and ovarian cancer (SEOC) (Group 1) and 16 patients had EOC alone (Group 2).
Results: Ovarian cancer substage and grade were compared between the two groups, and no significant differences were found. Most of the patients with SEEC had Grade 1 tumours ($n = 13$, 86.7%). In Group 1, nine (60.0%) patients had endometrial tumours with superficial myometrial invasion, and six (40.0%) patients had deep myometrial invasion. Median follow-up was 94 months. Ten-year disease-free survival rates were 92.9% for Group 1 and 84.6% for Group 2 ($p = 0.565$).
Conclusion: Patients with Stage 1 EOC have excellent long-term survival. The presence of SEEC does not influence the prognosis of patients with Stage 1 EOC, even in the presence of deep myometrial invasion.

Introduction

Ovarian cancer is the most lethal of all the gynaecological cancers [1]. Recent data have shown that ovarian cancer has two distinct histological types, and each type has a completely different pathogenesis [2]. Type 1 tumours arise from ovarian surface epithelium and mullerian inclusions, either from endosalpingiosis or invagination of the ovarian surface epithelium during repair of ovulation or implantation of cells from the endometrium. This process typically involves a relatively slow and multistep pathway, and accounts for many early-stage cancers such as endometrioid, clear cell, mucinous, and low-grade serous cancers. In contrast, the more common high-grade serous cancers (Type 2) have a phenotype that resembles the fallopian tube mucosa, and they commonly have p53 mutations. These tumours appear to develop rapidly, and are almost always at an advanced stage at presentation.

Endometrioid ovarian cancer (EOC) is a Type 1 tumour that has specific clinical and pathological features. It usually presents as early-stage disease and well-differentiated histology. Another distinct property of EOC is its frequent co-occurrence with synchronous endometrial tumours [3]. Synchronous endometrial and ovarian cancer (SEOC) is seen in approximately 10% of all women with ovarian cancer and 5% of all women with endometrial cancer [4]. Women with SEOC differ from women with primary endometrial or ovarian cancer alone, particularly in terms of prognosis. The prognostic effect of synchronous endometrial endometrioid cancer (SEEC) in the management of EOC has been a subject of debate in the literature. Therefore, this study sought to determine the prognostic effect of SEEC on Stage 1 EOC.

Materials and methods

After obtaining approval from the Institutional Review Board, the study population was identified by searching the gynaecologic oncology and pathology database. Thirty-one patients with Stage 1 EOC who underwent comprehensive surgical staging between January 2000 and November 2013 were included in the study. All patients underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and bilateral pelvic and

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http://dx.doi.org/10.1016/j.ejogrb.2016.03.010
0301-2115/

para-aortic lymph node dissection. The patients were divided into two groups based on the presence of SEEC in the uterus. For the elimination of confounding factors and to ensure homogeneity between the groups, only early-stage endometrioid uterine and ovarian cancers that were diagnosed simultaneously were chosen. Other pathological subgroups, patients with advanced-stage cancers and women who had undergone fertility-sparing surgery were excluded. Histopathological evaluation to differentiate synchronous carcinoma from metastatic carcinoma was based on the criteria of the World Health Organization [5] and the criteria of Scully et al. [6]. Pathological information, including histology, tumour size, bilaterality, International Federation of Gynecology and Obstetrics (FIGO) grade, depth of myometrial invasion, lymphovascular space invasion, and number of lymph nodes, was collected from surgical pathology reports. All patients were staged using FIGO 2009 criteria for ovarian cancer and endometrial cancer. Information regarding clinical presentation, laboratory values and treatment was retrieved from the patients' medical records. Patient follow-up commenced when the first cancer diagnosis was made, and terminated when the patient died or on the last contact with the outpatient clinic or via telephone (March 2015). All women underwent initial evaluation and surgical staging at the authors' gynaecologic oncology clinic by the same surgical team. Pathological specimens were examined by the same gynaecopathologists, in accordance with the criteria of Scully et al. [6], and the diagnosis was made simultaneously. The adjuvant therapy modality was adjusted based on the individual patient's needs according to surgical staging and the study protocol by the same gynaecologic oncology team after the final pathology report. As only one patient died due to disease during the follow-up period, it was not possible to provide overall survival data. Instead, disease-free survival was taken as the main conclusion of the study. Disease-free survival was defined as the interval between the date of diagnosis and the date of disease progression or death from any cause, or last contact with the patient. Statistical Package for the Social Sciences Version 17.0 (IBM Corp., Armonk, NY, USA) was used for data management and statistical analysis. The Kaplan–Meier method was used to assess survival outcomes.

Results

Fifteen women with FIGO Stage 1 EOC with SEEC were classed as Group 1 and 16 patients who had FIGO Stage 1 EOC alone were classed as Group 2. The mean age of all patients was 48.2 [standard deviation (SD) 8.6] years, the mean age of patients in Group 1 was 49 (SD 8.0), and the mean age of patients in Group 2 was 47.6 (SD 9.2) years. The two groups were similar in terms of age ($p = 0.685$). None of the patients had a family history of colon, gastric or breast cancer, and no secondary malignancies were detected during the follow-up period. The main presenting symptoms in Group 1 were abdominal swelling ($n = 5$), postmenopausal bleeding ($n = 4$) and menorrhagia ($n = 4$). Two of the patients in Group 1 had no major symptoms. The main presenting symptom in Group 2 was a pelvic mass ($n = 15$), and only one patient in Group 2 had no symptoms at all. There were five (33.3%) postmenopausal women in Group 1 and seven (43.7%) postmenopausal women in Group 2. Before surgery, nine patients in Group 1 were diagnosed with endometrioid carcinoma of the uterus following probe curettage.

Table 1 shows the histopathological characteristics and FIGO stages of endometrial and ovarian tumours of the patients in Groups 1 and 2. Three patients with positive peritoneal cytology in Group 1 were accepted as Stage 1c ovarian cancer as none of them had uterine invasion of more than half of the myometrium. The two groups were compared in terms of ovarian cancer substage and grade, and no significant differences were found ($p = 0.557$ and 0.885, respectively). The mean ovarian tumour size was significantly larger in Group 2 compared with Group 1 [15.8 (SD 7.7) cm vs 7.6 (5.4) cm, $p = 0.005$]. The mean CA-125 level was 71.3 (SD 85.6) mU/l and 629.1 (SD 1054) mU/l for Groups 1 and 2, respectively ($p = 0.081$). The mean number of lymph nodes extracted during surgery was 57.4 (SD 17.6) and 71.0 (SD 30.1) for Groups 1 and 2, respectively ($p = 0.192$). Seven (46.7%) patients in Group 1 received adjuvant therapy; of these, five (33.3%) patients had chemotherapy and two (13.3%) patients had vaginal cuff brachytherapy. Six (37.5%) patients in Group 2 received adjuvant chemotherapy.

Table 1
Characteristics of tumours in Groups 1 and 2.

	Endometrioid endometrial cancer (Group 1)	Endometrioid ovarian cancer (Group 1)	Endometrioid ovarian cancer (Group 2)
	n	*n*	*n*
2009 FIGO stage			
Ia	9	11	9
Ib	6	1	1
Ic	–	3	6
Histological grade			
1	13	12	12
2	1	2	2
3	1	1	2
Myometrial invasion			
<1/2	9	–	–
≥1/2	6	–	–
Lymphovascular space invasion			
Negative	1	–	–
Positive	14	–	–
Peritoneal cytology			
Negative	15	12	11
Positive	–	3	5
Largest tumour diameter			
	≤2 cm (*n* = 5) >2 cm (*n* = 6)	≤10 cm (*n* = 9) >10 cm (*n* = 3)	≤10 cm (*n* = 4) >10 cm (*n* = 10)
Unknown	4	3	2

FIGO, International Federation of Gynecology and Obstetrics.

The 10-year disease-free survival rates were 92.9% for Group 1 and 84.6% for Group 2. As survival rates for Stage 1 OEC and SEOC alone have been reported in previous publications, survival data related to EOC and EOC with SEEC are given in Table 2 [3,7–9]. Survival data were only retrieved from studies related to pure endometrioid histology. During the follow-up period, three recurrences were detected: one in Group 1 and two in Group 2. All three patients underwent surgery and subsequently received chemotherapy. Only one patient died due to disease, 103 months from the time of diagnosis.

Discussion

Approximately 1–2% of all women with gynaecological cancers have two or more simultaneous independent primary tumours involving the female genital tract. Some are coincidental tumours of completely different histological types, and each of them requires treatment on its own merit. However, synchronous tumours of similar or identical histology occur, and this is almost unique to the female genital tract [10]. It is important to distinguish between low-stage multiple primary tumours and tumours that have metastasized from one site to another due to completely different prognostic and management implications. Pathologists including Scully et al. [6] have delineated histological criteria to aid pathologists when evaluating these tumours. In the present study, the pathologists used these criteria to discriminate between double primaries and metastatic tumours, and no molecular or genetic analysis was undertaken. Considering the long follow-up period in this study and the length of survival, the validity of these pathological criteria