Clinical Presentation of Endometrioid Epithelial Ovarian Cancer with Concurrent Endometriosis: 
A Multicenter Retrospective Study

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Chi Heum Cho3, Sang-Yoon Park1, and Joo-Hyun Nam2

Abstract

Background: Endometrioid epithelial ovarian cancer (EOC) is frequently diagnosed in conjunction with 
endometriosis and is suggested to arise during the process of endometriosis. This study evaluates the clinical 
manifestations, including endometriosis-related symptoms and their relationships according to the coexis-
tence of endometriosis.

Methods: Using medical records, a retrospective analysis was conducted on 221 patients treated for EEOC 
at four tertiary educational hospitals between 2000 and 2008. The initial presenting symptoms, particularly 
those related to endometriosis, were examined in relation to the coexistence of endometriosis or other clinical 
variables.

Results: Endometriosis was identified in 82 (37.1%) of the 221 patients with EEOC. The most common 
symptoms were pelvic pain followed by gastrointestinal symptoms, palpable mass, abdominal distension, 
vaginal bleeding, and newly developed or exacerbated dysmenorrhea (18.1%) and dyspareunia (13.6%). Not-
tably, dysmenorrhea and dyspareunia were frequently observed in patients with endometriosis. Among 210 
patients identified with pretreatment serum CA-125, 54 (25.7%) displayed normal CA-125 levels (<35 units/
ml) and 23.3% and 29.9% of patients without and with endometriosis had normal CA-125 levels, respectively 
(P = 0.381). Additionally, 32.6% of the patients with early-stage EEOC displayed normal CA-125 levels.

Conclusions: In this large series of patients with EEOC, the main presenting symptoms were pelvic 
pain followed by gastrointestinal symptoms, palpable mass, abdominal distension, vaginal bleeding, 
and newly developed or exacerbated dysmenorrhea and dyspareunia. Dyspareunia and dysmenorrhea 
were more frequently detected in patients with endometriosis. Normal CA-125 levels cannot be applied 
as a marker to exclude EOC, particularly at the early stages. Cancer Epidemiol Biomarkers Prev; 19(2); 398–
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Introduction

Ovarian carcinoma is the leading cause of death from 
gynecologic malignancies. Annually, new diagnoses and 
mortalities from ovarian cancer are estimated at 21,650 
and 15,520, respectively, in the United States alone (1).

Although considerable research efforts have been direct-
ed toward improving treatment outcomes and survival 
in patients with ovarian cancer, effective screening tools 
with satisfactory sensitivity and false-positive rates have 
not been developed (2). The identification of acceptable 
screening tools to achieve a minimum positive predictive 
value of 10% and a sensitivity of 99.6% for screening the 
general population of postmenopausal women is a signif-
icant challenge (2, 3).

Ovarian cancer has diverse clinical and surgical mani-
festations based on the corresponding histology (4-8). En-
dometrioid epithelial ovarian cancer (EEOC) and ovarian 
clear cell carcinoma (OCCC) have some shared as well as 
some distinct risk factors related to endometriosis, and 
therefore, separate consideration of these ovarian cancers 
is suggested (9). The symptoms of ovarian cancer, such as 
abdominal swelling or pain, are generally vague (10). 
Logically, we can assume that endometriosis-related 
symptoms are more frequent in ovarian cancer–related 
endometriosis such as EEOC or OCCC. In an earlier 
study, we reported a high incidence of endometriosis-
related symptoms in patients with OCCC (11).
Although several reports support the theory that EEOC and OCCC arise in endometriosis (12-15), several differences in carcinogenesis and clinical manifestations between EEOC and OCCC have been suggested (7, 9). Endometrial cancer/hyperplasia is more frequently diagnosed with EEOC (9.1–38.6%) as a synchronous tumor compared with other epithelial ovarian cancers, including OCCC (16-18). The purpose of this study was to investigate the prevalence of the coexistence of endometriosis in patients with EEOC and their related clinical manifestations.

Materials and Methods

The study subjects consisted of 221 patients treated for EEOC between 2000 and 2008 at four tertiary educational hospitals in Korea. Data were obtained retrospectively from individual medical records. Histologic classification of ovarian cancer was based on the WHO system (19). Each case was staged according to the current International Federation of Gynecology and Obstetrics staging system (20). The presence of endometriosis was determined from H&E-stained sections of resected specimens. The coexistence of endometriosis was diagnosed by confirming the presence of ectopic endometrial glands or stroma. Age, parity, body mass index, previous diagnosis of endometriosis or infertility, age at menarche, menopausal status, presenting symptoms, International Federation of Gynecology and Obstetrics stage, serum CA-125 level, treatments for endometriosis (such as gonadotropin-releasing hormone agonists, danazol, and oral contraceptives), and the coexistence of other gynecologic diseases were retrospectively reviewed.

The distribution of patient characteristics was presented as median (range) for continuous variables and frequency (%) for categorical variables. The t test and one-way ANOVA were used for analysis of continuous variables, and Pearson’s χ² test was applied for categorical variables. All reported P values are two-sided, and the results were considered significant at P < 0.05. Statistical analyses were done using Stata 10 for Windows package (Stata Corp.).

Results

Clinical characteristics and presenting symptoms were statistically comparable among the individual hospitals. The clinical features of the 221 patients with EEOC are summarized in Table 1. The median age was 47 years. Overall, age was significantly higher in patients without endometriosis (50.0 versus 43.8 years; P < 0.001). Body mass index was also elevated in patients without endometriosis (23.8 versus 22.0 kg/m²; P = 0.007). Patients with endometriosis were more commonly diagnosed at the early stages (57.6% versus 76.8%; P = 0.004). Thirteen of the 82 patients (15.9%) with endometriosis had been previously diagnosed with endometriosis. On the other hand, only 1 of the 142 patients without endometriosis had a previous diagnosis. Among these 14 patients, 8 underwent laparoscopic operations and had a pathologic diagnosis. As expected, the rate of infertility was higher (5.0% versus 14.6%; P = 0.014) and the frequency of pregnancy and delivery was lower in patients with endometriosis. Moreover, endocrinological treatments, such as gonadotropin-releasing hormone agonists (0% versus 61.1%; P = 0.003) and oral contraceptives (6.5% versus 15.9%; P = 0.024), were more frequently used in patients with endometriosis. Only one patient without endometriosis used danazol. Age at menarche was not statistically different between the two groups. Climacteric women were more commonly classified into patient groups without endometriosis (50.4% versus 28.0%; P = 0.001). Approximately 10.9% (24 of 221) of the patients displayed synchronous endometrial cancer/hyperplasia. Distribution of endometrial cancer among the two groups was not statistically different (P = 0.348).

Preoperative CA-125 levels were measured in 210 patients (133 without endometriosis and 77 with endometriosis). The serum CA-125 level was not statistically different between the two groups (P = 0.381). A higher number of patients with early-stage EEOC contained CA-125 within the reference range compared with those with advanced-stage EEOC (32.6% (44 of 135) versus 13.3% (10 of 75); P = 0.002; data not shown). The serum CA-125 level was normal in 31 of 133 (23.3%) patients without endometriosis and in 23 of 77 (29.9%) patients with endometriosis (Table 1). Serum CA-125 was statistically different (P = 0.001) in patient groups according to the stage and coexistence of endometriosis (Table 2). In post hoc analyses, patients displaying advanced-stage EEOC without endometriosis had higher CA-125 levels compared with those diagnosed with early-stage EEOC without endometriosis (P = 0.002) and those with early-stage EEOC with endometriosis (P = 0.003). There was no difference in CA-125 levels among patients with and without endometriosis and advanced-stage EEOC (P = 0.570).

The main symptoms at initial presentation of the 221 patients with EEOC are shown in Table 3. The most common symptoms were pelvic pain (52.9%) followed by gastrointestinal symptoms (41.6%), palpable mass (40.3%), abdominal distension (39.4%), vaginal bleeding (19.9%), and newly developed or exacerbated endometriosis-related symptoms [dysmenorrhea (18.1%) and dyspareunia (13.6%)]. Incidental diagnosis was made in 13.1% of patients, and less than 10% displayed upper abdominal pain. The presenting symptoms appeared 1 to 4 months before patients were diagnosed with EEOC. The most long-standing symptoms were newly developed or exacerbated dyspareunia or dysmenorrhea (4 months). Vague symptoms, such as pelvic pain, gastrointestinal symptoms, and upper abdominal pain, appeared an average of 3 months before EEOC diagnosis. Vaginal bleeding was evident at a median of 2.5 months before EEOC...
diagnosis. The interval from manifestation to EEOC diagnosis was the shortest in the case of unusual symptoms such as palpable mass and abdominal distension. Symptoms did not differ statistically between the two patient groups based on the coexistence of endometriosis, except those related to endometriosis, such as newly developed or exacerbated dysmenorrhea and dyspareunia. Newly developed or exacerbated dysmenorrhea (12.2% versus 28.0%; \(P = 0.003\)) and dyspareunia (9.4% versus 20.7%; \(P = 0.017\)) were more frequent in patients with endometriosis. Upon evaluation of symptoms according to stage, pelvic pain (47.6% versus 62.8%; \(P = 0.030\)), gastrointestinal symptoms (31.5% versus 60.3%; \(P < 0.001\)), abdominal distension (27.3% versus 61.5%; \(P < 0.001\)), and upper abdominal pain (3.5% versus 15.4%; \(P = 0.002\)) were more common in patients with advanced-stage EEOC. Other symptoms, including newly developed or exacerbated dysmenorrhea and dyspareunia, were not significantly different between the two patient groups.

**Discussion**

In the present study, 37.1% (82 of 221) of patients presented with coexisting endometriosis and EEOC. This result is similar to previous reports (Table 4), including all stages of EEOC (28.4%; range, 13.6-42.9%; refs. 17, 18, 21-25). Endometriosis is frequently identified at all stages of EEOC (5.3%; range, 2.01-26.8%) compared with other epithelial ovarian cancers (21, 23, 24, 26). As depicted in Table 1, endometriosis was more commonly detected in early-stage EEOC (44.1%, 63 of 143), consistent with earlier

### Table 1. Clinical characteristics of patients with EEOC based on the coexistence of endometriosis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>EEOC ((n = 221))</th>
<th>EEOC without endometriosis ((n = 139))</th>
<th>EEOC with endometriosis ((n = 82))</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y), median (range)</td>
<td>47.0 (22-78)</td>
<td>50.0 (22-78)</td>
<td>43.8 (22-78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI, median (kg/m(^2))</td>
<td>23.1 (16.1-37.1)</td>
<td>23.8 (17.2-37.1)</td>
<td>22.0 (16.1-32.9)</td>
<td>0.007</td>
</tr>
<tr>
<td>FIGO stage, (n) (%)</td>
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<td></td>
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</tr>
<tr>
<td>I + II</td>
<td>143 (64.7)</td>
<td>80 (57.6)</td>
<td>63 (76.8)</td>
<td>0.004</td>
</tr>
<tr>
<td>III + IV</td>
<td>78 (35.3)</td>
<td>59 (42.4)</td>
<td>19 (23.2)</td>
<td></td>
</tr>
<tr>
<td>Previous diagnosis of endometriosis, (n) (%)</td>
<td>14 (6.3)</td>
<td>1 (0.7)</td>
<td>13 (15.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age at menarche, median (y)</td>
<td>13.0 (9.0-18.0)</td>
<td>13.0 (9.0-18.0)</td>
<td>13.0 (10.0-16.0)</td>
<td>0.470</td>
</tr>
<tr>
<td>No. of deliveries, median (range)</td>
<td>2 (0-7)</td>
<td>2 (0-7)</td>
<td>2 (0-5)</td>
<td>0.001</td>
</tr>
<tr>
<td>No. of pregnancies, median (range)</td>
<td>3 (0-12)</td>
<td>3 (0-12)</td>
<td>2 (0-7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Infertility, (n) (%)</td>
<td>19 (8.6)</td>
<td>7 (5.0)</td>
<td>12 (14.6)</td>
<td>0.014</td>
</tr>
<tr>
<td>Menopausal state, (n) (%)</td>
<td>93 (42.1)</td>
<td>70 (50.4)</td>
<td>23 (28.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Use of GnRH agonist, (n) (%)</td>
<td>5 (2.3)</td>
<td>0</td>
<td>5 (6.1)</td>
<td>0.003</td>
</tr>
<tr>
<td>Use of danazol, (n) (%)</td>
<td>1 (0.5)</td>
<td>1 (0.7)</td>
<td>0</td>
<td>0.441</td>
</tr>
<tr>
<td>Use of OCs &gt;3 mo, (n) (%)</td>
<td>22 (10.0)</td>
<td>9 (6.5)</td>
<td>13 (15.9)</td>
<td>0.024</td>
</tr>
<tr>
<td>Coexistences of endometrial cancer/ hyperplasia, (n) (%)</td>
<td>24 (10.9)</td>
<td>13 (9.4)</td>
<td>11 (13.4)</td>
<td>0.348</td>
</tr>
<tr>
<td>CA-125* (units/mL), median</td>
<td>102.5 (5.0-17,553)</td>
<td>128.0 (5.0-17,553)</td>
<td>69.0 (5.5-15,600)</td>
<td>0.263</td>
</tr>
<tr>
<td>CA-125* &lt;35 units/mL, (n) (%)</td>
<td>54 (25.7)</td>
<td>31 (23.3)</td>
<td>23 (29.9)</td>
<td>0.381</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; GnRH, gonadotropin-releasing hormone; OCs, oral contraceptives.

*CA-125 levels were measured in 210 patients, specifically in 133 patients without endometriosis and in 77 patients with endometriosis.

### Table 2. Serum CA-125 level based on the coexistence of endometriosis and stages in patients with EEOC

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum CA-125</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EEOC ((n = 210))</td>
<td>EEOC without endometriosis ((n = 133))</td>
</tr>
<tr>
<td>I + II</td>
<td>60.1 (5.5-3,610.0)</td>
<td>60.1 (5.8-3,610.0)</td>
</tr>
<tr>
<td>III + IV</td>
<td>342.0 (5.0-17,553.0)</td>
<td>379.0 (5.0-17,553.0)</td>
</tr>
</tbody>
</table>
Endometriosis and Endometrioid Ovarian Cancer

studies (16, 27). Our findings support the hypothesis that EEOC arises from endometriosis of the ovary (7, 12, 13, 25).

In 2004, Goff et al. (28) reported that ovarian cancer is not a silent disease, and severe and frequent symptoms of more recent onset warrant further diagnostic investigation in a prospective case-control study. More than two thirds of patients with ovarian cancer had recurring symptoms (median number of two symptoms), including back pain (45%), fatigue (34%), bloating (27%), constipation (24%), abdominal pain (22%), and urinary symptoms (16%; ref. 28). In 2005, Smith and colleagues investigated the target symptoms for ovarian cancer using records from the Surveillance, Epidemiology and End Results database linked to the Medicare claims record in California. The group reported that patients with ovarian cancer display target symptoms, such as abdominal swelling and pain, more than 6 months before diagnosis (10). The authors concluded that the evaluation of women with unexplained "target symptoms" should include pelvic imaging and/or measurement of CA-125 levels to facilitate earlier diagnosis of ovarian cancer (10). Therefore, investigation of symptoms in conjunction with other screening tools may yield more cost-effective screening tools for ovarian cancer. However, it must be considered that the target symptoms in the study are relatively vague, such as abdominal pain (30.6%), abdominal swelling (16.5%), gastrointestinal symptoms (8.4%), and pelvic pain (5.4%; ref. 10).

Endometriosis is frequently diagnosed along with EEOC and OCCC. However, the symptoms specific for endometriosis-associated epithelial ovarian cancer remain to be established (9). Recently, we reported unique symptoms including hard palpable mass (32.6%) and newly developed or exacerbated dysmenorrhea (32.6%) in patients with OCCC (11). In the present study, pelvic pain (52.9%) was the most common indication in patients with EEOC followed by gastrointestinal symptoms (41.6%), palpable mass (40.3%), abdominal distension (39.4%), vaginal bleeding (19.9%), and upper abdominal pain (7.7%). The incidence of vaginal bleeding was relatively high (19.9%), considering that 10.9% of patients with EEOC have coexisting endometrial hyperplasia or cancer. Newly developed or exacerbated endometriosis-related symptoms [dysmenorrhea (18.1%) and dyspareunia (13.6%)] were not the main symptoms in patients with EEOC, particularly those without endometriosis. The presenting symptoms are distinct between not only EEOC and ovarian cancer but also EEOC and OCCC in terms of pattern and frequency (10, 11). Although endometriosis is suggested as the common origin of EEOC and OCCC, the differences between the two ovarian carcinoma types may be attributed to distinct molecular pathologies and clinical manifestations (7, 9, 29-31). The symptoms of ovarian cancer have thus far been described as silent or vague. However, these authors propose "different symptoms by different histologies of cancers in the same ovary." These findings should be helpful in establishing programs for the early detection and screening of ovarian cancers.

Serum CA-125 is commonly used in routine clinical practice and is elevated in the preclinical asymptomatic phase of the disease, with raised levels detected in 25% of serum samples collected 5 years before ovarian cancer diagnosis (32). Preoperative CA-125 can be used to predict severe endometriosis and malignant disease of the ovary (33, 34). In general, the sensitivity of CA-125 in predicting ovarian cancer is 81% to 91% (35-38). We assumed a higher incidence of elevated serum CA-125 in patients with EEOC because a significant number of patients displayed

### Table 3. Presenting symptoms of patients with EEOC based on the coexistence of endometriosis and stage

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>EEOC (n = 221)</th>
<th>Interval from symptoms to diagnosis of EEOC (mo), median (range)</th>
<th>Coexistence of endometriosis</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No (n = 139)</td>
<td>Early (n = 143)</td>
</tr>
<tr>
<td>Pelvic pain</td>
<td>117 (52.9%)</td>
<td>3.0 (0.1-60.0)</td>
<td>73 (52.5%)</td>
<td>88 (47.6%)</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>92 (41.6%)</td>
<td>3.0 (0.3-60.0)</td>
<td>58 (41.7%)</td>
<td>49 (28.8%)</td>
</tr>
<tr>
<td>Palpable mass</td>
<td>89 (40.3%)</td>
<td>1.0 (0.3-12.0)</td>
<td>54 (38.8%)</td>
<td>56 (39.2%)</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>87 (39.4%)</td>
<td>1.0 (0.3-5.0)</td>
<td>57 (41.0%)</td>
<td>39 (27.3%)</td>
</tr>
<tr>
<td>Vaginal bleeding</td>
<td>44 (19.9%)</td>
<td>2.5 (0.3-20.0)</td>
<td>30 (21.6%)</td>
<td>27 (18.9%)</td>
</tr>
<tr>
<td>Dysmenorrhea*</td>
<td>40 (18.1%)</td>
<td>4.0 (1.0-60.0)</td>
<td>17 (12.2%)</td>
<td>26 (14.7%)</td>
</tr>
<tr>
<td>Dyspareunia*</td>
<td>30 (13.6%)</td>
<td>4.0 (1.0-24.0)</td>
<td>13 (9.4%)</td>
<td>16 (11.2%)</td>
</tr>
<tr>
<td>Incidental diagnosis</td>
<td>29 (13.1%)</td>
<td>—</td>
<td>15 (10.8%)</td>
<td>23 (16.1%)</td>
</tr>
<tr>
<td>Upper abdominal pain</td>
<td>17 (7.7%)</td>
<td>3.0 (0.3-36.0)</td>
<td>11 (7.9%)</td>
<td>5 (3.5%)</td>
</tr>
</tbody>
</table>

NOTE: Fisher’s exact test.
*Newly developed or exacerbated.

Pelvic pain (52.9%), 3.0 (0.1-60.0) 73 (52.5%) 44 (53.7%) 0.870 68 (47.6%) 49 (62.8%) 0.030
Gastrointestinal symptoms 92 (41.6%) 3.0 (0.3-60.0) 58 (41.7%) 34 (41.5%) 0.969 45 (31.5%) 47 (60.3%) <0.001
Palpable mass 89 (40.3%) 1.0 (0.3-12.0) 54 (38.8%) 35 (42.7%) 0.398 56 (39.2%) 33 (42.3%) 0.669
Abdominal distension 87 (39.4%) 1.0 (0.3-5.0) 57 (41.0%) 30 (36.6%) 0.516 39 (27.3%) 48 (61.5%) <0.001
Vaginal bleeding 44 (19.9%) 2.5 (0.3-20.0) 30 (21.6%) 14 (17.1%) 0.417 27 (18.9%) 17 (21.8%) 0.604
Dysmenorrhea* 40 (18.1%) 4.0 (1.0-60.0) 17 (12.2%) 23 (28.0%) 0.003 26 (18.2%) 14 (17.9%) 0.966
Dyspareunia* 30 (13.6%) 4.0 (1.0-24.0) 13 (9.4%) 17 (20.7%) 0.017 16 (11.2%) 14 (17.9%) 0.161
Incidental diagnosis 29 (13.1%) — 15 (10.8%) 14 (17.1%) 0.182 23 (16.1%) 6 (7.7%) 0.067
Upper abdominal pain 17 (7.7%) 3.0 (0.3-36.0) 11 (7.9%) 6 (7.3%) 0.872 5 (3.5%) 12 (15.4%) 0.002
comorbidity with endometriosis. Contrary to our predictions, approximately a quarter of patients displayed CA-125 levels within the reference range in the present study. Similarly, the CA-125 level was normal in about a third of patients with OCCC (11). The higher incidence of normal serum CA-125 seems to be associated with the higher proportion of early-stage disease in patients with EEOC or OCCC. Therefore, we should bear in mind that normal levels of CA-125 cannot be effectively used as a marker to exclude ovarian cancer in these patients.

Endometriosis is a common disease (7-15%) in all women of reproductive age (39). The incidence of ovarian cancer (0.72-3.92%) and EEOC (0.25-0.77%) in patients with endometriosis is higher than that in the general population (Table 4). Endometriosis is a risk factor for cancer overall [relative risk (RR), 1.04-1.2], breast cancer (RR, 1.3), ovarian cancer (RR, 1.43-1.9), endocrine tumor (RR, 1.36), hematologic malignancies (RR, 1.4), non-Hodgkin lymphoma (RR, 1.24), and brain tumor (RR, 1.22; refs. 15, 40). In ovarian cancer, EEOC (RR, 2.2-2.53) and OCCC (RR, 3.0-3.37) are more high-risk histologies compared with other epithelial ovarian cancers (9, 26). This might be explained by the shared pathophysiology between endometriosis and cancer, such as immune alterations and hormonal imbalance (14).

There are two reasons for the higher incidence of EEOC and OCCC in patients with endometriosis. First, direct transformation, a transition from benign to malignant epithelium, is often evident (17, 22, 25). Second, iron released by hemorrhage in the endometrial cyst induces

<table>
<thead>
<tr>
<th>Table 4. Literature review</th>
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<tr>
<td><strong>(A) Prevalence of ovarian cancer or EEOC in patients with endometriosis</strong></td>
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<tr>
<td>Author</td>
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<tr>
<td>Brinton</td>
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<td>Kobayashi</td>
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<table>
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<tr>
<th><strong>(B) Prevalence of coexisting endometriosis in patients with EEOC</strong></th>
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<tr>
<td>Author</td>
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<tr>
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<tr>
<td>Valenzuela</td>
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<td>Jimbo</td>
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Abbreviations: EC, endometrial cancer; FU, follow-up; OC, ovarian cancer; SCSEOC, Shizuoka Cohort Study on Endometriosis and Ovarian Cancer; TFBTME, transition from benign to malignant epithelium.
persistent oxidative stress and frequent DNA mutations (41). In the current study, 37.1% of patients with EEOC displayed coexisting endometriosis in a routine pathologic examination. We believe that endometriosis will be more frequently identified in EEOC cases in a prospective setting (11).

Fourteen patients in our study had a previous history of endometriosis, most displaying coexisting endometriosis. However, the majority of patients diagnosed with endometriosis before EEOC detection had moderate to severe endometriosis requiring surgical management. Eight of the 14 patients previously diagnosed with endometriosis were subjected to laparoscopic procedures. Only six patients were diagnosed based on clinical manifestations. The symptoms of endometriosis seem different from subclinical to those requiring surgical management (42). Therefore, a significant proportion of patients with mild symptoms might not be diagnosed before the diagnosis of EEOC.

Selection bias and other confounders found in retrospective studies were other possibilities, and we made an effort to minimize these as much as possible. Symptoms were collected based on a retrospective review of medical charts. Possible missing data may suggest an underestimation of some of the parameters of interest. However, our data revealed consistent and characteristic symptoms in patients with EEOC from large databases from four training hospitals. A prospective study might reveal a higher incidence of symptoms suggestive of EEOC. This issue will be addressed by the Korean Outcome Research and Analysis of Gynecologic malignancy, which has collected prospective data similar to the Surveillance, Epidemiology, and End Results program in the United States.

In conclusion, the presenting symptoms in patients with EEOC are pelvic pain followed by gastrointestinal symptoms, palpable mass, abdominal distension, vaginal bleeding, endometriosis-related symptoms, and upper abdominal pain. Newly developed or exacerbated endometriosis-related symptoms, such as dysmenorrhea and dyspareunia, were frequently identified in patients with endometriosis. Approximately one quarter of patients with EEOC and one third of patients with early-stage EEOC had normal CA-125 levels. Therefore, normal levels of CA-125 do not seem effective as a marker to exclude EEOC, particularly at the early stages.

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No potential conflicts of interest were disclosed.

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**References**

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