ORIGINAL ARTICLE: ENDOMETRIOSIS

Development of ovarian cancer after excision of endometrioma

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Objective: To determine the prevalence rate of subsequent development of ovarian cancer after excision of endometrioma.
Design: Retrospective cross-sectional study.
Setting: University hospital.
Patient(S): A total of 485 women with endometrioma.
Intervention(s): Excisions of endometrioma were performed between 1995 and 2004. Data were collected from medical records in 2013.
Main Outcome Measure(s): Age, revised American Society for Reproductive Medicine score, cyst diameter, follow-up periods, endometrioma recurrence, and development of ovarian cancer.
Result(s): Recurrence of endometrioma was recorded in 121 patients (24.9% of the entire cohort), and 4 patients (0.8% of the entire cohort) developed ovarian cancer. All ovarian cancers developed from a recurrent endometrioma (3.3% of patients who experienced recurrence). Recurrence of endometrioma was significantly associated with ovarian cancer development.
Conclusion(s): Ovarian cancers can develop after excision of endometrioma and are more likely to arise from recurrent endometrioma. Special care such as rigorous follow-up should be practiced to manage patients who experience recurrence of endometrioma. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Cancer, cystectomy, endometriosis, ovary

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Endometriosis is defined as the presence of endometrial-like tissue external to the uterine cavity. It is a chronic inflammatory condition that affects women in their reproductive years and is associated with pelvic pain and infertility (1). Ovarian endometrioma is the most common form of endometriosis and accounts for 55% of this disorder (2). Regardless of its symptoms, surgery is frequently selected to treat endometrioma because medical treatment alone is often inadequate. Excision of endometrioma (cystectomy) has been shown to reduce pain and enhance fertility (3). In addition, cystectomies are preferred over oophorectomies because most women with endometrioma are of reproductive age.

Although endometriosis is considered to be a benign condition, malignant transformation of endometriosis was reported as early as 1925 by John Sampson (4). Endometriotic implants are observed throughout the pelvis; however, endometriosis-associated malignancies typically arise from endometriomas. Epidemiologic, histopathologic, and molecular data suggest that endometrioma may serve as precursor lesions for specific subtypes of ovarian cancer (5).

Several studies have demonstrated the occurrence of malignancies among patients with endometriosis; however, most studies used either self-reporting (6) or the national register (7, 8), and the impact of the therapeutic methods on subsequent cancer development was often not reported or fully understood. The aim of this study was to investigate whether the excision of endometrioma affects the subsequent development of ovarian cancer. We also investigated factors that are associated with the

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development of cancer after excision of endometrioma. For this purpose we conducted a retrospective study using medical records from patients who underwent laparoscopic excision of endometrioma at a single institute.

MATERIALS AND METHODS

Sample

A total of 485 patients underwent laparoscopic excision of endometrioma at the University of Tokyo Hospital between 1995 and 2004, and all these patients were included in the present study. The minimal cut-off for diameter, as an indication for surgery in our institute, is 4 cm, and all patients in the present study met this indication. The patients were consecutively followed up, and their records were retrospectively studied until June 2013. Four patients who were diagnosed with ovarian cancer during the follow-up period were studied in detail. The study protocol was approved by the University of Tokyo's review board. All patients gave informed consent to participate in the research before surgery. The patients' clinical characteristics are summarized in Table 1.

Surgery

Laparoscopic excisions of endometrioma were performed as previously described (9, 10). After the ovary was freed from any adhesion, the capsule of the cyst was completely stripped away from the normal ovarian tissue. Endometriotic peritoneal implants were either excised using scissors or coagulated using bipolar electro-coagulation.

Diagnosis of Recurrence and Ovarian Cancer

In the postoperative period, all patients were advised to follow up every 3–6 months, and transvaginal ultrasonography was performed at each visit. The diagnosis of endometrioma recurrence was made as described in our previous study (9, 10). Recurrence is defined as the presence of cysts with a typical aspect detected by transvaginal ultrasonography (11) and a cyst diameter >2 cm. A diagnosis of recurrence was made when the cyst did not disappear after several successive examinations. We did not have any well-defined indication for the second surgery. In addition, all recurrent cysts were individually managed on the basis of, for example, their size and patient's age. The diagnosis of ovarian cancer was made by pathologic evaluation of the specimen that was removed by the surgery.

Statistical Analysis

Patient characteristics (age at the first laparoscopy, infertility, preoperative pain, previous medical treatment for endometriosis, medical treatment before laparoscopy, presence of adenomyosis, presence of uterine myoma, revised American Society for Reproductive Medicine [rASRM] score, bilateral/unilateral involvement, postoperative pain, postoperative fertility treatment, postoperative pregnancy, and recurrence of endometrioma) between the two cohorts—cancer-free patients and patients who developed carcinoma—were compared using the Mann-Whitney *U* test and Fisher's exact test, followed by a multivariate regression analysis. A survival curve, to illustrate the period after laparoscopic excision of endometrioma and the occurrence of ovarian cancer development, was plotted using a Kaplan-Meier plot. Statistical analyses were performed using Ekuseru-Toukei 2008 software (Social Survey Research Information). A P value of $<.05$ was considered statistically significant.

TABLE 1

Clinical details for 485 patients.

Factor	n (%)
Patient background at laparoscopy	
Age (y)	
<20	1 (0.2)
20–29	128 (26.4)
30–39	314 (64.7)
>40	42 (8.7)
Mean ± SD	32.8 ± 5.1
Gravida	
0	369 (76.1)
1	65 (13.4)
2	40 (8.2)
3 or more	11 (2.3)
Parity	
0	411 (84.7)
1	43 (8.9)
2	26 (5.4)
3 or more	5 (1.0)
Infertility	186 (38.4)
Preoperative pain	383 (79.0)
History of medical treatment for endometriosis	
No	327 (67.4)
Yes	158 (32.6)
GnRHa	141 (29.1)
Danazol	30 (6.2)
OC	8 (1.6)
Medical treatment before laparoscopy	
No	411 (84.7)
Yes	74 (15.3)
GnRHa	64 (13.2)
Danazol	6 (1.2)
OC/progestin	4 (0.8)
Laparoscopic findings	
Presence of adenomyosis	49 (10.1)
Presence of uterine myoma	125 (25.8)
rASRM score, mean ± SD	56.1 ± 30.8
Largest cyst diameter (cm), mean ± SD	5.7 ± 2.3
Bilateral involvement	193 (39.8)
Postoperative conditions	
Postoperative observation period, median ± SD	4 y ± 4 y, 7 mo
Postoperative pain	18 (3.7)
Postoperative fertility treatment	181 (37.3)
Postoperative medical treatment	
No	428 (88.2)
Yes	57 (11.8)
GnRHa	20 (4.1)
Danazol	5 (1.0)
OC	32 (6.6)
Postoperative pregnancy	135 (27.8)
Recurrence of ovarian endometrioma	121 (24.9)
Ovarian cancer after excision of endometrioma	4 (0.8)

Note: GnRHa = gonadotropin-releasing hormone agonist; OC = oral contraceptive.

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