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Cumulative Recurrence Rate and Risk Factors for Recurrent Abdominal Wall Endometriosis after Surgical Treatment in a Single Institution

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Purpose: This study aimed to evaluate the cumulative recurrence rate and risk factors for recurrent abdominal wall endometriosis (AWE) after surgical treatment.

Materials and Methods: A retrospective cohort study was conducted at a single gynecological surgery center between January 2004 and December 2020. Patients who were surgically treated and followed up for at least 6 months after surgery were selected.

Results: Eighteen patients with pathologically diagnosed AWE were included in this study. The median follow-up duration was 22.5 months (range, 6–106). The median age was 37 years (range, 22–48), and 33.3% of the patients were nulliparous. Among the patients included in our study, 55.6% complained of a mass with cyclic pain, and 27.8% had a palpable mass. In addition, 22.2% of patients experienced recurrence with 17.5±9.7 months of mean time to recurrence. The cumulative recurrence rates at 24 and 60 months after surgical treatment of AWE were 23.8% and 39.1%, respectively. There were no statistically significant risk factors for the recurrence of AWE, including postoperative medical treatment.

Conclusion: The recurrence rate of AWE appears to be correlated with the follow-up duration. There was no statistically significant risk factor for the recurrence of AWE. Unlike ovarian endometriosis, postoperative hormonal treatment does not seem to lower the recurrence of AWE. The findings of the current study may help healthcare providers in counselling and managing patients with AWE.

Key Words: Abdominal wall endometriosis, recurrence, risk factor, postoperative hormonal treatment

INTRODUCTION

Endometriosis is defined as the presence of endometrial tissue; glands and stroma outside the uterine cavity, primarily in the pelvic peritoneum and ovaries. It is an estrogen-dependent chronic inflammatory disorder which causes chronic pelvic pain and infertility. Despite extensive investigation and predominant theories, the pathogenesis of endometriosis remains mostly unknown. Endometriosis affects the pelvic region, such as the ovaries, ligaments, and peritoneal surfaces, and less commonly occurs in the gastrointestinal tract, urinary system, abdominal wall, thoracic cavity, and central nervous system.[1,2]

Abdominal wall endometriosis (AWE) describes the involvement of endometriosis in the abdominal wall, including lesions secondary to a surgical procedure and spontaneous lesions.[2] The incidence rate of AWE has been estimated to be 0.04%–12%.[3,4] Most patients with AWE complain of cyclic abdominal pain, as well as a palpable and tender mass with swelling.[5]

Horton, et al.[6] studied 445 cases of AWE. In their systematic review, 57%, 11%, and 13% of the cases were associated with Cesarean section, hysterectomy, and other surgeries, respectively. Spontaneous AWE found at the umbilicus or in the groin constituted 20% of cases; 4.3% of recurrence rate (95% confi-

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dence interval 1.2%–7.4%) was reported.[6] In a recent study, the recurrence rate was 15% in AWE and perineal scar endometriosis.[7] Local excision of the lesion is recommended for appropriate diagnosis and treatment. Extensive resection with negative margins is required to prevent postoperative recurrence.[7] In the majority of published articles, the postoperative follow-up period in individual patients has not been described; as a result, studies related to cumulative recurrence rate and risk factors for recurrence after surgery in AWE are limited. In the present study, we evaluated the cumulative recurrence rate and risk factors for recurrent AWE endometriosis after surgical treatment in a single institution.

MATERIALS AND METHODS

A retrospective cohort study was performed on patients diagnosed with AWE who were followed up for at least 6 months after surgical treatment in a single gynecological surgery center between January 2004 and December 2020. AWE was defined as endometrial tissue superficial to the peritoneum, including scar endometriosis and spontaneous lesions such as inguinal and perineal endometriosis, as previously reported.[2,6] During the study period, 56 patients were clinically diagnosed with AWE. Among these patients, eight women were recommended for surgical treatment, but lost to follow-up; five women decided expectant management, nine women had medical treatment, and 34 women underwent surgical treatment. Among the 34 patients who received surgical treatment, 18 were followed-up for at least 6 months and included in this study (Fig. 1). One patient diagnosed with clear cell carcinoma arising from AWE on postoperative biopsy was also included in our analysis.

Data including the age at the time of surgery, parity, body mass index, presenting symptoms, previous surgical history, previous history of endometriosis surgery, interval between recent surgery and AWE surgery, size of the mass (the diameter of the largest mass in centimeters), location of the AWE, presence of ovarian endometriosis, duration of preoperative medical treatment, duration of postoperative medication use, time to recurrence, and follow-up duration were collected using a medical chart review. The size of lesion was confirmed by ultraso-

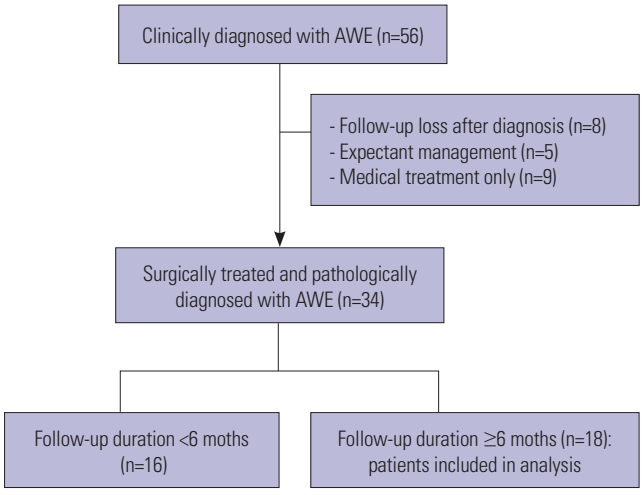

Fig. 1. Flow diagram of patient selection process. AWE, abdominal wall endometriosis.

Table 1. Baseline Characteristic of Patients with AWE (n=18)

Characteristics	Value
Age at surgery (yr)	36.4±5.7 (37, 22–48)
Parity	
Nulliparous	6 (33.3)
Parous	12 (66.7)
Body mass index (kg/m^2)	21.9±4.6 (21.0, 17.9–38.4)
Presenting symptom	
Palpable mass	5 (27.8)
Mass with cyclic pain	10 (55.6)
Mass with persistent pain	1 (5.6)
Mass with cyclic bleeding	1 (5.6)
Pain with cyclic bleeding	1 (5.6)
Previous surgical history (including episiotomy during NSVD)	
No surgical history	3 (16.7)
C/S	10 (55.6)
NSVD	3 (16.7)
Laparoscopy	8 (44.4)
Laparotomy	1 (5.6)
Associated endometriosis during previous surgery	7 (38.9)
Interval between recent surgery and AWE surgery (yr)	7.1±4.4 (6.0, 1–19)
Size of largest diameter of AWE lesion (cm)	3.5±1.9 (3.1, 1.5–9.0)
Location of AWE	
C/S scar	10 (55.6)
Episiotomy site	1 (5.6)
Inguinal area	3 (16.7)
Laparoscopic trocar site (including umbilicus)	4 (22.2)
Associated ovarian endometrioma during AWE surgery	4 (22.2)
Preoperative medical treatment before AWE surgery	1 (5.6)
Duration of preoperative medical treatment (months)	42 in one patient
Postoperative medical treatment after AWE surgery	8 (44.4)
Duration of postoperative medical treatment (months)	12.8±11.0 (7.5, 3–35) in 8 patients
Recurrence	4 (22.2)
Time to recurrence (months)	17.5±9.7 (16.0, 9–29)
Follow-up duration (months)	31.8±26.9 (22.5, 6–106)

AWE, abdominal wall endometriosis; C/S, Cesarean section; NSVD, normal spontaneous vaginal delivery.
Data are presented as mean±standard deviation (median, range) or n (%).

nography or CT performed before surgery. The duration of preoperative or postoperative medication was calculated using the sum of individual medication use, such as gonadotropin-releasing hormone agonist (GnRH agonist), dienogest (DNG), oral contraceptives, or levonorgestrel-intrauterine system. Time to recurrence was defined as the time in months from the surgery to detect a newly developed AWE lesion, which was confirmed by imaging studies with or without symptoms.

This study was approved by the Institutional Review Board and the ethics committee of CHA Gangnam Medical Center on the Use of Human Subjects in Research (2021-10-005-001). Informed consent for the study was waived due to its retrospective nature.

Statistical analysis was performed using the SPSS software (version 25.0; IBM Corp., Armonk, NY, USA), and categorical variables were compared using the chi-square and Fisher's exact tests. Quantitative variables were compared using the Mann-Whitney U test after normality test for data using the Shapiro-Wilk test. The Kaplan-Meier method was used to evaluate the cumulative probability of recurrence and reoperation. Multivariate analyses using the Cox proportional hazards models, including the significant variables in univariate analysis, were performed to obtain a subset of independent risk factors for recurrent AWE. Among these variables, those with a p-value <0.2 underwent multivariate regression analyses. Statistical significance was set at $p<0.05$.

Table 2. Analysis of Possible Risk Factors for Recurrent AWE (n=18)

Characteristics	No recurrence (n=14)	Recurrence (n=4)	*p* value
Age at surgery (yr)	35.3±5.4 (37, 22–42)	40.5±5.4 (39.5, 35–48)	0.149
Parity			0.245
Nulliparous	6 (42.9)	0 (0)	
Parous	8 (57.1)	4 (100)	
Body mass index (kg/m^2)	20.9±1.9 (20.9, 18.1–25.0)	25.5±9.0 (22.8, 17.9–38.4)	0.457
Presenting symptom			0.391
Palpable mass	4 (28.6)	1 (25)	
Mass with cyclic pain	8 (57.1)	2 (50)	
Mass with persistent pain	0	1 (25)	
Mass with cyclic bleeding	1 (7.1)	0 (0)	
Pain with cyclic bleeding	1 (7.1)	0 (0)	
Previous surgical history and location of AWE (including episiotomy during NSVD)			0.249
No surgical history	3 (21.4)	0 (0)	
C/S	6 (42.9)	4 (100)	
NSVD	1 (7.1)	0 (0)	
Laparoscopy	4 (28.6)	0 (0)	
Associated endometriosis during previous surgery			>0.999
No	8 (57.1)	3 (75)	
Yes	6 (42.9)	1 (25)	
Interval between recent surgery and AWE surgery (years)	6.0±3.1 (5.0, 1–12)	10.0±6.7 (9.0, 3–19)	0.265
Size of largest diameter of AWE lesion (cm)	3.1±1.1 (3.1, 1.5–5.0)	4.9±3.3 (4.5, 1.7–9.0)	0.365
Location of AWE			0.249
C/S scar	6 (42.9)	4 (100)	
Episiotomy site	1 (7.1)	0 (0)	
Inguinal area	3 (21.4)	0 (0)	
Laparoscopic trocar site (including umbilicus)	4 (28.6)	0 (0)	
Associated ovarian endometrioma during AWE surgery			>0.999
No	11 (78.6)	3 (75)	
Yes	3 (21.4)	1 (25)	
Preoperative medical treatment before AWE surgery			>0.999
No	13 (92.9)	4 (100)	
Yes	1 (7.1)	0 (0)	
Postoperative medical treatment after AWE surgery			>0.999
No	8 (57.1)	2 (50)	
Yes	6 (42.9)	2 (50)	

AWE, abdominal wall endometriosis; C/S, Cesarean section; NSVD, normal spontaneous vaginal delivery.
Data are presented as mean±standard deviation (median, range) or n (%).

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RESULTS

A total of 18 patients were recruited. The median follow-up duration was 22.5 months (range, 6–106). Table 1 shows the baseline characteristics of the patients with AWE. The median age was 37 years (range, 22–48), and 33.3% of the patients were nulliparous. Among the study subjects, 55.6% complained of a mass with cyclic pain and 27.8% had a palpable mass. Interestingly, all three patients (16.7%) without a surgical history had lesions in the inguinal area. In addition, 22.2% of patients experienced recurrence within a mean period of 17.5±9.7 months. Seven out of 18 patients had previously been diagnosed with pelvic endometriosis by surgery.

To analyze the possible risk factors for recurrent AWE, baseline characteristics of the two groups (without recurrence and with recurrence groups) were compared, as shown in Table 2. No statistically significant differences were observed between the two groups.

Using the Kaplan-Meier method, the cumulative recurrence rates at 24 and 60 months after surgical treatment of AWE were calculated as 23.8% and 39.1%, respectively (Fig. 2).

Cox regression analysis was performed on univariate analysis for independent risk factors for recurrent AWE (Table 3). The results showed no statistically significant risk factors for the recurrence of AWE.

Among our patients, one woman was diagnosed with clear cell carcinoma. The initial symptom of this patient was a palpable abdominal mass, which had increased in size during the previous year. The patient underwent local excision, and the final pathology revealed clear cell carcinoma. During a detailed evaluation, inguinal lymph node metastasis was suspected. Subsequently, the patient underwent total laparoscopic hysterectomy with bilateral salpingo-oophorectomy with pelvic lymph node dissection, and metastatic carcinoma was confirmed in the left inguinal lymph node. Despite six cycles of adjuvant paclitaxel-carboplatin chemotherapy, recurrent disease was confirmed in the left inguinal lymph nodes and ribs of the patient. She was transferred to another hospital for radiotherapy.

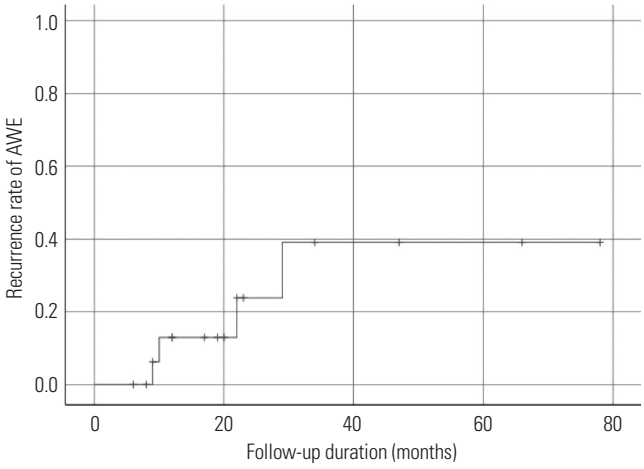

Fig. 2. Cumulative recurrence rate of AWE using the Kaplan-Meier analysis. AWE, abdominal wall endometriosis.

DISCUSSION

In the present study, we found that the cumulative recurrence rates at 24 and 60 months after surgical treatment of AWE were 23.8% and 39.1%, respectively. Univariate analysis of risk factors for recurrent AWE showed no statistically significant factors; mass size, cyclic symptoms, previous operation type, interval between recent surgery and AWE surgery, pre- and postoperative medical treatment, and association with ovarian endometrioma were not risk factors for AWE recurrence in our study.

To date, most articles on AWE have been published with a focus on clinical manifestations. Most of the patients had a history of surgical procedures, complaints of pain with a palpable, tender mass, and/or cyclical pain and swelling.[5] In suspected cases, fine-needle aspiration, ultrasonography with Doppler, computed tomography, and magnetic resolution imaging could be helpful, but not accurate.[6,8] However, in patients with a classic presentation suggestive of AWE, no further studies are necessary, and these studies may even result in treatment delay.[6,8]

We reviewed nine articles published after year 2000 and presented postoperative recurrence rates. A total of 218 patients with AWE, including perineal endometriosis, are listed in Table 4. Most of the patients underwent surgical treatment and were diagnosed pathologically, but five patients did not undergo surgery. In this review of Table 4, the recurrence rates were 0%–15% except our study, which was relatively lower than that in our study (22.2%).[3,7-11] The follow-up duration varied from 1.1 to 235 months, and two studies did not provide any clear infor-

Table 3. Univariate and Multivariate Analyses for Independent Risk Factors of Recurrent AWE Using the Cox Regression Method

Risk factors of recurrence	Univariate	*p* value
	HR (95% CI)	
Age >37 years (vs. ≤37 years)	4.426 (0.456–42.970)	0.200
Parous (vs. Nulliparous)	58.309 (0.016–211985.722)	0.331
BMI >21 kg/m^2 (vs. ≤21 kg/m^2)	3.596 (0.372–34.806)	0.269
Cyclic Sx (vs. non-cyclic Sx)	0.442 (0.061–3.231)	0.422
Previous C/S (vs. no)	60.611 (0.018–209588.582)	0.324
Previous endo op (vs. no)	0.790 (0.080–7.797)	0.840
Interval >6 years between recent surgery and AWE surgery (vs. ≤6 years)	7.592 (0.768–75.081)	0.083
Size >3.1 cm (vs. ≤3.1 cm)	1.106 (0.155–7.911)	0.920
C/S scar (vs. other site)	0.016 (0.000–57.052)	0.324
Associated ovarian endometriosis (vs. no)	1.125 (0.117–10.855)	0.919
Preoperative medical treatment (vs. no)	0.045 (0.000–1990788.781)	0.804
Postoperative medical treatment (vs. no)	1.551 (0.218–11.054)	0.661

HR, hazard ratio; CI, confidence interval; Sx, symptom; C/S, Cesarean section; endo op, endometriosis operation; AWE, abdominal wall endometriosis.

Table 4. A review of Reported Articles Published after 2000 in English on Postoperative Recurrence Rates of Abdominal Wall Endometriosis

Study	Number of patients	Mean age (yr)	Surgical treatment (%)	Postoperative recurrence rate (%)	Follow-up duration (range, months)	Risk factor for recurrence
Blanco, et al.[9]	12	29.4	100	0	4–36	-
Francica, et al.[10]	12	31	100	0	4–23	-
Zhao, et al.[3]	64	29.8	96.9 (62/64)	7.81 (5/64)	1.1–235 (mean 83.7)	Size and depth of lesion
Gunes, et al.[11]	11	28.2	100	0	Mean 21.8	-
Rao, et al.[12]	6	33.3	100	0	12–60	-
Goel, et al.[13]	6	33	100	0	9–144	-
Khan, et al.[8]	34	35.2	100	5.88 (2/34)	36–65 (median 50.5)	-
Lopez-Soto, et al.[14]	33	35.4	90.9 (30/33)	9.09 (3/33)	12–36	-
Metalliotakis, et al.[7]	40	36.5	100	15 (6/40)	-	-
Current study	18	37	100	22.2 (4/18)	6–106 (median 22.5)	Not found

mation about the follow-up duration. Only one study analyzed the risk factors for recurrence. According to a retrospective study by Zhao, et al.,[3] five out of 64 women showed recurrence after surgical treatment. The risk factors for recurrence were lesion diameter and mass involving the muscle or peritoneum (p<0.001, p=0.018, and p=0.003, respectively).[3] However, in our study, the mass size was not a risk factor for recurrence. Due to the retrospective nature of our study, we did not evaluate the characteristics of the tissue involved in AWE. Considering that the treatment of choice for AWE was local resection with a negative margin, the possibility of a larger or deeper lesion might be difficult to remove completely.[8] This might have affected the recurrence. Large-scale prospective studies are required to confirm these possible risk factors.

Purvis and Tyring[15] reported poor results in medical treatment. Danazol temporarily alleviated the symptoms, but pain returned after the cessation of drugs. GnRH agonists were effective in relieving symptoms, but patients experienced menopausal side effects, such as hot flashes.

Rani, et al.[16] reviewed 27 cases of abdominal scar endometriosis. Two patients received oral progestogen therapy with temporary pain relief, but were ultimately treated by surgical excision. Rani, et al.[16] recommended complete surgical excision as the treatment of choice. A few studies have demonstrated pain control and lesion volume reduction by using DNG in patients with endometriosis involving the rectosigmoid, bladder, and other extragenital areas.[17-21] In our study, two patients underwent preoperative medical treatment. One patient had a history of Cesarean delivery 5 years ago. There was no change in mass size with 2 months of DNG use after the diagnosis of AWE, and the patient decided to undergo surgical treatment. One patient had a history of laparoscopic cyst enucleation for endometrioma 9 years ago. During a total of 40 months of DNG use, growing lesions of AWE resulted in surgical treatment. Eight patients underwent postoperative medical treatment with a GnRH agonist and/or DNG after AWE surgery, and two patients experienced recurrent AWE. The two patients received postoperative GnRH analogues for 6 months, wherein recurrence occurred at 9 and 26 months, respectively. In the univariate analysis, preoperative and postoperative medical treatments did not decrease recurrence. Therefore, surgical treatment may be preferable for medical treatment. Early detection of the lesion and surgical treatment are important in patients with suspected AWE.

The current study had some strengths in that it was the first to analyze the cumulative recurrence rates over a follow-up period of at least 6 months after surgery, and that it aimed to identify the risk factors for AWE recurrence. However, this study also had several limitations. First, the current study was performed retrospectively. Most AWE usually occurs as a second process in surgical scars. Since AWE is a rare disease entity, the number of subjects who were surgically treated and followed up for at least 6 months in this study were too small to generalize the results. Second, we did not evaluate the tissue involved in AWE, which could be a possible risk factor for recurrence due to its retrospective nature. Third, most patients were lost to follow-up after surgical treatment. We evaluated postoperative medical treatment as one of the possible risk factors for recurrence; however, in many cases, the duration of medical treatment was relatively short. This study may provide information to the patients, and also help in patient counselling and management. In the future, large-scale prospective multicentre studies are required to confirm the clinical effectiveness of postoperative medical treatment in AWE.

In conclusion, the recurrence rate of AWE appears to be correlated with follow-up duration. Unlike ovarian endometriosis, postoperative hormonal treatment does not seem to lower the recurrence of AWE. The possibility of clear cell carcinoma arising from AWE, accurate diagnosis, and definite surgical treatment with negative margins should be considered in AWE patients.

AUTHOR CONTRIBUTIONS

Conceptualization: Su Jin Kim, Seok Ju Seong, and Mi-La Kim. Data curation: Su Hyeon Choi and Nara Lee. Formal analysis: Seyeon Won and Sohyun Shim. Investigation: Miseon Kim, Su Jim Kim, and Mi Kyoung Kim. Methodology : Miseon Kim, Sohyun Shim, and Seok Ju

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Seong. Administration: Mi Kyoung Kim and Su Hyeon Choi. Resources: Nara Lee and Seyeon Won. Software: Su Jin Kim. Supervision: Mi-La Kim. Validation: Seyeon Won and Nara Lee. Visualization: Mi Kyoung Kim and Sohyun Shim. Writing—original draft: Su Jin Kim, Su Hyeon Choi, and Miseon Kim. Writing—review & editing: Seok Ju Seong and Mi-La Kim. Approval of final manuscript: all authors.

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