Influence of laterality on endometriosis severity in patients with unilateral endometrioma: a retrospective study.

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Abstract

Background: We compared the revised American Society for Reproductive Medicine (ASRM) scores determined during laparoscopic surgery to evaluate the effect of the location of the endometrioma (right vs. left ovary) on the severity of endometriosis. Methods: The medical records of 151 patients, including 58 right-sided and 93 left-sided cases, who underwent an initial laparoscopic surgery for unilateral ovarian endometrioma were reviewed retrospectively. We extracted the ASRM scores determined during surgery and some representative factors related to endometriosis that are separate from the tumour characteristics, such as the coexistence of uterine fibroids, adenomyoma, or other ovarian tumours, a history of use of assisted reproductive technology (ART), and tumour marker values. A statistical analysis was performed to assess the impact of each factor. We classified the ASRM scores into 4 categories to compare the tendency towards endometrial lesion spread with a focus on the “sidedness” of the endometrioma. We defined contralateral endometrial lesion (CEL), Douglas pouch endometrial lesion (DEL), same endometrial lesion (SEL) and peritoneal endometrial lesion (PEL). Results: The ASRM scores of patients with a right-sided endometrioma were significantly higher than patients with a left-sided endometrioma (41.5 ± 22.1 points vs. 32.9 ± 15.8 points, $p<0.05$). The higher ASRM scores of the patients with right-sided endometrioma may be caused by the frequent detection of endometrial lesions in the left tube, left ovary and Douglas pouch. According to the statistical analysis, the coexistence of uterine fibroids also exerted significant positive effects on increasing the ASRM score. Conclusions: Higher ASRM scores are possible in patients with right-sided endometrioma. The laterality of endometriosis severity should be considered.

Background

Endometriosis is one of the most common gynaecological diseases and is known to affect 2–10% of reproductive-age women [1, 2]. While many patients are asymptomatic [3], endometriosis is frequently associated with infertility and pain symptoms, including chronic pelvic pain, dysmenorrhoea, dyspareunia, and dyschezia [4]. Previous studies have revealed a relationship between symptom severity and disease stage according to the revised American Society for Reproductive Medicine (ASRM) scoring system [5]. In most cases, the diagnosis of endometrioma is obtained during an outpatient ultrasound examination [6], and laparoscopic surgeries are often performed to treat pelvic pain and subfertility [7]. During surgery, ovarian endometrioma, superficial implantation and deep infiltrating endometriosis are detected. The most frequent site of endometriotic lesions detected during surgery was the ovary [8]. According to some studies, left-sided endometriomas are more common than right-sided endometriomas [9]. This tendency is believed to be due to anatomical asymmetries in the pelvic organs, including the presence of the sigmoid colon and more frequent ovulation of right ovary caused by the varying paths of the vein [9, 10]. However, the recognition of this laterality is insufficient. Therefore, we aimed not only to verify this laterality but also to evaluate the effect of the side of endometrioma on disease severity. Specifically, the ASRM scores determined during laparoscopic surgery were compared.

Methods

Patient selection criteria

This study was reviewed and approved by the Human Ethics Committee of the University of Teikyo (trial registration number: 18-233). The medical records of 151 female patients with unilateral endometrioma, including 58 right-sided and 93 left-sided cases, from June 1, 2014, to December 31, 2019, were reviewed retrospectively. We defined the former cases as the right-sided endometrioma group (REG, n = 58) and the latter cases as the left-sided endometrioma group (LEG, n = 93). In this study, we did not include patients with recurrent endometriosis. As shown in Figure 1, 151 of the 302 patients who underwent laparoscopic surgery for new onset endometrioma detected during outpatient examinations were excluded for the following reasons: 95 patients were excluded because they were diagnosed with bilateral endometrioma and 56 patients were excluded for other reasons, including a lack of cystic lesions detected during surgery (n = 23); a diagnosis of other main ovarian cystic diseases, such as mature cystic teratoma (n = 8); ruptured endometrioma (n = 4); and prior abdominal surgery (n = 21). Since patients meeting the last criterion (prior abdominal surgery) were excluded after patients meeting other criteria were excluded, this number may be an underestimation (n = 21). Among the 151 remaining patients, we performed 123 laparoscopic cystectomies, including 9 that were performed simultaneously with laparoscopic myomectomies; 9 laparoscopic hysterectomies; 23 laparoscopic salpingo-oophorectomies, including 3 surgeries performed simultaneously with laparoscopic hysterectomies; and 5 laparoscopic-assisted cystectomies, including 3 surgeries performed simultaneously with laparoscopic-assisted myomectomies.

Collection of patient characteristics

After extracting the medical records of these 151 patients, the following patient characteristics were collected: 1) size of the ovarian endometrioma before and during surgery; 2) ASRM score (points) [5]; 3) patient's age at the time of the operation; 4) presence of adhesions predicted before the operation; 5) history of use of assisted reproductive technology (ART); 6) presence of complicated adenomyomas, uterine fibroids or other ovarian tumours; and 7) serum carbohydrate antigen 125 (CA125) level (U/ml). Magnetic resonance imaging (MRI) was performed on almost all patients (148/151 cases) to assess the size of the endometrioma. MRI was also used to predict adhesions, particularly in the Douglas pouch. In this study, ART included both in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Twenty-eight of these 151 patients used hormone drugs, including oral contraceptives, gonadotropin-releasing hormone agonists and other drugs. However, the indications for the use of hormone drugs varied, and thus this factor was not considered in the present study.

Classification of endometrial lesions

We divided the endometrial lesions based on the location of the endometrioma to compare the tendency of endometrial lesion spread between patients with right or left ovarian endometrioma. Briefly, the so-called ASRM score chart, in which the severity of endometriosis is standardized by roughly classifying

endometrial lesions [5], was divided into four parts. First, we calculated the total ASRM score for the uterine adnexa on the same side as the ovarian endometrioma and excluded the score for the endometrioma itself, as shown in Figure 2-A. Second, a similar calculation was performed for the uterine adnexa on the contralateral side of the ovarian endometrioma (Figure 2-B). The remaining endometrial lesions were divided into peritoneal (Figure 2-C) or Douglas pouch endometrial lesions (Figure 2-C). In summary, by referencing the sheet of “Revised ASRM classification of endometriosis, 1996.” [5], we classified the ASRM scores into the following four categories: 1) “same endometrial lesions (SELs)”, including Ovary-ENDOMETRIOSIS-Superficial, Ovary-ADHESIONS and Tube-ADHESIONS on the same side, as the main ovarian endometrioma; 2) “contralateral endometrial lesions (CELs)”, including Ovary-ENDOMETRIOSIS-Superficial, Ovary-ADHESIONS and Tube-ADHESIONS on the contralateral side of the main ovarian endometrioma; 3) “peritoneal endometrial lesions (PELs)”, including Peritoneum-ENDOMETRIOSIS; and 4) “Douglas pouch endometrial lesions (DELs)”, including POSTERIOR CULDESAC OBLITERATION. As an example, this classification is shown in Figure 2 for REG. The SEL (Figure 2-A), CEL (Figure 2-B), PEL (Figure 2-C) and DEL (Figure 2-C) scores are the total scores in each cell, as indicated by an italicized letter and thick-bordered box. In the patients with left ovarian endometrioma, the SEL and CEL scores were reversed. In this analysis, the theoretical maximum values of SEL, CEL, PEL and DEL were 36, 36, 10 and 40 points, respectively. We not only compared each average value of SEL, CEL, PEL and DEL between patients in the REG and LEG but also counted each number of patients with these four lesions in both the REG and LEG.

Statistical analysis

The primary outcomes included the difference in the ASRM scores detected during laparoscopic surgery between the patients with right- and left-sided endometriomas. We assessed the influences of the following 8 factors on the ASRM score: 1) “right-sided endometrioma”; 2) “predicted adhesion”, which was defined as the detection of the possible presence of an adhesion in a patient during a pelvic examination or MRI; 3) “ART history”, which was defined as patients who underwent ART; 4) “adenomyoma”, which was defined as the current presence of adenomyoma based on clinical images; 5) “uterine fibroid”, which was defined as the current presence of a uterine fibroid based on clinical images; 6) “other ovarian tumour”, which was defined as the current presence of an ovarian tumour other than endometrioma based on clinical images; 7) “positive marker”, which was defined as serum CA125 levels $\geq$ 35 U/ml; and 8) “large endometrioma”, which was defined as a tumour size of at least 50 mm (described in Table 2). All 151 patients were divided into two groups based on the presence (= 1) or absence (= 0) of these 8 factors. The difference in the ASRM score was compared using Welch’s t-test. We also performed a multivariate regression analysis using the least squares method to reduce confounding factors and confirm this difference. These statistical analyses were performed using JMP version 12 for Windows (SAS Institute, Inc., Tokyo, Japan). The total values of SEL, CEL, PEL and DEL between patients in the REG and LEG were also compared with Welch’s t-test. The data are presented as means ± standard deviations. A p-value less than 0.05 was considered statistically significant.

Results

Patient characteristics

The 151 patients with unilateral endometrioma comprised 58 right-sided and 93 left-sided cases (REG and LEG). The average endometrioma size measured before and during surgery, patient age and ASRM score were 56.2 ± 23.2 mm, 58.9 ± 24.4 mm, 36.7 ± 7.2 years and 36.2 ± 18.9 points, respectively. The representative symptoms were dysmenorrhoea (n = 77), infertility (n = 51), pelvic pain (n = 38), coital pain (n = 7) and other symptoms, although the symptoms overlapped in some cases.

By comparing the REG and LEG in a univariate analysis (Table 1), a significantly higher ASRM score was detected for the REG (41.5 ± 22.1 points vs. 32.9 ± 15.8 points, p = 0.0068). The endometrioma sizes before surgery (63.8 ± 23.8 mm vs. 57.7 ± 22.1 mm, p = 0.11) and during surgery (64.0 ± 26.6 mm vs. 55.7 ± 22.4 mm, p = 0.051), and the patients' age (36.0 ± 6.6 years vs. 37.2 ± 7.5 years, p = 0.34) did not differ significantly.

Influential factors increasing the ASRM scores

We compared 8 factors using Welch's t-test and a multivariate regression analysis to identify the significant factors associated with the severity of endometriosis (Table 2). We extracted the following 8 factors collected before surgery: 1) "right-sided endometrioma" (n = 58); 2) "predicted adhesion" (n = 32), which was defined as the possible presence of an adhesion detected during a pelvic examination or MRI; 3) "ART history" (n = 14), which was defined as patients who underwent ART; 4) "adenomyoma" (n = 16), which was defined as the current presence of adenomyoma based on clinical images; 5) "uterine fibroid" (n = 60), which was defined as the current presence of uterine fibroids based on clinical images; 6) "other ovarian tumour" (n = 13), which was defined as the current presence of an ovarian tumour other than endometrioma based on clinical images; 7) "positive marker" (n = 85), which was defined as serum CA125 levels ≥ 35 U/ml; and 8) "large endometrioma" (n = 82), which was defined as a tumour size of at least 50 mm. Welch's t-test revealed that "right-sided endometrioma" (41.5 ± 22.1 points vs. 32.9 ± 15.8 points, p = 0.012) and "uterine fibroid" (40.4 ± 21.8 points vs. 33.5 ± 16.3 points, p = 0.037) were significant factors contributing to higher ASRM scores. The factor "adenomyoma" also had the tendency to increase the ASRM score (47.3 ± 23.0 points vs. 34.9 ± 18.0 points, p = 0.053). A multivariate regression analysis of the 8 factors using the least squares method indicated significant differences in 3 factors (right-sided endometrioma: p = 0.028, uterine fibroid: p = 0.033, adenomyoma: p = 0.027). However, the other 5 factors did not show significant differences. These results supported the hypothesis that the laterality of endometrioma affected the severity of endometriosis independent of the other 2 significant factors. Comparisons of the REG and LEG revealed the following findings: 26/58 patients in the REG and 34/93 patients in the LEG exhibited "uterine fibroid" (p = 0.32), and 9/58 patients in the REG and 7/93 patients in the LEG exhibited "adenomyoma" (p = 0.12).

Laterality of endometrial lesion spread

We compared the total values of SEL, CEL, PEL and DEL between patients in the REG and LEG to detect the tendency towards the spread of endometrial lesions. The actual maximal values of SEL, CEL, PEL and DEL were 32, 34, 7 and 40 points for patients in the REG and 32, 9, 6 and 40 points for patients in the LEG, respectively. The numbers of SEL, CEL, PEL and DEL cases were 51, 23, 26 and 30, respectively, in the REG (n=58) and 80, 24, 45 and 35, respectively, in the LEG (n=93). The proportion of patients with CEL or DEL was significantly higher among the REG than among the LEG. When comparing the scores of these 4 lesions, the CEL (3.5 ± 6.9 points vs. 1.0 ± 2.1 points, p = 0.0091) and DEL (9.5 ± 15.8 points vs. 4.2 ± 10.4 points, p = 0.026) scores were significantly higher among patients in the REG. The SEL (7.9 ± 7.1 points vs. 7.0 ± 7.0 points, p = 0.42) and PEL (1.3 ± 1.8 points vs. 1.2 ± 1.7 points, p = 0.69) scores did not differ significantly.

Discussion

One classically proposed pathogenic theory, i.e., the retrograde menstruation hypothesis [11], suggests that the tendency towards a frequent left-sided disease is attributed to the presence of the sigmoid colon [9]. In fact, more cases of left-sided endometrioma were detected at our hospital (93 vs. 58) after excluding 95 cases of bilateral endometrioma. In this study, the possible effect of laterality on the severity of endometriosis was also investigated because the stage of endometriosis is considered closely related to its symptoms, particularly infertility [12, 13], although we were limited because we were unable to assess the severity by comparing patients' symptoms. As an index of severity, we compared the ASRM scores of two groups, i.e., REG and LEG. In this comparison, by excluding patients with bilateral endometrioma, we aimed to determine the main endometriosis lesion in each case. As expected, the ASRM score of patients in the REG was significantly higher than patients in the LEG, and this difference reached approximately 10 points (41.5 ± 22.1 points vs. 32.9 ± 15.8 points, p = 0.012). Similarly, "uterine fibroid" exerted a significant effect on the high ASRM scores and "adenomyoma" showed a similar tendency. The likely explanation is that endometriosis, adenomyosis and uterine fibroids can co-occur [1, 2, 14, 15]. Based on these results from the multivariate analysis, we ensured that the ratios of patients with "uterine fibroid" and "adenomyoma" were not significantly different before subsequently comparing the REG and LEG in more detail.

By classifying the endometrial lesions into 4 patterns (SEL, CEL, PEL and DEL), the detailed characteristics of the endometrial lesions were also compared between the REG and LEG. In this analysis, the more frequent endometrial lesions in the Douglas pouch and the left ovary or tube increased the severity of endometriosis in the REG (Table 3). Of these lesion types, DEL was detected in more than 50% of the patients in the REG (30/58 patients) and exerted a greater effect on the ASRM score (9.5 ± 15.8 points; Table 3). Unfortunately, the possibility that the main endometrial lesion in these 30 cases was located in the Douglas pouch cannot be excluded because the pathogenesis of endometriosis is multifactorial and endometriosis does not always arise from the ovary [16]. Additionally, because endometrial lesions in the Douglas pouch are difficult to detect during a simplified outpatient examination, we mainly focused on "endometrioma". However, the anatomical distribution of endometriotic lesions may also be consistent with the retrograde menstruation theory [11]. In addition to

some severe symptoms, such as pelvic pain, these lesions are also associated with more difficult surgery [17]; thus, the differentiation between right or left endometrioma is meaningful.

Conclusions

We examined the associations between the laterality of ovarian endometrioma and its severity. Patients with right-sided endometrioma tended to have higher ASRM scores than patients with left-sided endometrioma. A detailed analysis of the distribution of endometrial lesions revealed the possible involvement of anatomical asymmetries in pelvic organs.

List Of Abbreviations

ASRM: American Society for Reproductive Medicine, REG: right-sided endometrioma group, LEG: left-sided endometrioma group, ART: assisted reproductive technology, CA125: carbohydrate antigen 125, MRI: magnetic resonance imaging, IVF: in vitro fertilization, ICSI: intracytoplasmic sperm injection, SELs: same endometrial lesions, CELs: contralateral endometrial lesions, PELs: peritoneal endometrial lesions, DELs: Douglas pouch endometrial lesions

Declarations

Ethical approval and consent to participate

This retrospective study was approved by the Institutional Review Board of Teikyo University. The study registry number, registry name and date of registration are as follows: 18-233, Clinical outcomes and carcinogenic risk of ovarian endometriomas: a retrospective analysis, 2019/3/20.

Consent for publication

Written informed consent was obtained from the patients for the publication of any images. A copy of the written informed consent form is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

The authors agree to make all data of this study freely available.

Competing interests

The authors have no competing interests to declare.

Funding

The authors declare that no funding was received for this study.

Authors' contributions

WI collected and analysed the data and wrote the manuscript. AT and ON supervised the entire study. MH, AT, AS, RM and HT performed all operations. AF and ON determined the methods of all operations and supervised all medical practice. All authors read and approved the final manuscript.

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Tables

Table 1: Patient characteristics

We extracted the patient's age, ASRM score, tumour size measured before and during surgery from the medical records of the 93 patients in the LEG and 58 patients in the REG. The data are presented as the means ± standard deviations and this difference was compared using Welch's t-test.

	LEG	REG	P-value
Total number (n)	93	58	
Average age (years)	37.2 ± 7.5	36.0 ± 6.6	0.33
ASRM score	32.9 ± 15.8	41.5 ± 22.1	0.01
Endometrioma size before surgery (mm)	57.7 ± 22.1	63.8 ± 22.8	0.11
Endometrioma size during surgery (mm)	55.7 ± 22.4	64.0 ± 26.6	0.05

Table 2: Influences of endometriosis-related factors on the ASRM score.

For the 151 patients, we extracted the following 8 factors collected before surgery: 1) "right-sided endometrioma"; 2) "predicted adhesion", which was defined as the possible presence of an adhesion based on a pelvic examination or MRI; 3) "ART history", which was defined as patients who underwent ART; 4) "adenomyoma", which was defined as the current presence of adenomyoma based on clinical images; 5) "uterine fibroid", which was defined as the current presence of a uterine fibroid based on clinical images; 6) "other ovarian tumour", which was defined as the current presence of an ovarian tumour other than endometrioma based on clinical images; 7) "positive marker", which was defined as serum CA125 levels ≥ 35 U/ml; and 8) "large endometrioma", which was defined as a tumour size of at least 50 mm. In Table 2, we show the number of patients with each factor. Because several factors overlapped in some cases,

we divided the patients into two groups according to the presence or absence of each factor and used Welch's t-test to assess the effects of the 8 factors. Then, we compared the average ASRM scores (points) between these two groups based on these factors. The p-values calculated using Welch's t-test are shown in Table 2. Among the 8 factors, 2 factors, including "right-sided endometrioma" and "uterine fibroid", were significantly different. The factor of "adenomyoma" also indicated the tendency of a high ASRM score.

Factors	N	ASRM score (Positive vs. Negative)	P-value
Right-sided Endometrioma	58	41.5 ± 22.1 vs. 32.9 ± 15.8	0.01
Uterine fibroid	60	40.4 ± 21.8 vs. 33.5 ± 16.3	0.04
Adenomyoma	16	47.3 ± 23.0 vs. 34.9 ± 18.0	0.05
ART history	14	40.0 ± 14.8 vs. 35.9 ± 19.3	0.35
Large endometrioma	82	37.3 ± 18.7 vs. 35.0 ± 19.2	0.45
Positive marker	85	37.0 ± 18.0 vs. 35.2 ± 20.1	0.57
Predicted adhesion	32	36.0 ± 14.9 vs. 36.3 ± 19.9	0.92
Other ovarian tumour	13	36.3 ± 20.9 vs. 36.2 ± 18.8	0.99

Footnote

ART: assisted reproductive technology

Table 3: Distribution of endometrial lesions.

We classified the ASRM scores into four categories, including SEL, CEL, PEL, and DEL, to compare the tendency of endometrial lesions to spread between patients with right or left ovarian endometrioma. In Table 3, we compared the average of these scores (points) between the REG and LEG using Welch's t-test (Note: n = the number of patients with each endometrial lesion).

Lesion	Right ovarian endometrioma	Left ovarian endometrioma	P-value
CEL	3.5 ± 6.9 (n = 23)	1.0 ± 2.1 (n = 24)	0.01
DEL	9.5 ± 15.8 (n = 30)	4.2 ± 10.4 (n = 35)	0.03
SEL	7.9 ± 7.1 (n = 51)	7.0 ± 7.0 (n = 80)	0.42
PEL	1.3 ± 1.8 (n = 26)	1.2 ± 1.7 (n = 45)	0.69

Footnote

CEL: contralateral endometrial lesion, DEL: Douglas pouch endometrial lesion, SEL: same endometrial lesion, PEL: peritoneal endometrial lesion

Figures

Figure 1: Flowchart of data collection criteria.

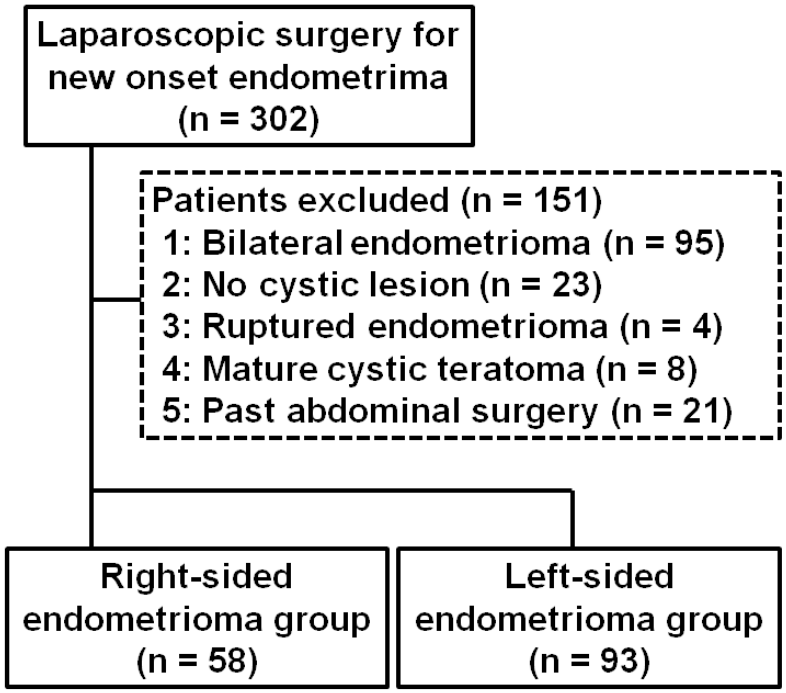

Figure 1

Flowchart of data collection criteria. Of the 302 patients, 151 were excluded for the following reasons: 95 patients were excluded because they were diagnosed with bilateral endometrioma, and 56 patients were excluded for other reasons, including no cystic lesion detected during surgery (n = 23); other main ovarian cystic diseases, such as mature cystic teratoma (n = 8); ruptured endometrioma (n = 4); and past abdominal surgery (n = 21). This last factor (past abdominal surgery) was excluded after excluding other

factors. Then, the medical records of 151 female patients with unilateral endometrioma, including 58 right-sided and 93 left-sided cases, were reviewed retrospectively.

Figure 2: Classification of endometrial lesions in patients with right-side endometrioma

A. Same endometrial lesion (SEL)

	ENDOMETRIOSIS	< 1cm	1 - 3 cm	> 3 cm
Peritoneum	Superficial	1	2	4
	Deep	2	4	6
Ovary	***R Superficial***	***1***	***2***	***4***
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	Partial		Complete
		4		40
	ADHESIONS	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
Ovary	***R Filmy***	***1***	***2***	***4***
	Dense	***4***	***8***	***16***
	L Filmy	1	2	4
	Dense	4	8	16
Tube	***R Filmy***	***1***	***2***	***4***
	Dense	***4***	***8***	***16***
	L Filmy	1	2	4
	Dense	4	8	16

B. Contralateral endometrial lesion (CEL)

	ENDOMETRIOSIS	< 1cm	1 - 3 cm	> 3 cm
Peritoneum	Superficial	1	2	4
	Deep	2	4	6
Ovary	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	***1***	***2***	***4***
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	Partial		Complete
		4		40
	ADHESIONS	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
Ovary	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	***1***	***2***	***4***
	Dense	***4***	***8***	***16***
Tube	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	***1***	***2***	***4***
	Dense	***4***	***8***	***16***

C. Peritoneal endometrial lesion (PEL) and Douglas pouch endometrial lesion (DEL)

	ENDOMETRIOSIS	< 1cm	1 - 3 cm	> 3 cm
Peritoneum	***Superficial***	***1***	***2***	***4***
	Deep	***2***	***4***	***6***
Ovary	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	***Partial***		***Complete***
		4		***40***
	ADHESIONS	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
Ovary	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
Tube	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16

Figure 2

Classification of endometrial lesions in patients with right-sided endometrioma. In addition to the right or left endometriomas that are generally treated as deep endometriosis, we classified the ASRM scores into the following four categories: 1) “same endometrial lesions (SELs)”, including ovarian and tubal

endometrial lesions on the same side as the main ovarian endometrioma; 2) “contralateral endometrial lesions (CELs)”, including ovarian and tubal endometrial lesions on the contralateral side of the main ovarian endometrioma; 3) “peritoneal endometrial lesions (PELs)”; and 4) “Douglas pouch endometrial lesions (DELs)”. For illustration, the classification of SEL (A), CEL (B), PEL (C) and DEL (C) in the REG is shown using the Chart of Revised ASRM score [5]. The scores of SEL, CEL, PEL and DEL are the total values of the scores in each cell, as indicated by an italic letter and thick-bordered box. In the LEG, the scores of SEL and CEL are reversed.