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INTERVENTIONAL

Comparison of the therapeutic efficacy and ovarian reserve between catheter-directed sclerotherapy and surgical excision for ovarian endometrioma

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Abstract

Objectives To compare the efficacies of catheter-directed sclerotherapy (CDS) with 99% ethanol and surgery for ovarian endometrioma and their impact on the ovarian reserve.

Methods From January 2011 to June 2019, 71 patients who underwent surgical excision ($n = 51$) or CDS ($n = 20$) for symptomatic ovarian endometriomas were reviewed. To analyze the effect on the ovarian reserve, serum anti-Müllerian hormone (AMH) levels were compared before and after the procedure. Symptoms, serum cancer antigen 125 (CA-125), lesion size, recurrence, hospitalization, and complications were reviewed retrospectively.

Results During a mean follow-up of 22.3 months (range, 6 to 94 months), no significant difference in symptom relief was found between CDS and surgery (95.0% [19/20] and 92.2% [47/51], respectively, $p > 0.999$). The hospital stay was shorter with CDS than with surgery (2.6 ± 0.6 days and 4.1 ± 0.5 days, respectively, $p < 0.001$). There was no significant difference in serum AMH levels before and after CDS (2.3 (interquartile range (IQR) 1.1–5.3) ng/mL and 2.6 (IQR 0.9–4.9) ng/mL, respectively, $p = 0.243$), but there was a significant decrease in serum AMH in the surgery group (3.0 (IQR 1.3–5.5) ng/mL and 1.6 (IQR 0.7–3.2) ng/mL, respectively, $p < 0.001$). CA-125 decreased in both CDS and surgery groups ($p = 0.001$ and < 0.001, respectively). Two minor complications occurred in the surgery group, while no complication was observed in the CDS group.

Conclusions The therapeutic efficacy of CDS appears to be comparable to that of surgical resection for ovarian endometrioma. Ovarian function was well-preserved, and a shorter hospital stay was required in patients who underwent CDS.

Key Points

- *There was no significant difference in symptom relief between CDS and surgery (95.0% [19/20], 92.2% [47/51], respectively, p > 0.999).*
- *No significant difference in serum AMH levels was seen before and after CDS (2.3 (1.1, 5.3)* ng/mL, 2.6 (0.9, 4.9)* ng/mL, respectively, p = 0.243), whereas serum AMH levels significantly decreased after surgical resection (3.0 (1.3, 5.5)* ng/mL, 1.6 (0.7, 3.2)* ng/mL, respectively, p < 0.001). *Median (25 quartiles, 75 quartiles)*
- *The hospitalization period was shorter with CDS than with surgery (2.6 ± 0.6 days, 4.1 ± 0.5 days, respectively, p < 0.001).*

Keywords Sclerotherapy · Catheters · Ovary · Endometriosis · Ovarian reserve

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Abbreviations

AMH	Anti-Müllerian hormone
CDS	Catheter-directed sclerotherapy
NDS	Needle-directed sclerotherapy
CA-125	Serum cancer antigen 125

Introduction

Endometriosis is defined as endometrial-like tissue outside the normal uterus, commonly involving the ovaries and pelvic peritoneum [1]. The prevalence of endometriosis is 6–10% in women of reproductive age and ~ 50% in women with infertility in the USA [2]. It is associated with chronic pelvic pain and infertility. Dysmenorrhea and dyspareunia are the most commonly reported symptoms [3]. Up to 44% of patients with endometriosis present with ovarian endometrioma [4]. In patients with ovarian endometrioma, infertility is caused by an injury to the healthy ovary and tubo-ovarian structures [5].

Surgical excision is considered to be the standard treatment for endometriosis, but an inevitable decline in the ovarian reserve after surgery has been reported [6]. It is assumed that damage to the normal ovarian tissue or excessive electrocoagulation during surgery adversely affects the ovarian function [6–8]. Ultrasound-guided aspiration and sclerotherapy were introduced as less-invasive procedures in 1988 [9]. To date, sclerotherapy has been performed using a needle, but this has inherent technical limitations, such as instability of the needle during the procedure causing poor aspiration and spillage of endometrial tissue or sclerosing agents into the peritoneal cavity. Due to these reasons, needle-directed sclerotherapy (NDS) showed limited therapeutic efficacy and a relatively high rate of complications and wide range of recurrence rates [10–16]. To overcome the limitations of NDS, catheter-directed sclerotherapy (CDS) was devised, and its technical advantages were translated into better therapeutic outcomes, with little to no damage to the ovarian reserve, in a small prospective study [10].

The objective of this study was to compare the therapeutic efficacies of CDS and surgical excision for ovarian endometrioma and their impact on the ovarian reserve.

Materials and methods

Patients

This retrospective study was approved by the Institutional Review Board of our institution with a waiver of the need to obtain informed consent because of its retrospective nature. From January 2011 to June 2019, electronic medical records and picture archiving and communication system were searched to collect patients who underwent surgery or CDS for symptomatic ovarian endometrioma measuring from 3 to 10 cm. Seventy-one patients were included in this study, excluding those without measured serum AMH (anti-Müllerian hormone), those who were lost to follow-up, or those who had a follow-up period less than 6 months (Fig. 1). To investigate the impact on the ovarian reserve, patients whose serum AMH levels were analyzed before and after CDS or surgery were included. Patients who were lost to follow-up or had a follow-up period of less than 6 months were excluded. The patients' age, previous surgical history for ovarian endometrioma, symptoms, serum cancer antigen 125 (CA-125), lesion size and characteristics, recurrence, hospitalization, follow-up periods, and complications were reviewed. Table 1 shows the baseline characteristics.

Procedure details

The access route was determined based on the visibility of the lesion on ultrasound (US). In cases with a well-visualized lesion on transabdominal US and no intervening vital structures between the abdominal wall and the lesion, transabdominal access was used. Otherwise, the procedure was performed via transvaginal access (Fig. 2). For transvaginal access, patients were placed in a lithotomy position, and the US probe with an in-plane needle guidance adaptor was inserted into the vagina after sterilization with povidone iodine. An 18-gauge, 20-cm needle (Chiba Biopsy Needle; Cook) was used to puncture the endometrioma. After successful puncture of the lesion, a 0.035-in. hydrophilic guidewire (Terumo) was inserted through the needle under fluoroscopy guidance, and the needle was changed for an 8.5-F pigtail catheter (Dawson-Mueller Drainage Catheter; Cook). After meticulous aspiration of the endometrial contents, the contrast agent was injected into the lesion to rule-out rupture of the lesion. Once no rupture was confirmed, 99% ethanol was injected carefully at a quarter of the aspirated volume, and the maximum dose of ethanol was 100 cc. Patients were instructed to change their positions every 5 min (supine, prone, and bilateral decubitus) after their catheters were clamped. The ethanol was aspirated out as much as possible after 20 min, and subsequently, catheters were removed. To rule-out the possibility of malignancy, all patients underwent preprocedural contrast-enhanced magnetic resonance imaging, and the aspirates were sent to the pathology lab for cytologic examination. For those who underwent transabdominal access, the procedure was performed in the same manner, except for their position (supine position for transabdominal access). All surgical resections were performed laparoscopically under general anesthesia. Resection of the endometrioma was performed by aspirating the cystic content and removing the cystic wall by means of a stripping technique.

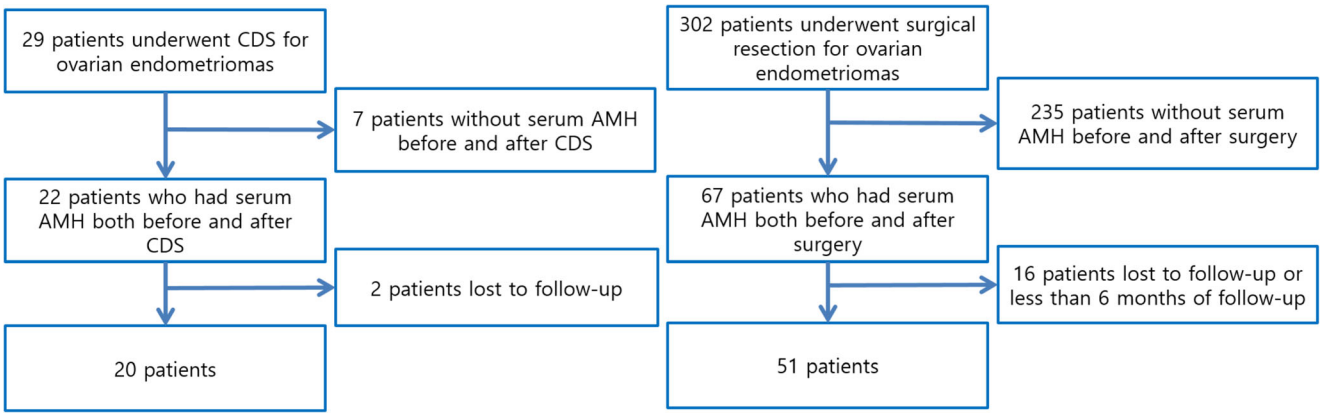

Fig. 1 Flowchart of inclusion and exclusion criteria of patients who underwent catheter-directed sclerotherapy or surgery

Preprocedural MRI

Preprocedural MRI examination (1.5-T Signa HD/HDx; GE Healthcare) of the pelvis was performed for all patients who underwent CDS. Axial and sagittal fast spin-echo T2-weighted images (repetition time msec/effective echo time msec, 4400/120; matrix size, 384 × 224; field of view, 300 × 300 mm; section thickness, 5 mm) and contrast-enhanced sagittal T1-weighted images were obtained. Enhanced images were acquired 2 min after intravenous infusion of 10 cc gadolinium contrast agent (Dotarem; Guerbet) [10].

Data analysis

Patients were followed-up with US 1, 3, and 6 months after CDS/surgery and annually thereafter to assess changes in the cyst size and recurrence. Serum AMH levels before and 6 months after CDS/surgery were measured to observe the impact on the ovarian reserve. Serum CA-125 was reviewed to measure the therapeutic efficacies before and after CDS/surgery at the same time points. Visual analog scale was used to assess pain before and after the procedure. Complications were recorded in all cases.

Statistical analysis

Based on the variable's characteristics, the two-sample *t* test or Mann–Whitney *U* test was used for continuous variables based on normality and the chi-square test or Fisher's exact test for categorical variables. The paired *t* test or Wilcoxon signed-rank test was used to compare serum AMH, CA-125, and lesion size before and after CDS/surgery based on normality. Kolmogorov–Smirnov test was used for testing normality. All statistical analyses were performed using SPSS 25.0 (IBM) software. A p value < 0.05 was considered statistically significant.

Results

The technical success of CDS was 100%, and intra-procedural pain was well-tolerated with non-narcotic analgesics. In the CDS

Table 1 Baseline characteristics of catheter-directed sclerotherapy and surgery

Parameters	CDS ($n = 20$)	Surgery ($n = 51$)	p value
Age (years)	30.6 ± 7.4	33.2 ± 7.3	0.179[a)]
Preprocedural AMH (ng/mL)*	2.3 (1.1, 5.3)	3.0 (1.3, 5.5)	0.766[d)]
Preprocedural CA-125 (U/mL)*	46.2 (25.5, 102.2)	28.7 (23.7, 63.9)	0.097[d)]
Preprocedural lesion size (mm)	58.3 ± 13.7	51.9 ± 20.5	0.083[a)]
Previous surgical history for ovarian endometrioma	8/20 (40.0%)	3/51 (5.9%)	0.001[b)]
Location of lesions			0.769[c)]
Unilateral	14/20 (70.0%)	38/51 (74.5%)	
Bilateral	6/20 (30.0%)	13/51 (25.5%)	
Follow-up periods (months)*	26.9 (9.5, 34.3)	18.2 (10.2, 27.5)	0.588[d)]

AMH, anti-Müllerian hormone; *CA-125*, cancer antigen 125

Mean ± standard deviation; *Median (25 quartiles, 75 quartiles)

[a)] Two-sample *t* test was used; [b)] Fisher's exact test was used; [c)] Pearson's chi-square test was used; [d)] Mann–Whitney *U* test was used

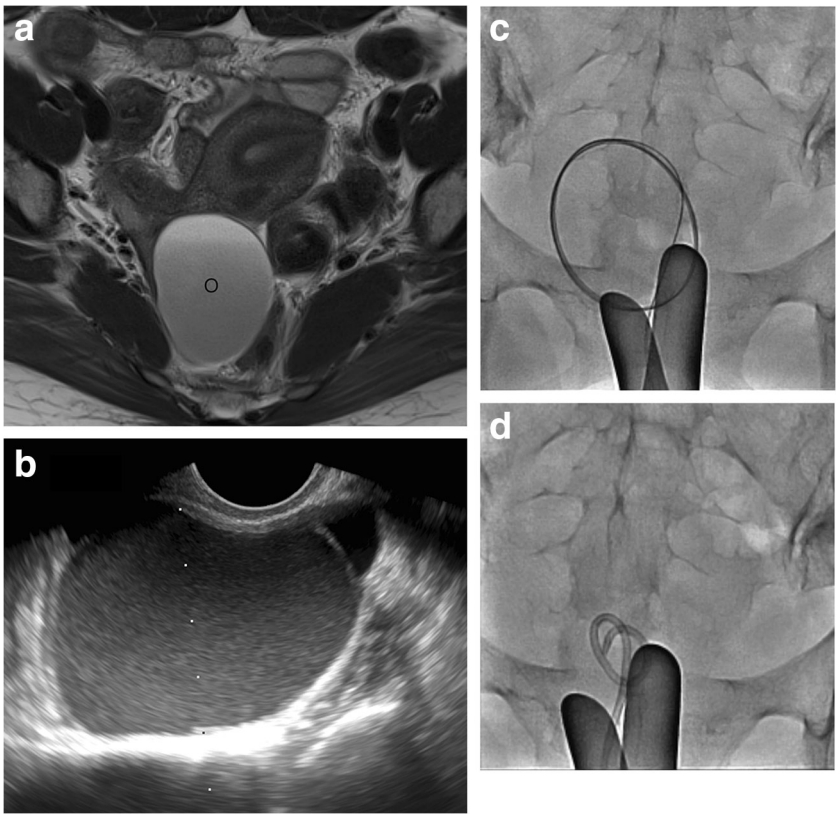

Fig. 2 Catheter-directed sclerotherapy of a 36-year-old woman with primary ovarian endometrioma. **a** The T2-weighted image shows a 5.6-cm, well defined unilocular cystic mass which was diagnosed as endometrioma (O). **b** Transvaginal ultrasound reveals the same cystic lesion which contained heterogenous materials. **c** A 0.035-in. hydrophilic guidewire (Terumo) was inserted in the lesion after puncture using an 18-Gauge needle. **d** An 8.5-F pigtail catheter (Dawson-Mueller Drainage Catheter; Cook) is placed into the lesion

group, all the aspirates consisted of hemosiderin-laden macrophages, which was consistent with endometrioma and negative for malignancy. None of the lesions showed any enhancing solid portions within the cysts on magnetic resonance imaging.

The mean lesion size had decreased after CDS compared with that before CDS ($p < 0.001$). No significant difference in the rates of symptom relief between CDS and surgery ($p > 0.999$) was observed. The mean pain scores in the CDS arm decreased from 5.79 ± 1.36 to 1.26 ± 0.87 ($p < 0.001$). A significant correlation was noted between the rates of size reduction and symptom score reduction ($p = 0.011$) (Fig. 3). There was no significant difference in the serum AMH level before and 6 months after CDS ($p = 0.243$), but a significant reduction in the serum AMH level was observed in the surgical group ($p < 0.001$). Serum CA-125 levels had decreased significantly in both CDS and surgery groups after 6 months ($p = 0.001$ and < 0.001, respectively). Table 2 summarizes the outcomes of CDS and surgery.

During the mean follow-up of 23.7 months, no procedure-related complications or recurrence occurred in the CDS group. There were two minor complications (wound infection), and four cases in the surgery group were recurrent (recurred at 280, 807, 1349, and 1094 days after surgery, respectively) during the mean follow-up of 21.7 months. The CDS group required shorter hospitalization compared with the surgery group ($p < 0.001$). Table 3 summarizes the comparison between CDS and surgery.

Discussion

Ovarian endometrioma is a common, debilitating condition, affecting 17–44% of women with endometriosis [4]. While surgical resection was considered as the mainstay treatment, in this study, the ovarian reserve was well-preserved in patients whose endometriomas were treated with CDS while therapeutic efficacy was comparable to surgery. CA-125 was decreased significantly in the CDS group as well as in the surgery group, and almost all patients experienced symptom relief except only one patient in the CDS group. Also, there were no short-term recurrence and procedure-related complication in the CDS group.

In CDS, the drainage catheter is securely placed into the lesion, and the content can be evacuated more effectively. Furthermore, CDS allows patients to change their position with the catheter clamped, which can maximize the exposure of the cystic wall to ethanol. Sclerotherapy using ethanol showed its efficacy by combinations of cytotoxic damage, coagulation, and cell dehydration [17]. Therefore, the more prolonged exposure of endometriomas to ethanol, the higher chance to maximize cell damage [5]. With these technical advantages, CDS resulted in excellent treatment outcomes in the present study.

Prior studies reported that a decrease in serum AMH, which is a surrogate marker for ovarian reserve, was inevitable with surgery due to damage to the ovary [7, 18]. However,

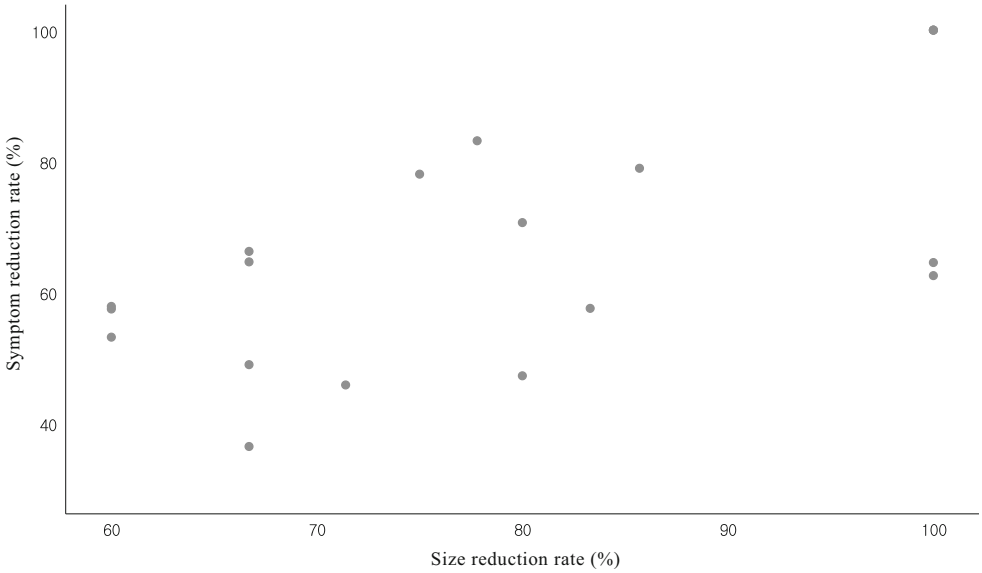

Fig. 3 Scatterplot demonstrates positive relationship between size reduction rate and symptom score reduction rates ($p = 0.571$, $p = 0.011$)

image-guided sclerotherapy targets the lesion only, thus sparing the normal ovarian tissue and minimizing the adverse effect on the ovary. The number of anterior follicles even increased after sclerotherapy for recurrent endometrioma because decreased perfusion to the ovary by the mass had improved after treatment [11, 19]. In this study, it was obvious that the ovarian reserve was well-preserved with sclerotherapy as there was no significant difference in the serum AMH level before and after sclerotherapy.

Surgical excision for recurrent ovarian endometrioma has technical challenges due to adhesion from the initial surgery. In contrast, CDS is not affected by postoperative adhesion as long as the lesion is visualized on US. In the current study, despite the significantly higher proportion of recurrent ovarian endometrioma in the CDS group, the therapeutic efficacy was comparable to that of surgery. Therefore, for such patients, CDS may be particularly useful.

Furthermore, the mean hospital stay was significantly shorter in the CDS group than in the surgery group. This is because CDS was performed under local anesthesia and intraprocedural pain was well-managed with non-narcotic analgesics. This may also suggest the possibility of CDS as a less-invasive alternative to surgery.

There were several limitations to this study. First, the sample size was small, and the follow-up period was short. This is because CDS was first devised 4 years before, and future follow-up data would provide deeper insights into its long-term control of ovarian endometrioma. Second, due to its retrospective study design, some outcomes of interest could not be evaluated. Symptoms were written in descriptive terms in many patients of the surgical arm and objective pain scores were not available in the electronic medical records. Also, although it was obvious that CDS outperformed surgery in terms of preservation of the ovarian reserve, the direct impact of this difference on fertility could not be investigated. Third, how long and what kind of the medical treatment prior to surgery or CDS could not be provided, because the majority of patients were referred from outside hospitals. This might have caused unintentional bias. Finally, there was lack of comparison for patients who were not treated by surgery or CDS.

In conclusion, CDS seems to be as effective as surgery for ovarian endometrioma. Compared with surgical excision, the

Table 2 Outcomes of catheter-directed sclerotherapy or surgery

	Before	After	*p* value
CDS			
Serum AMH (ng/mL)*	2.3 (1.1, 5.3)	2.6 (0.9, 4.9)	0.243[a)]
Serum CA-125 (U/mL)*	46.2 (25.5, 102.2)	21.5 (12.1, 41.6)	0.001[a)]
Lesion size (mm)	58.5 ± 13.9	17.8 ± 12.0	< 0.001[b)]
Surgery			
Serum AMH (ng/mL)*	3.0 (1.3, 5.5)	1.6 (0.7, 3.2)	< 0.001[a)]
Serum CA-125 (U/mL)*	28.7 (23.7, 63.9)	8.8 (6.4, 11.2)	< 0.001[a)]

CDS, catheter-directed sclerotherapy; *AMH*, anti-Müllerian hormone; *CA-125*, cancer antigen 125

Mean ± standard deviation; *Median (25 quartiles, 75 quartiles)

[a)] Wilcoxon signed-rank test was used; [b)] Paired *t* test was used

Table 3 Comparison between catheter-directed sclerotherapy and surgery

	CDS ($n = 20$)	Surgery ($n = 51$)	p value
Symptom relief	19/20 (95.0%)	47/51 (92.2%)	> 0.999[a)]
Hospitalization days	2.6 ± 0.6	4.1 ± 0.5	< 0.001[b)]
Complications	0	2/51 (3.9%)	
Recurrence	0	4/51 (7.8%)	

CDS, catheter-directed sclerotherapy

Mean ± standard deviation

[a)] Fisher's exact test was used; [b)] Two-sample t test was used

ovarian reserve was well-maintained, and shorter hospitalization was required in patients treated with CDS. Future randomized trials are warranted to investigate the long-term effect of CDS and further comparisons with surgery.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Kichang Han.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap Fourteen of the 20 patients who had undergone CDS have been previously reported [13]. The prior study was a single-arm study lacking a control group, whereas in this manuscript, we compared CDS with surgical resection.

Methodology
- Retrospective
- Observational
- Performed at one institution

References

1. Giudice LC (2010) Clinical practice. Endometriosis. N Engl J Med 362:2389–2398
2. Eskenazi B, Warner ML (1997) Epidemiology of endometriosis. Obstet Gynecol Clin North Am 24:235–258
3. Vercellini P, Vigano P, Somigliana E, Fedele L (2014) Endometriosis: pathogenesis and treatment. Nat Rev Endocrinol 10:261–275
4. Chapron C, Vercellini P, Barakat H, Vieira M, Dubuisson JB (2002) Management of ovarian endometriomas. Hum Reprod Update 8:591–597
5. Cohen A, Almog B, Tulandi T (2017) Sclerotherapy in the management of ovarian endometrioma: systematic review and meta-analysis. Fertil Steril 108:117–124.e115
6. Busacca M, Riparini J, Somigliana E et al (2006) Postsurgical ovarian failure after laparoscopic excision of bilateral endometriomas. Am J Obstet Gynecol 195:421–425
7. Raffi F, Metwally M, Amer S (2012) The impact of excision of ovarian endometrioma on ovarian reserve: a systematic review and meta-analysis. J Clin Endocrinol Metab 97:3146–3154
8. Somigliana E, Berlanda N, Benaglia L, Vigano P, Vercellini P, Fedele L (2012) Surgical excision of endometriomas and ovarian reserve: a systematic review on serum antiMüllerian hormone level modifications. Fertil Steril 98:1531–1538
9. Akamatsu N, Hirai T, Masaoka H, Sekiba K, Fujita T (1988) Ultrasonically guided puncture of endometrial cysts–aspiration of contents and infusion of ethanol. Nihon Sanka Fujinka Gakkai Zasshi 40:187–191
10. Han K, Seo SK, Kim MD et al (2018) Catheter-directed sclerotherapy for ovarian endometrioma: short-term outcomes. Radiology 289:854–859
11. Hsieh CL, Shiau CS, Lo LM, Hsieh TT, Chang MY (2009) Effectiveness of ultrasound-guided aspiration and sclerotherapy with 95% ethanol for treatment of recurrent ovarian endometriomas. Fertil Steril 91:2709–2713
12. Noma J, Yoshida N (2001) Efficacy of ethanol sclerotherapy for ovarian endometriomas. Int J Gynaecol Obstet 72:35–39
13. Wang SM, Cai HQ, Dong XQ et al (2015) Correlation between ovarian chocolate cyst and serum carbohydrate antigen 125 level and the effect of ultrasound-guided interventional sclerotherapy on serum carbohydrate antigen 125 level. J Obstet Gynaecol Res 41:92–98
14. Aflatoonian A, Rahmani E, Rahsepar M (2013) Assessing the efficacy of aspiration and ethanol injection in recurrent endometrioma before IVF cycle: a randomized clinical trial. Iran J Reprod Med 11:179–184
15. Gatta G, Parlato V, Di Grezia G et al (2010) Ultrasound-guided aspiration and ethanol sclerotherapy for treating endometrial cysts. Radiol Med 115:1330–1339
16. Ikuta A, Tanaka Y, Mizokami T et al (2006) Management of transvaginal ultrasound-guided absolute ethanol sclerotherapy for ovarian endometriotic cysts. J Med Ultrason (2001) 33:99–103
17. Albanese G, Kondo KL (2010) Pharmacology of sclerotherapy. Semin Interv Radiol 27:391–399
18. Celik HG, Dogan E, Okyay E et al (2012) Effect of laparoscopic excision of endometriomas on ovarian reserve: serial changes in the serum antiMüllerian hormone levels. Fertil Steril 97:1472–1478
19. Lee KH, Kim CH, Lee YJ, Kim SH, Chae HD, Kang BM (2014) Surgical resection or aspiration with ethanol sclerotherapy of endometrioma before in vitro fertilization in infertile women with endometrioma. Obstet Gynecol Sci 57:297–303