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Optimal management of large endometriomas (≥ 4 cm) before IVF: ethanol sclerotherapy, cystectomy, or no intervention?

Yavuz Emre Şükür[1,2*], Necati Berk Kaplan[1], Batuhan Aslan[1,3], Nilüfer Akgün[3,4], Batuhan Özmen[1,2], Murat Sönmezer[1,2], Bülent Berker[1,2], Cem Somer Atabekoğlu[1,2] and Ruşen Aytaç[1,2]

Abstract

Background The optimal management strategy for large (≥ 4 cm) endometriomas prior to in vitro fertilization (IVF) remains uncertain. This study aimed to compare the cumulative live birth rate (CLBR) among three approaches: no intervention, ethanol sclerotherapy (EST), and laparoscopic cystectomy.

Methods This retrospective cohort study included 90 infertile women undergoing their first IVF cycle at a university-based infertility center between 2020 and 2023. Patients were grouped based on endometrioma management: IVF with no intervention (OMA in situ group, $N=39$), IVF after EST (EST group, $N=20$), or IVF after cystectomy (Cystectomy group, $N=31$). The primary outcome was CLBR per initiated cycle. Secondary outcomes included oocyte and embryo yield, fertilization and implantation rates, and cycle cancellation rate. Statistical analysis included one-way ANOVA and chi-square tests, with significance set at $P<0.05$.

Results The EST group demonstrated a significantly higher CLBR (65%) compared to the OMA in situ (30.8%) and cystectomy (29%) groups ($P=0.017$). Oocyte yield was higher in the EST group (10.1 ± 3.9) than in the OMA in situ (5.7 ± 4.3) and cystectomy (4.2 ± 3.5) groups ($P<0.001$). Fertilization and implantation rates were similar across groups, but the number of good-quality embryos was higher following EST. The cycle cancellation rate was greatest in the cystectomy group (35.5%). Fresh embryo transfer pregnancy rates were higher in the EST and cystectomy groups compared to no intervention (66.7% and 55% vs. 32.4%, respectively; $P=0.044$). Ovarian reserve was better preserved in the EST group, with no significant change in AMH levels post-procedure.

Conclusions Ethanol sclerotherapy prior to IVF improves cumulative live birth outcomes compared to both no intervention and cystectomy in patients with large endometriomas. It enhances oocyte yield, reduces cycle cancellations, and preserves ovarian reserve, supporting its use as a favorable management strategy in IVF planning.

Trial registration This study was approved by the Institutional Review Board of Ankara University School of Medicine (Approval ID i018525, Date 17 February 2025) and is retrospectively registered.

Keywords Cumulative live birth rate, Endometrioma, Ethanol sclerotherapy, In vitro fertilization, Ovarian reserve

*Correspondence:
Yavuz Emre Şükür
yesukur@gmail.com
[1]Department of Obstetrics and Gynecology, School of Medicine, Ankara University, Cebeci Hastanesi, Dikimevi, Ankara, Türkiye
[2]Reproductive Health Diagnosis Treatment Education Research and Application Center, Ankara University, Ankara, Türkiye
[3]The Graduate School of Health Sciences, Ankara University, Ankara, Türkiye
[4]Department of Obstetrics and Gynecology, University of Health Science, Etlik City Hospital, Ankara, Türkiye

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Introduction

Endometriosis is a chronic, estrogen-dependent inflammatory disease characterized by the presence of endometrial tissue outside the uterus. The main clinical manifestations are pain and infertility [1]. While the link between endometriosis and infertility is well established, the underlying mechanisms are complex and multifactorial including anatomical alterations in the pelvic cavity, impaired folliculogenesis, granulosa cell dysfunction, immune dysregulation, and defects in fertilization or implantation [2]. Evidence from assisted reproductive technology (ART) studies suggests that endometriosis may also impair oocyte quality through disruptions in steroid metabolism, oxidative stress responses, and cell cycle regulation [3, 4]. Abnormal inflammation, local estrogen production, and progesterone resistance further contribute to reduced endometrial receptivity [5, 6].

Endometriomas can potentially impact IVF outcomes in three keyways: reducing the number of retrievable oocytes, impairing oocyte quality, and decreasing implantation chances. The presence of endometriomas has been linked to reduction in ovarian reserve, likely due to the chronic inflammatory environment they create [7]. Additionally, large endometriomas may limit follicular access during IVF, reducing the number of oocytes retrieved and consequently affecting cumulative outcomes, even if per-embryo transfer success rates remain unchanged [8–10]. Two recent meta-analyses by Gayete-Lafuente et al. and Alshehre et al. evaluated the impact of presence of endometriomas on IVF outcomes and reported similar live birth rates between patients with and without endometriomas [8, 9]. However, their analyses were conducted per cycle rather than cumulatively. Given the observed reduction in the number of oocytes retrieved and good quality embryos, cumulative live birth rates could potentially be diminish. While some studies suggest that endometriomas negatively influence oocyte and embryo quality, two recent meta-analyses indicate no significant impact [8, 9]. To assess their effect on implantation rates, donor oocyte cycles provide the most reliable evidence. A recent meta-analysis suggests a slight negative effect of endometriomas on implantation, though this remains inconclusive [11].

In infertile women with endometriomas scheduled for IVF, laparoscopic cystectomy is recommended if the patient experiences pain or if the endometrioma is expected to complicate oocyte retrieval [10]. If endometriomas negatively impact oocyte and embryo quality or implantation, surgery could potentially improve outcomes. However, laparoscopic cystectomy is known to significantly reduce ovarian reserve [12]. While studies suggest that IVF success rates per embryo transfer or cycle may remain unchanged post-surgery, most available data do not focus on cumulative outcomes [13]. Additionally, although surgery may not alter overall outcomes in the general IVF population, it increases cycle cancellation rates, which could have a particularly detrimental impact on certain patients [14].

Ethanol sclerotherapy (EST), though an established technique for managing endometriomas, has recently gained renewed attention and is increasingly preferred as a preliminary procedure for patients planning IVF [15–21]. Recent studies suggest that IVF outcomes are improved in patients undergoing EST prior to IVF compared to those who do not [20–22]. Furthermore, comparisons between EST and cystectomy before IVF have shown similar or more favorable results for EST [17–19, 23]. However, existing studies have not adequately assessed cumulative success rates.

Briefly, the presence of endometriomas during IVF may reduce the number of oocytes retrieved, leading to fewer embryos for transfer and lower cumulative live birth rates. Laparoscopic cystectomy may improve oocyte quality and implantation, but it also significantly reduces ovarian reserve, potentially further lowering cumulative outcomes. Ethanol sclerotherapy (EST) offers an alternative approach, eliminating endometriomas while better preserving ovarian reserve. This study aims to compare the cumulative live birth rates (CLBR) among three primary approaches for patients with large endometriomas undergoing IVF: IVF with the endometrioma left in situ, IVF after EST, and IVF following laparoscopic cystectomy.

Materials and methods

Study design and patient selection

This single-center retrospective cohort study reviewed data from infertile women with at least one endometrioma ≥ 4 cm who underwent intracytoplasmic sperm injection following a GnRH antagonist cycle at the Infertility Centre, Ankara University Cebeci Hospital, between January 2020 and December 2023. The study protocol was approved by the Institutional Review Board of Ankara University School of Medicine (i01-85-25, 02.17.2025). Patients in the control group underwent IVF with the endometrioma in situ (OMA in situ). Patients in the first study group underwent IVF following ethanol sclerotherapy for endometrioma/s (EST), while those in the second study group underwent IVF following laparoscopic endometrioma cystectomy (Cystectomy). The choice of management strategy for each patient was made at the discretion of the primary physician. Only the first fresh IVF cycle for each patient, along with the frozen-thawed embryo transfer (FET) cycles performed using embryos obtained from that cycle, were included in the study. Data related to both fresh IVF and FET cycles were extracted from patient files and the hospital database. The inclusion criteria were: female age 20–40 years,

a GnRH antagonist cycle, and utilization of all available embryos. The exclusion criteria included: utilization of long or natural cycle protocols, progestin-primed ovarian stimulation, presence of adenomyosis, untreated hydrosalpinx, untreated thyroid dysfunction or hyperprolactinemia, and severe male factor infertility, and an interval of more than 12 months since cystectomy. The 12-month limit was chosen because patients' return after surgery can sometimes be delayed, and beyond this period the potential beneficial effects of cystectomy may diminish, endometriosis may recur, and, in order to minimize the potential impact of the natural decline in ovarian reserve on the outcomes, these patients were excluded.

Ethanol sclerotherapy procedure

All patients underwent transvaginal ultrasound-guided aspiration of one or more endometriomas, as previously described in detail [24]. The procedure was performed by an experienced reproductive surgeon (YEŞ) with the patient in the lithotomy position under sedation or local anesthesia. To prevent pelvic infections, prophylactic antibiotics were administered, consisting of 2 g of cefazolin administered intravenously during the procedure, followed by oral doxycycline twice daily for one week. The size, number, and laterality of the endometriomas were recorded prior to the procedure.

Using ultrasound guidance, a single-lumen 16G needle was employed to puncture the cyst transvaginally. The cyst contents were fully aspirated, and the aspirated volume was documented. The first sample of the aspirated cyst fluid was sent for cytological analysis. The cyst cavity was then flushed with saline solution until the aspirated fluid became clear. If aspiration was challenging due to thick content, flushing with small volumes of saline was initiated earlier. Following this, 96.5% ethanol was injected into the cyst cavity at 60% of the aspirated volume to avoid overdistension, rupture, or leakage. If the cyst ruptured during aspiration or flushing, the procedure was abandoned. If ethanol leakage into the pelvis was suspected, ethanol injection was immediately discontinued, and the leaked ethanol was aspirated from the Douglas pouch. The ethanol was left in the cyst for 10 min before being completely aspirated, and the final volume was recorded. In cases where ethanol loss exceeded 5 mL, patients were monitored in the hospital for at least six hours. As per our clinical protocol, EST patients were scheduled for IVF within 3 months to ensure complete resolution and minimize the risk of recurrence.

Laparoscopic cystectomy procedure

All cystectomies were performed by experienced reproductive surgeons under general anesthesia using a standard laparoscopy technique. After inspection of the pelvic cavity, endometriomas were identified and carefully incised. The cyst wall was stripped from the normal ovarian cortex by traction and counter-traction, aiming to preserve healthy ovarian tissue. Hemostasis was achieved using bipolar cautery with minimal thermal damage, and copious irrigation was applied. The excised cyst wall was retrieved for histopathological examination.

Ovarian stimulation and IVF procedures

Before the initiation of treatment, all patients underwent a transvaginal ultrasound on day 2 of their menstrual cycle, and baseline hormonal profiles were assessed. Ovarian stimulation was carried out using recombinant FSH (Gonal-F; Merck-Serono, Geneva, Switzerland) and/or human menopausal gonadotropin (hMG; Menopur; Ferring GmbH, Wittland, Kiel, Germany), starting on the second day of the menstrual cycle at an initial dose of 225–300 IU/day. The dose was adjusted individually based on ovarian response, as assessed by estradiol levels and ultrasound. The GnRH antagonist cetrorelix 0.25 mg/day (Cetrotide; Merck-Serono, Geneva, Switzerland) was initiated on a fixed schedule starting on the sixth day of stimulation and continued throughout the stimulation period. The final oocyte maturation trigger was administered when at least one follicle reached a diameter of ≥ 18 mm or at least two follicles measured ≥ 17 mm, using one of the following regimens: 250 µg of choriogonadotropin alpha (hCG trigger) (Ovitrelle, Merck-Serono, Bari, Italy), 0.2 mg of triptorelin acetate (GnRH agonist trigger) (Gonapeptyl; Ferring GmbH, Kiel, Germany), or 250 µg of choriogonadotropin alpha combined with 0.2 mg of triptorelin acetate (dual trigger). Transvaginal ultrasound-guided oocyte pick-up (OPU) with a double-lumen needle was performed 36 h after the trigger. Standard intracytoplasmic sperm injection (ICSI) was conducted on metaphase II (MII) oocytes.

The criteria for embryo grading were previously described elsewhere [25]. Briefly, embryos were classified as top quality when they had four or five blastomeres on day 2, at least seven blastomeres on day 3, absence of multinucleated blastomeres, and less than 10% fragmentation at the cleavage stage [26]. Blastocyst-stage embryos were graded based on Gardner and Schoolcraft's criteria, which evaluate the developmental stage of the embryo as well as the morphology of the trophoblast and inner cell mass [27]. Top-quality blastocysts were graded as AA, AB, BA, or BB. In the present study, none of the embryos underwent preimplantation genetic testing for aneuploidies.

Embryo transfer (ET) was performed using soft embryo catheters under transabdominal ultrasound guidance. A maximum of two embryos were transferred in accordance with national regulations on embryo transfer policy. In fresh ET cycles, luteal phase support was initiated on the day of oocyte retrieval with 600 mg/day

of vaginal progesterone (Progestan, 200 mg vaginal capsules; Koçak Farma, Tekirdağ, Türkiye) and continued until the 10th week of gestation for women who achieved clinical pregnancy. In FET cycles, luteal phase support was administered with 800 mg/day of vaginal progesterone (Progestan 200 mg vaginal tablets; Koçak Farma, Tekirdağ, Türkiye) ± daily subcutaneous progesterone (Progestan dex 25 mg; Koçak Farma, Tekirdağ, Türkiye).

Outcome measures

The primary outcome measure was the cumulative live birth rate per initiated IVF cycle. The cumulative live birth rate was defined as the number of deliveries with at least one live birth resulting from one initiated IVF cycle, including all cycles in which fresh and/or frozen embryos are transferred, until one delivery with a live birth occurs or until all embryos are used, whichever occurs first [28]. Live birth was defined by a live birth after 22 weeks of gestation [28]. The secondary outcome measures were the number of mature oocytes collected, fertilization rate, number of top-quality embryos, implantation rate (number of intrauterine gestational sacs divided by the number of transferred embryos), clinical pregnancy rates, and cycle cancellation rate. Clinical pregnancy was defined as the visualization of fetal heartbeat on ultrasound at 7 weeks.

Statistical analyses

Data analyses were performed by using SPSS Version 21.0 (IBM Corporation, Armonk, NYC, USA). Samples were tested with the Shapiro-Wilk test to determine normality of distributions. According to the results, parametric tests were preferred. Continuous variables are presented as mean±standard deviation, and categorical variables are presented as frequency (percentage). Continuous variables were compared with one-way ANOVA test. Categorical variables were compared with the chi-square test or Fisher's exact test where appropriate. A P value of < 0.05 was considered statistically significant. When there is a statistically significant difference, a post hoc analysis was performed in between all group pairs to define the source of statistical significance.

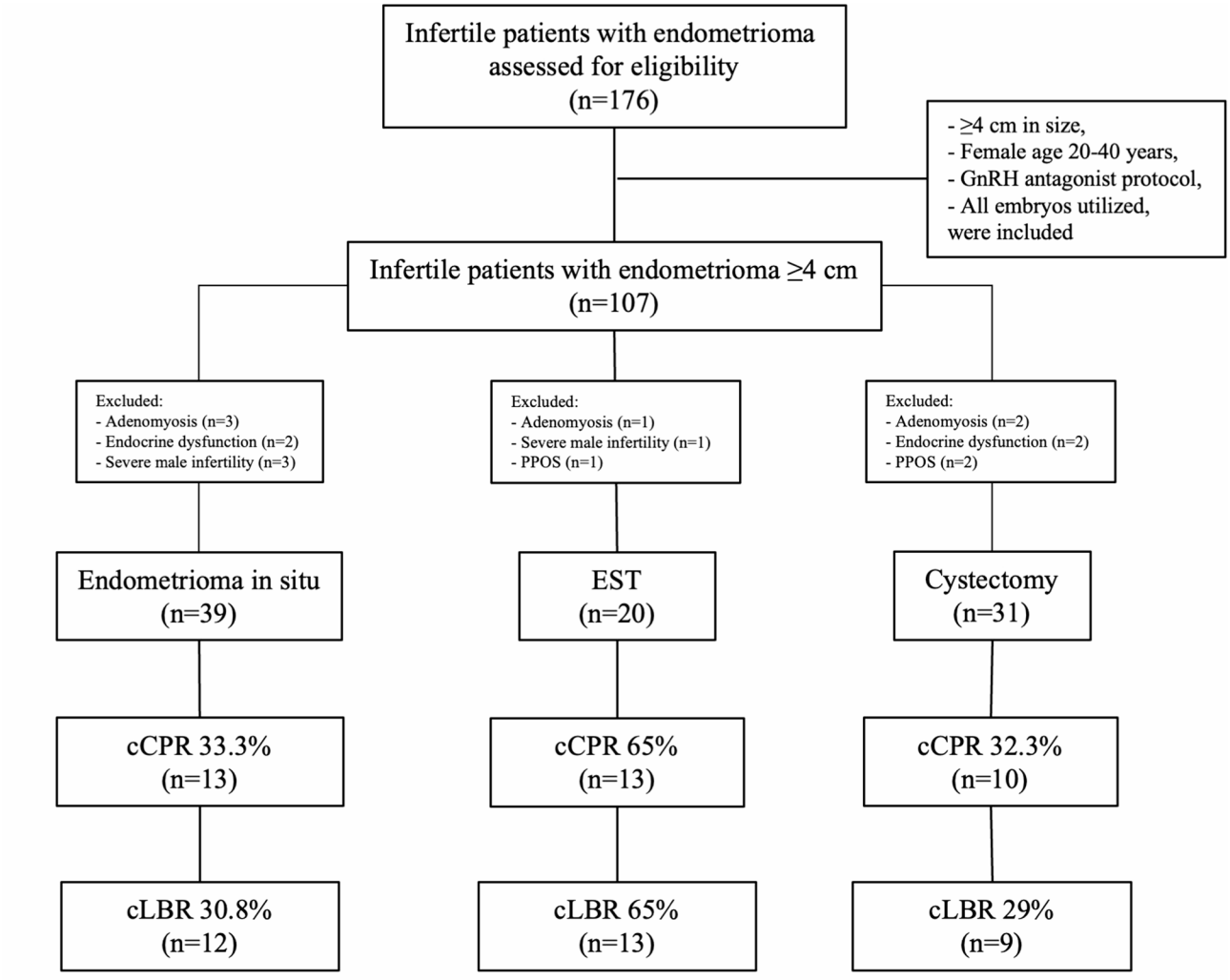
Results

Between January 2020 and December 2023, 176 patients with endometriomas underwent their first IVF cycle. Among them, 107 patients with at least one endometrioma measuring ≥ 4 cm were assessed for eligibility. After applying the inclusion and exclusion criteria, 90 patients were included in the final analysis: 39 patients underwent IVF with endometriomas in situ, 20 patients underwent IVF following EST procedure, and 31 patients underwent IVF following laparoscopic cystectomy (Fig. 1). The demographic characteristics of the groups, including age, BMI, duration of infertility, number of previous IVF cycles, and history of prior endometriosis surgery were comparable. Serum AMH levels at presentation, when IVF was planned, did not differ significantly between groups (Table 1). However, the largest endometrioma was significantly smaller in the OMA in situ group compared to the EST and Cystectomy groups ($P < 0.001$). Additionally, the number of endometriomas and the bilaterality rate were significantly higher in the EST group compared to the OMA in situ and Cystectomy groups ($P = 0.001$ and $P = 0.004$, respectively) (Table 1).

The comparison of IVF cycle characteristics between the groups is summarized in Table 2. All parameters, except baseline AFC, and serum estradiol level on the day of trigger, were comparable among the groups. The baseline AFC was significantly higher in the EST group compared to both the OMA in situ and Cystectomy groups (10.7 ± 5.4 vs. 6.5 ± 3.6 vs. 5.4 ± 2.9, respectively; $P < 0.001$). In the EST group, the serum preoperative and postoperative AMH levels were 2.6 ± 1.5 ng/ml and 2.3 ± 1.5 ng/ml, respectively ($P = 0.576$). In contrast, in the Cystectomy group, the serum preoperative and postoperative AMH levels were 1.9 ± 0.9 ng/ml and 0.9 ± 0.6 ng/ml, respectively ($P = 0.001$).

Table 3 summarizes the comparison of outcome parameters among the groups (Endometrioma in situ, EST, and Cystectomy). The numbers of total oocytes retrieved were 7.4 ± 5.3, 12.6 ± 4.6, and 5.1 ± 3.6, respectively, and the numbers of MII oocytes were 5.7 ± 4.3, 10.1 ± 3.9, and 4.2 ± 3.5, respectively, with both being significantly higher in the EST group ($P < 0.001$). Fertilization rates were similar across groups; however, the numbers of total embryos (2.6 ± 2.7, 3.9 ± 2.5, and 1.4 ± 1.7) and good-quality embryos (2.1 ± 2.1, 2.8 ± 2.1, and 1.3 ± 1.3) were significantly higher in the EST group compared with the Cystectomy group ($P = 0.001$ and $P = 0.020$, respectively). The cycle cancellation rates differed significantly among the groups, with the highest rate observed in the Cystectomy group (12.8% vs. 10% vs. 35.5%; $P = 0.028$). Both implantation rates and pregnancy rates per ET were comparable across the groups. However, the pregnancy rate following fresh ET was significantly lower in the OMA in situ group compared to the other groups ($P = 0.044$). The cumulative CPR's were 33.3% in the OMA in situ group, 65% in the EST group, and 32.3% in the Cystectomy group ($P = 0.035$). Similarly, the CLBR's were 30.8% in the OMA in situ group, 65% in the EST group, and 29% in the Cystectomy group ($P = 0.017$).

No major complications were observed following the EST procedures. One patient was hospitalized one day after the procedure due to mild fever and was treated with intravenous antibiotics. Another patient experienced moderate pelvic pain six hours post-procedure, which was managed with intravenous hydration and



Note: PPOS: progestin primed ovarian stimulation ;EST: ethanol sclerotherapy; cCPR: cumulative clinical pregnancy rate; cLBR: cumulative live birth rate.

Fig. 1 Flow chart of the study population

analgesics. There were no recurrences observed at the time of the IVF procedures. All laparoscopic cystectomies were completed successfully without conversion to laparotomy or major/minor complications, and all patients were discharged on postoperative day 1.

Discussion

The present study was conducted to compare the cumulative outcomes of the first IVF cycle in patients with endometriomas ≥ 4 cm, either with OMA in situ, following EST, or following laparoscopic cystectomy. According to the results of our study, the EST group yielded significantly higher numbers of oocytes, MII oocytes, and good-quality embryos compared to the other two groups. Consequently, the CLBR was also higher in the EST group. However, fertilization and implantation rates were similar across all groups. In the cystectomy group, the higher cycle cancellation rate was a notable finding.

Previous studies on EST have shown considerable variability in technique, patient selection criteria, and follow-up duration, all of which may influence recurrence rates and IVF outcomes [29]. However, previous studies comparing IVF outcomes between EST and direct IVF have consistently reported approximately twice the CPR or LBR in the EST group [20–22]. However, none of these studies assessed cumulative success rates. Unlike our study, they found similar numbers of retrieved oocytes across groups [20–22]. This discrepancy may stem from their inclusion of patients with smaller or unilateral endometriomas, whereas our study specifically focused on patients with larger endometriomas (≥ 4 cm), likely contributing to the higher number of retrieved oocytes

Table 1 Comparison of the demographic characteristics between the study groups

	OMA in situ *N*=39	EST *N*=20	Cystectomy *N*=31	*P* value
Age, years	33±5.5	32.5±4.1	31.6±5.2	0.499
BMI, kg/m^2	23.1±4	25.5±4.1	23.2±3.3	0.054
Duration of infertility, years	3.6±2.5	4.8±2.8	4.4±2.8	0.190
No. of previous pregnancies	0.3±0.6	0.2±0.6	0.3±0.6	0.882
No. of previous IVF cycles	0.6±0.8	0.3±0.7	0.8±0.9	0.112
Previous endometriosis surgery, *n* (%)	2 (5.1)	2 (10)	5 (16.1)	0.313
Baseline serum AMH level, ng/ml	2.1±1.3	2.6±1.5	1.9±0.9	0.219
Largest OMA size, cm	4.5±0.9	6±1.7	5.6±1.3	<0.001[a]
Total no. of OMA's	1.6±0.7	2.5±1.3	1.7±0.8	0.001[b]
Bilateral OMA, *n* (%)	10 (25.6)	14 (70)	15 (48.4)	0.004

EST ethanol sclerotherapy, *BMI* body mass index, *IVF* in vitro fertilization, *OMA* endometrioma

[a] The statistical significance stems from the differences between groups A vs. B (*P*<0.001) and A vs. C (*P*=0.001)

[b] The statistical significance stems from the differences between groups A vs. B (*P*=0.001) and B vs. C (*P*=0.008)

Table 2 Comparison of ovarian stimulation cycle parameters between the study groups

	OMA in situ *N*=39	EST *N*=20	Cystectomy *N*=31	*P* value
Baseline FSH, IU/l	9.2±3	9.1±4.6	10±5.5	0.744
Baseline LH, IU/l	5.7±2.1	6.9±3.7	5.4±3.2	0.259
Baseline estradiol, pg/ml	53.1±29.8	45±10.9	52±38	0.631
Baseline progesterone, ng/ml	0.6±0.3	0.4±0.2	0.6±0.3	0.144
Baseline antral follicle count	6.5±3.6	10.7±5.4	5.4±2.9	<0.001[a]
Gonadotropin starting dose, IU	277±50	255±38	270±63	0.448
Duration of stimulation, days	10.1±1.6	10.7±1.6	9.8±2.3	0.240
Total gonadotropin dose, IU	2701±683	2558±679	2678±1117	0.769
Estradiol on the DoT, pg/ml	1803±1241	2017±703	1246±913	0.033[b]
Progesterone on the DoT, ng/ml	0.9±0.5	1±0.6	1±0.5	0.440
LH on the DoT, IU/l	3.8±3.1	4.1±4.9	5.8±8	0.346
Type of trigger, *n* (%)				0.544
GnRH agonist	3 (7.7)	4 (20)	2 (6.5)	
Recombinant hCG	27 (69.2)	12 (60)	23 (74.2)	
Dual	9 (23.1)	4 (20)	6 (19.4)	

EST ethanol sclerotherapy, *FSH* follicle stimulating hormone, *LH* luteinizing hormone, *OMA* endometrioma, *DoT* day of trigger

[a] The statistical significance stems from the differences between groups A vs. B (*P*=0.001), and B vs. C (*P*<0.001)

[b] The statistical significance stems from the difference between groups B vs. C (*P*=0.043)

Table 3 Comparison of in vitro fertilization cycle outcome parameters

	OMA in situ *N*=39	EST *N*=20	Cystectomy *N*=31	*P* value
No. of oocytes collected	7.4±5.3	12.6±4.6	5.1±3.6	<0.001[a]
No. of MII oocytes collected	5.7±4.3	10.1±3.9	4.2±3.5	<0.001[b]
Fertilization rate, %	71.1±26.9	58.4±19.9	63±27.9	0.205
Total no. of embryos	2.6±2.7	3.9±2.5	1.4±1.7	0.001[c]
No. of grade 1–2 embryos	2.1±2.1	2.8±2.1	1.3±1.3	0.020[d]
Cycle cancellation, n (%)	5 (12.8)	2 (10)	11 (35.5)	0.028
Implantation rate, %	21.7±36	41.7±30.9	34.6±39.4	0.102
Pregnancy per ET, n (%)	14 (30.4)	13 (59.1)	13 (50)	0.055
Pregnancy per fresh ET, n (%)	11 (32.4%)	11 (66.7%)	11 (55)	0.044
Cumulative CPR, n (%)	13 (33.3)	13 (65)	10 (32.3)	0.035
Cumulative LBR, n (%)	12 (30.8)	13 (65)	9 (29)	0.017

EST ethanol sclerotherapy, *OMA* endometrioma, *ET* embryo transfer, *CPR* clinical pregnancy rate, *LBR* live birth rate

[a] The statistical significance stems from the differences between groups A vs. B (*P*<0.001) and B vs. C (*P*<0.001)

[b] The statistical significance stems from the differences between groups A vs. B (*P*<0.001) and B vs. C (*P*<0.001)

[c] The statistical significance stems from the difference between groups B vs. C (*P*=0.001)

[d] The statistical significance stems from the difference between groups B vs. C (*P*=0.017)

and embryos in the EST group. Comparative studies on EST and cystectomy before IVF have reported either similar or superior outcomes for EST [17–19, 23]. Two studies, consistent with our findings, observed a higher oocyte yield in the EST group [19, 23]. A very recent meta-analysis by Lavadia et al. reported that EST was associated with higher numbers of total and MII oocytes, greater embryo yield, and increased clinical pregnancy rates compared with cystectomy [30]. As shown in numerous previous studies, our results confirm that, unlike cystectomy, EST does not negatively impact ovarian reserve [17, 18, 31–34]. Taken together, these findings suggest that EST provides a quantitative advantage in IVF outcomes compared to both cystectomy and no intervention.

According to our study, EST has no impact on oocyte quality. Indirect markers, such as fertilization and high-quality embryo rates, were comparable between the groups. Previous studies have also reported similar fertilization rates when comparing EST with both OMA in situ and cystectomy groups [11, 17, 18, 20, 21]. Only Aflatoonian et al. assessed top-quality embryo rates, finding a significantly higher rate with EST compared to OMA in situ [22]. Furthermore, we did not observe a statistically significant positive effect of EST on implantation rates. Similarly, three other comparative studies assessed

implantation rates but failed to demonstrate a beneficial effect [18, 20, 23].

Our study's most significant finding is the higher CLBR in the EST group, likely due to the increased number of retrieved oocytes and embryos. Another key result is the higher success rate of fresh ET in both the EST and cystectomy groups compared to the OMA in situ group. This may be explained by reduced inflammation following these procedures, as endometriosis is known to induce inflammation and angiogenesis in the uterine environment, potentially affecting endometrial receptivity [35, 36]. Although they did not demonstrate a quantitative benefit, in line with our findings, Rabattu et al. also suggested that the increased CPR associated with EST may be attributed to reduced inflammation, which could improve implantation and oocyte quality [21]. Moreover, supraphysiologic steroid hormone levels during ovarian stimulation may negatively impact endometrial receptivity [35, 37, 38]. A recent meta-analysis also found that frozen-thawed ET leads to better reproductive outcomes than fresh ET in patients with endometriosis [39].

The main strength of our study is the direct comparison of three management approaches for large endometriomas before IVF, with CLBR as the primary outcome, providing a comprehensive evaluation of treatment success. The inclusion of a well-defined cohort and standardized IVF protocols enhances internal validity. Additionally, restricting the study to patients undergoing their first IVF cycle and using an accurate definition of CLBR, along with assessing both quantitative and qualitative markers, further strengthens its findings. However, the retrospective design introduces potential selection bias, and the relatively small sample size and the absence of sample size calculation limits generalizability. Moreover, the imbalance in endometrioma size and number between the groups is another limitation. However, including patients with larger and multiple endometriomas in the EST group reinforces the robustness of the findings. Another limitation of the study was that the choice of management strategy was left to the discretion of the primary physician, which might have been influenced by several factors such as endometriosis severity, symptoms, previous surgical history, and physician experience. Although no physician adhered exclusively to a specific treatment option, in selected patients this may have affected the outcomes. However, given the retrospective design, we were not able to assess these specific factors at the decision-making step, and we had no opportunity to assign patients to treatment groups; instead, we compared IVF outcomes, which were performed in a standardized manner for all patients.

In conclusion, EST before IVF significantly improves CLBR compared to both no intervention and cystectomy in patients with endometriomas ≥ 4 cm. Ethanol sclerotherapy prior to IVF was associated with a higher oocyte and embryo yield and lower cycle cancellation rates without compromising ovarian reserve. These findings suggest that EST may be a preferred approach for optimizing IVF outcomes in infertile patients with large endometriomas. Further prospective studies with larger sample sizes are warranted to confirm these results and assess long-term ovarian function post-EST.

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Authors' contributions
Y.E.Ş., N.B.K., B.A., and M.S. conceptualized the study. B.A., N.A., and N.B.K. contributed to data collection. Y.E.Ş., N.A. and B.Ö. performed statistical analyses. Y.E.Ş., B.A., B.B. and C.S.A. contributed to manuscript editing. B.Ö., M.S., B.B., C.S.A. and R.A. supervised the study. All authors reviewed and approved the final version of the manuscript.

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Data availability
Data supporting the findings of this study are available from the corresponding author, Dr. Yavuz Emre Şükür (yesukur@gmail.com), upon reasonable request. Due to inclusion of ultrasonographic images, the data cannot be shared publicly.

Declarations

Ethics approval and consent to participate
This study was approved by the Institutional Review Board of Ankara University School of Medicine (Approval ID: i01-85-25, Date: 17 February 2025). All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Written informed consent was obtained from all patients. No animal experiments were conducted.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References
1. Eskenazi B, Warner ML. Epidemiology of endometriosis. Obstet Gynecol Clin North Am. 1997;24(2):235–58.
2. Gupta S, Goldberg JM, Aziz N, Goldberg E, Krajcir N, Agarwal A. Pathogenic mechanisms in endometriosis-associated infertility. Fertil Steril. 2008;90(2):247–57.
3. Falconer H, Sundqvist J, Gemzell-Danielsson K, Von Schoultz B, D'hooghe T, Fried G. IVF outcome in women with endometriosis in relation to tumour necrosis factor and anti-Müllerian hormone. Reprod Biomed Online. 2009;18(4):582–8.
4. Orazov MR, Radzinsky VY, Ivanov II, Khamoshina MB, Shustova VB. Oocyte quality in women with infertility associated endometriosis. Gynecol Endocrinol. 2019;35(sup1):24–6.
5. Brosens I, Brosens JJ, Benagiano G. The eutopic endometrium in endometriosis: are the changes of clinical significance? Reprod Biomed Online. 2012;24(5):496–502.

6. Fox C, Morin S, Jeong J-W, Scott RT Jr, Lessey BA. Local and systemic factors and implantation: what is the evidence? Fertil Steril. 2016;105(4):873–84.
7. Kasapoglu I, Ata B, Uyaniklar O, Seyhan A, Orhan A, Oguz SY, et al. Endometrioma-related reduction in ovarian reserve (ERROR): a prospective longitudinal study. Fertil Steril. 2018;110(1):122–7.
8. Gayete-Lafuente S, Vilà Famada A, Albayrak N, Espinós Gómez JJ, Checa Vizcaíno M, Moreno-Sepulveda J. Indirect markers of oocyte quality in patients with ovarian endometriosis undergoing IVF/ICSI: a systematic review and meta-analysis. Reprod Biomed Online. 2024;49(3):104075.
9. Alshehre SM, Narice BF, Fenwick MA, Metwally M. The impact of endometrioma on in vitro fertilisation/intra-cytoplasmic injection IVF/ICSI reproductive outcomes: a systematic review and meta-analysis. Arch Gynecol Obstet. 2021;303(1):3–16.
10. Group motEGC, Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, et al. ESHRE guideline: endometriosis. Hum Reprod Open. 2022;2022(2):hoac009.
11. Paffoni A, Casalechi M, De Ziegler D, Cicinelli E, Somigliana E, Viganò P, et al. Live birth after oocyte donation in vitro fertilization cycles in women with endometriosis: a systematic review and meta-analysis. JAMA Netw Open. 2024;7(1):e2354249.
12. Younis JS, Shapso N, Fleming R, Ben-Shlomo I, Izhaki I. Impact of unilateral versus bilateral ovarian endometriotic cystectomy on ovarian reserve: a systematic review and meta-analysis. Hum Reprod Update. 2019;25(3):375–91.
13. Wu CQ, Albert A, Alfaraj S, Taskin O, Alkusayer GM, Havelock J, et al. Live birth rate after surgical and expectant management of endometriomas after in vitro fertilization: A systematic Review, Meta-Analysis, and critical appraisal of current guidelines and previous Meta-Analyses. J Minim Invasive Gynecol. 2019;26(2):299–e3113.
14. Şükür YE, Özmen B, Yakıştıran B, Atabekoğlu CS, Berker B, Aytaç R, et al. Endometrioma surgery is associated with increased risk of subsequent assisted reproductive technology cycle cancellation; a retrospective cohort study. J Obstet Gynaecol. 2021;41(2):259–62.
15. Akamatsu N, Hirai T, Masaoka H, Sekiba K, Fujita T. Ultrasonically guided puncture of endometrial cysts–aspiration of contents and infusion of ethanol. Nihon Sanka Fujinka Gakkai Zasshi. 1988;40(2):187–91.
16. Honde C, Agostini A, Pivano A, Piechon L, Courbiere B, Netter A. [Management of endometriomas in france: A survey of practices]. Gynecol Obstet Fertil Senol. 2023;51(9):408–14.
17. Alborzi S, Askary E, Keramati P, Moradi Alamdarloo S, Poordast T, Ashraf MA, et al. Assisted reproductive technique outcomes in patients with endometrioma undergoing sclerotherapy vs laparoscopic cystectomy: prospective cross-sectional study. Reprod Med Biol. 2021;20(3):313–20.
18. Antonaci D, Schiavi MC, Carletti V, Yacoub V, Morgani C, Grilli D, et al. Laparoscopic stripping versus endometrioma ethanol sclerotherapy in women with endometrioma awaiting IVF: a long-term analysis of ovarian reserve and pregnancy outcome. Minerva Obstet Gynecol. 2022;74(5):410–8.
19. Lee K-H, Kim C-H, Lee Y-J, Kim S-H, Chae H-D, Kang B-M. Surgical resection or aspiration with ethanol sclerotherapy of endometrioma before in vitro fertilization in infertilie women with endometrioma. Obstet Gynecol Sci. 2014;57(4):297–303.
20. Miquel L, Preaubert L, Gnisci A, Resseguier N, Pivano A, Perrin J, et al. Endometrioma ethanol sclerotherapy could increase IVF live birth rate in women with moderate-severe endometriosis. PLoS ONE. 2020;15(9):e0239846.
21. Rabattu A, Swierkowski-Blanchard N, Paillusson B, Drioueche H, Fauconnier A, Fathallah K. Ethanol sclerotherapy of endometriomas prior to IVF/ICSI improves progressive pregnancy and live birth rate. J Gynecol Obstet Hum Reprod. 2024;53(10):102835.
22. Aflatoonian A, Rahmani E, Rahsepar M. Assessing the efficacy of aspiration and ethanol injection in recurrent endometrioma before IVF cycle: A randomized clinical trial. Iran J Reprod Med. 2013;11(3):179–84.
23. Yazbeck C, Madelenat P, Ayel J, Jacquesson L, Bontoux L, Solal P, et al. Ethanol sclerotherapy: a treatment option for ovarian endometriomas before ovarian stimulation. Reprod Biomed Online. 2009;19(1):121–5.
24. Şükür YE, Aslan B, Varlı B, Özcan P, Daniilidis A, Kalaitzopoulos DR. Ethanol sclerotherapy for endometriomas in infertile women: a narrative review. J Clin Med. 2024;13(24):7548.
25. Yaprak E, Şükür YE, Özmen B, Sönmezer M, Berker B, Atabekoğlu C, et al. Endometrial compaction is associated with the increased live birth rate in artificial frozen-thawed embryo transfer cycles. Hum Fertil (Camb). 2023;26(3):550–6.
26. Medicine ASiR, Embryology ESIGo. The Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting†. Hum Reprod. 2011;26(6):1270–83.
27. Gardner DK. In-vitro culture of human blastocysts. Towards reproductive certainty: fertility and genetics beyond 1999. 1999:378-88.
28. Zegers-Hochschild F, Adamson GD, Dyer S, Racowsky C, de Mouzon J, Sokol R, et al. The international glossary on infertility and fertility care, 2017. Fertil Steril. 2017;108(3):393–406.
29. Cohen A, Almog B, Tulandi T. Sclerotherapy in the management of ovarian endometrioma: systematic review and meta-analysis. Fertil Steril. 2017;108(1):117–e245.
30. Lavadia CMM, Jeong HG, Ryu KJ, Park H. Ovarian reserve and IVF outcomes after ethanol ovarian sclerotherapy in women with endometrioma: a systematic review and meta-analysis. Reprod Biomed Online. 2025;51(1):104840.
31. Azizova A, Ciftci TT, Gultekin M, Unal E, Akhan O, Bozdag G, et al. Ethanol sclerotherapy in the management of ovarian endometrioma: technical considerations for catheter- and needle-directed sclerotherapy. Cardiovasc Intervent Radiol. 2024;47(7):891–900.
32. Ghasemi Tehrani H, Tavakoli R, Hashemi M, Haghighat S. Ethanol sclerotherapy versus laparoscopic surgery in management of ovarian endometrioma; a randomized clinical trial. Arch Acad Emerg Med. 2022;10(1):e55.
33. Koo JH, Lee I, Han K, Seo SK, Kim MD, Lee JK, et al. Comparison of the therapeutic efficacy and ovarian reserve between catheter-directed sclerotherapy and surgical excision for ovarian endometrioma. Eur Radiol. 2021;31(1):543–8.
34. Lee JK, Ahn SH, Kim HI, Lee YJ, Kim S, Han K, et al. Therapeutic efficacy of catheter-directed ethanol sclerotherapy and its impact on ovarian reserve in patients with ovarian endometrioma at risk of decreased ovarian reserve: a preliminary study. J Minim Invasive Gynecol. 2022;29(2):317–23.
35. Evans J, Hannan NJ, Edgell TA, Vollenhoven BJ, Lutjen PJ, Osianlis T, et al. Fresh versus frozen embryo transfer: backing clinical decisions with scientific and clinical evidence. Hum Reprod Update. 2014;20(6):808–21.
36. Velarde MC, Aghajanova L, Nezhat CR, Giudice LC. Increased mitogen-activated protein kinase kinase/extracellularly regulated kinase activity in human endometrial stromal fibroblasts of women with endometriosis reduces 3',5'-cyclic adenosine 5'-monophosphate inhibition of cyclin D1. Endocrinology. 2009;150(10):4701–12.
37. Asoglu MR, Celik C, Bahceci M. Frozen blastocyst transfer improves the chance of live birth in women with endometrioma. Gynecol Endocrinol. 2020;36(10):902–6.
38. Weinerman R, Mainigi M. Why we should transfer frozen instead of fresh embryos: the translational rationale. Fertil Steril. 2014;102(1):10–8.
39. Chang Y, Shen M, Wang S, Li X, Duan H. Association of embryo transfer type with infertility in endometriosis: a systematic review and meta-analysis. J Assist Reprod Genet. 2022;39(5):1033–43.

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