



Published By : PERINASIA
The Indonesian Society of Perinatology

The Outcome of Ethanol Directed Sclerotherapy for the Management of Endometrioma: A Systematic Review



I Gusti Ngurah Agung Trisnu Kamajaya^{1*}, Anom Suardika², Putu Doster Mahayasa²,
Nyoman Gede Budiana³, Gede Bagus Kantwa Abhimantra⁴

¹Obstetric and Gynecologic Resident, Faculty of Medicine, Universitas Udayana, Bali, Indonesia

²Fertility Endocrinology and Reproduction Consultant, Obstetric and Gynecologic Departments, Prof IGNG Ngoerah Hospital/ Faculty of Medicine, Universitas Udayana, Bali, Indonesia

³Oncology Gynecology Consultant, Obstetric and Gynecologic Departments, Prof IGNG Ngoerah Hospital/ Faculty of Medicine, Universitas Udayana, Bali, Indonesia

⁴Medical Doctor, Mataram Faculty of Medicine, Universitas Mataram, Lombok, Indonesia

*Corresponding Author :
I Gusti Ngurah Agung Trisnu Kamajaya;
Obstetric and Gynecologic Resident,
Faculty of Medicine, Universitas Udayana, Bali, Indonesia;
kamajayatr@gmail.com

Received: 2024-08-02
Accepted: 2024-10-09
Published: 2024-11-06

ABSTRACT

Background and Objectives: Ovarian endometriomas, commonly known as chocolate cysts, are prevalent gynecological conditions associated with chronic pelvic pain and infertility. Current standard treatment, laparoscopic cystectomy, poses risks such as reduced ovarian reserve. Ethanol-directed sclerotherapy has emerged as a minimally invasive alternative aiming to preserve ovarian tissue while treating endometriomas. This systematic review evaluates the outcome of ethanol directed sclerotherapy for the management of endometrioma.

Methods: Following PRISMA guidelines, databases including PubMed, EMBASE, and Cochrane were searched in January 2024 using "endometrioma and sclerotherapy." Inclusion criteria encompassed studies reporting success rate (SR), RR, and pregnancy rate (PR) post-treatment. Nine studies involving 499 patients were analyzed.

Results: Ethanol sclerotherapy demonstrated >80% SR in six studies and <30% RR in seven studies, indicating efficacy in reducing recurrence. However, its impact on ovarian reserve remains inconclusive. Pregnancy outcomes were inconsistently reported, with one study achieving 100% PR, while others ranged from 0% to >30%. Variability in techniques, such as ethanol concentration and retention time, likely influenced outcomes.

Conclusions: Ethanol sclerotherapy offers a promising alternative to surgery, showing lower RR and potential preservation of ovarian function. Despite these benefits, inconsistencies in procedural protocols and limited data on long-term fertility outcomes necessitate further research. Standardized guidelines and larger cohort studies are essential to establish sclerotherapy's role in endometrioma management, especially for fertility preservation.

Keywords: Ovarian Endometrioma, Ethanol Directed Sclerotherapy, Recurrence Rate and Succession Rate.

Cite This Article: Kamajaya, I.G.N.A.T., Suardika, S., Mahayasa, P.D., Budiana, N.G., Abhimantra, G.B.K. 2024. The Outcome of Ethanol Directed Sclerotherapy for the Management of Endometrioma: A Systematic Review. *Indonesian Society Of Perinatology* 5(2): 62-66. DOI: 10.51559/inajperinatol.v5i2.56

INTRODUCTION

Endometriosis is a common estrogen-dependent inflammatory gynecological disorder characterized by the abnormal presence of endometrial tissue outside the uterine cavity. Endometriomas, primarily located in the ovaries, represent a more advanced stage of the disease. These lesions, often referred to as chocolate cysts due to the thick, dark brown fluid they contain, can cause chronic pain, dyspareunia, dysmenorrhea, and infertility, frequently necessitating surgical management. This review explores the evaluation and treatment of endometriomas, highlighting the critical role of interprofessional collaboration in diagnosing and managing patients with this condition. Endometriomas indicate a

more severe progression of endometriosis and may result in complications, including reduced ovarian reserve.¹

The treatment of ovarian endometriomas aims to alleviate symptoms that diminish quality of life, such as dysmenorrhea while safeguarding ovarian reserve by minimizing ovarian damage through hormonal therapies or surgical approaches. Milder forms of endometriosis can be effectively managed using oral contraceptive pills, various progesterone formulations (e.g., oral pills or intrauterine devices), gonadotropin-releasing hormone (GnRH) agonists (e.g., leuprolide), or androgenic agents (e.g., danazol). Once a patient's endometriosis progresses to the point of developing an endometrioma, surgical intervention is

often favored. Surgical excision remains the usual therapy; however, it is certain that electrocoagulation or the removal of healthy ovarian tissue around the endometrioma would result in a decrease in ovarian reserve. Research indicates that women have reduced levels of anti-Müllerian hormone (AMH) after cystectomy, a hormone used by reproductive experts to assess ovarian reserve. Reportedly, 2 to 3% of individuals experience ovarian failure after the removal of bilateral endometriomas.¹ Consequently, these are significant concerns when evaluating the appropriateness of surgery for each patient, considering their reproductive aspirations.

Numerous research teams have investigated various approaches for

the treatment of endometrioma. Sclerotherapy is among the most prevalent treatments. Sclerotherapy involves injecting alcoholic substances into the endometrioma's pseudocapsule in order to destroy it.² Ethanol sclerotherapy has been shown to retain ovarian reserve by precisely targeting endometriomas without damaging normal ovarian tissue. Furthermore, a significant reduction in cyst size alleviates the mass impact on the ovary and correlates with improved ovarian reserve.³ According to a recent meta-analysis assessing the effectiveness of ultrasound-guided sclerotherapy for endometrioma, it is a secure and practical method for managing pain, infertility, and recurrence.⁴

A sclerosing agent should be injected into the cyst by the practitioner, followed by either flushing or retention of the solution to ensure effective treatment.⁴ Bacterial surface proteins may be denatured and the lipid components of their capsules dissolved by hydrosoluble dehydrating antiseptic solutions. Ethanol is often chosen among sclerosing medicines because of its exceptional efficacy in treating hepatic and renal cysts. Sclerotherapy is usually well tolerated by patients and may be done under either local or general anaesthesia. Its benefits—such as quick recovery, affordability, and scheduling simplicity—make it a viable option for minimally invasive procedures such as ethanol sclerotherapy for ovarian endometriomas.² The outcome of ethanol-directed sclerotherapy in the treatment of endometrioma is assessed in this systematic study.

MATERIALS AND METHODS

Since this study didn't use any human participants for interventions, it was exempt from ethical approval. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement's recommendations were followed in the pre-design of the technique. Patients having at least one ovarian endometrioma that was diagnosed by imaging or surgery, the study published in the last ten years were the subject of the included research. The interventions analyzed were sclerotherapy using ethanol or similar sclerosing agents, compared with surgical

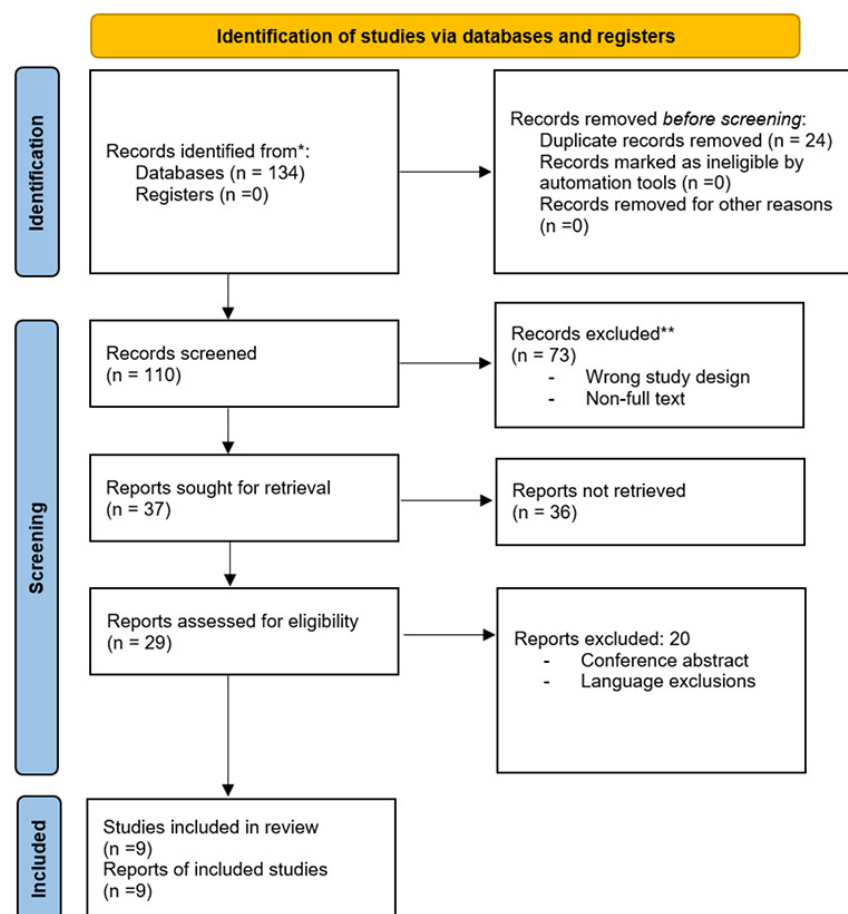


Figure 1. Prisma Flowchart.

interventions, conservative management, or no treatment. Outcomes of interest included success rate (SR), defined as the proportion of healed patients among the total treated; recurrence rate (RR), representing the proportion of patients experiencing recurrence during follow-up; and pregnancy rate (PR), reflecting the proportion of women achieving pregnancy among those trying to conceive. Eligible study designs included randomized controlled trials (RCTs), cohort studies (prospective or retrospective), case-control studies, and systematic reviews with original data reporting.

Studies were excluded if they were non-original (e.g., editorials or commentaries), preclinical or animal studies, abstract-only publications, or articles not published in English. Additionally, studies without sufficient data on relevant outcomes were excluded. A comprehensive search was conducted in January 2024 using PubMed, EMBASE, Scopus, Google Scholar,

ClinicalTrials.gov, and the Cochrane Central Register of Controlled Trials. Search terms included "Endometrioma," "Ovarian cyst," "Sclerotherapy," "Ethanol," "Recurrence rate," "Pregnancy rate," and "Success rate," combined using Boolean operators (AND, OR). The search strategy was adapted for each database, and only studies published in English were considered. Grey literature and unpublished studies were identified by reviewing conference abstracts and contacting authors when additional data were needed.

A full-text review of papers judged possibly eligible was done after two independent reviewers screened titles and abstracts to determine research eligibility. Discussion was used to settle any disagreements. Standardised forms were used to obtain data on research characteristics, population demographics, interventions, comparators, and results. The research selection procedure,

including the justifications for exclusions at each level, is depicted in the PRISMA flowchart (Figure 1). Potential conflicts of interest were evaluated for each included study, and SR, RR, and PR were computed as percentages. Where appropriate, risk rates and 95% CIs were also examined.

RESULTS

The database search initially identified 134 articles that matched the search criteria. After excluding records without full-text availability, duplicates, and studies

with unsuitable designs, 37 articles were deemed eligible. Of these, 29 met the inclusion criteria and were incorporated into the systematic review. Among these, 9 were non-comparative, single-arm studies focusing exclusively on sclerotherapy. Table 2 summarizes the countries where the studies were conducted, the publication years, study designs, number of participants, substances used, and procedural characteristics. The publication years ranged from 2014 to 2022, with a total of 499 patients with endometriomas

included in the analysis.

Based on the characteristics of these patients, it was found that the average patient diagnosed with endometrioma was 30 years old and above, with the largest cyst reaching 8.7 ± 3.9 cm. This condition can also cause infertility which was evaluated in two studies in this article. A total of 499 patients were included in this systematic review from nine of the selected studies presented the Success Rate (SR), Recurrence Rate (RR), and Pregnancy Rate (PR). These

Table 1. Risk of Bias Analysis

Study	Years	Selection Bias	Performance Bias	Detection Bias	Risk of Bias
Garcia-Tejedor et al., ⁵	2015	Low	Low	Moderate (limited reporting on PR)	Low
Begum et al., ⁶	2015	Low	Moderate (variable ethanol use)	Moderate	Low
Wang et al., ⁷	2014	Low	Low	Moderate (PR not reported)	Low
Han et al., ³	2018	Moderate (small sample size)	Low	Moderate	Low
Aflatoonian et al., ⁸	2020	Moderate (retrospective design)	Low	Moderate	Moderate (incomplete follow-up)
Miquel et al., ⁹	2020	Low	Moderate	Moderate	Low
Huang et al., ¹⁰	2021	Moderate (non-randomized cohorts)	Moderate	Low	Low
Lee et al., ¹¹	2022	Moderate (small sample size)	Low	Low	Moderate (limited follow-up)
Meng et al., ¹²	2022	Low	Moderate (unique isolation method)	Moderate (PR not reported)	Low

Table 2. Characteristics of studies included

Author,	Years	Country	Study Type	Procedure	Substance
Garcia-Tejedor et al., ⁵	2015	Spain	Prospective cohort	US-guided sclerotherapy	Ethanol -Instilled 66% of cyst fluid volume
Begum et al., ⁶	2015	Bangladesh	Prospective cohort	US-guided sclerotherapy	Ethanol- 95%. Instilled and removed 75% of aspirated fluid.
Wang et al., ⁷	2014	China	Prospective cohort	US-guided sclerotherapy	Ethanol- 95%. Instilled 50% of cyst fluid volume
Han et al., ³	2018	South Korea	Prospective cohort	Catheter-directed sclerotherapy	Ethanol- 95%. Instilled 25% of cyst fluid volume
Aflatoonian et al., ⁸	2020	Iran	Retrospective cross-sectional	Sclerotherapy with retention of ethanol (n = 27); no retention (n=16)	Ethanol- 98%. Instilled 60% of cyst fluid volume
Miquel et al., ⁹	2020	France	Retrospective cohort	US-guided sclerotherapy	Ethanol- 96%. Instilled 60% of cyst fluid volume
Huang et al., ¹⁰	2021	Taiwan	Retrospective cross-sectional	Sclerotherapy with retention of ethanol and CA-125 91 U/mL (n = 44); no retention and CA-125 91 U/mL (n = 80)	Ethanol- 95%. Instilled variable 3–10 mL of cyst fluid volume
Lee et al., ¹¹	2022	South Korea	Retrospective cohort	Catheter-directed sclerotherapy	Ethanol- 99%. Instilled 25% of cyst fluid volume
Meng et al., ¹²	2022	China	Prospective cohort	US-guided pelvic artificial isolation with fluid	Ethanol- 95%. Instilled 33% of cyst fluid volume

Table 3. Patient characteristics

Author	Years	Age (Years)	Cyst Size (Cm)	Duration infertility (Years)
Garcia-Tejedor et al., ⁵	2015	37 ± 5.8	6.58 ± 1.64mm	NA
Begum et al., ⁶	2015	32.28 ± 2.17	6.75 ± 1.64 cm	NA
Wang et al., ⁷	2014	38 ± 12	6.8 ± 1.7 cm	NA
Han et al., ³	2018	30.1 ± 6.1	5.8 ± 2.2	NA
Aflatoonian et al., ⁸	2020	31.47 ± 4.93	4.52 ± 1.27	7.95 ± 4.08
Miquel et al., ⁹	2020	EST group: 31.5 ± 4.5 Non-EST group: 33.0 ± 3.8	NA	EST group: 4.4 ± 3.1 Non-EST group: 4.3 ± 2.4
Huang et al., ¹⁰	2021	Retained group: 31.1 Non-retained group: 29.3	Retained group: 5.5 ± 1.4 Non-retained group: 5.8 ± 1.7	NA
Lee et al., ¹¹	2022	36.8 ± 5.0	8.7 ± 3.9	NA
Meng et al., ¹²	2022	35	6.35	NA

Note: Ethanol sclerotherapy (EST); Non- Ethanol sclerotherapy (NEST)

studies consist of interventions ranging from catheter-directed sclerotherapy, Sclerotherapy with retention of ethanol, and US-guided sclerotherapy. A total of six studies presented 100% SR, while one study presented a >80% SR and < 80% data in sclerotherapy with ethanol instilled of cyst fluid. The RR found 5 studies with 0-30% and one study with more than 30% recurrence rate in which retention of ethanol sclerotherapy was the procedure after 12 months of follow-up. Regarding the reproductive outcomes, one study reported a 100% pregnancy rate (PR), while three studies observed PRs exceeding 30%. In contrast, one study reported a PR of less than 30%, including a study with a 0.0% PR following ethanol injection at two-thirds of the cyst fluid volume. These results are detailed in **Table 4**.

DISCUSSION

One treatment that is becoming more popular for endometriomas is sclerosing. According to the findings, using this strategy results in a higher SR. Recurrence rates (RR), which address the chronic nature of the pathology while minimising treatment-related events, and pregnancy rates (PR), which indirectly assess potential iatrogenic damage caused by the treatment, should be the main focus of any meaningful comparison between surgical techniques and sclerotherapy, in our opinion. Sclerotherapy for endometriomas is linked to a varied RR, ranging from 0.0% to 44.1%, according to the findings from this systematic review. Differences in the approach, such as the selection of

Table 4. Clinical and Reproductive outcomes after sclerotherapy of ovarian endometrioma.

Author	Years	Success Rate (%)	Recurrence Rate (%)	Pregnancy Rate (%)
Garcia-Tejedor et al., ⁵	2015	100	12.1	0.0
Begum et al., ⁶	2015	79.2	11.3	33.9
Wang et al., ⁷	2014	100	0.0	N/A
Han et al., ³	2018	100	0.0	100
Aflatoonian et al., ⁸	2020	N/A	44.1	39.5
Miquel et al., ⁹	2020	87.0	2.7	37.3
Huang et al., ¹⁰	2021	N/A	22.5	23.3
Lee et al., ¹¹	2022	100	5.5	N/A
Meng et al., ¹²	2022	100	N/A	N/A

the sclerosing agent, its concentration, the volume infused, and the retention period, may be the cause of variation in the results, especially with regard to RR and PR. Ethanol, a sclerosing agent, damages the pseudo capsule of endometrioma, resulting in cytotoxicity, thrombosis, and hypertonic dehydration in the cells.^{1,3} It appears that the complete degradation of the pseudo capsule's cytoarchitecture may be linked to lengthy ethanol retention times and minor dilutions. However, due to data heterogeneity among investigations, it was not possible to determine the best ethanol retention length or dilution percentage. It is crucial to highlight that women with endometriomas often demonstrate a diminished ovarian reserve, which may contribute to a decreased response to Assisted Reproductive Technology (ART) in terms of pregnancy outcomes.²

Nevertheless, the ovarian tissue and antral follicle count are influenced by surgical interventions, as evidenced by the modifications of Anti-Müllerian Hormone (AMH).² Recurrent surgeries

may lead to the development of adhesion syndrome, a condition that can significantly impact fertility. Similarly, ethyl alcohol instillation carries the risk of causing follicular injury. However, the considerable variability among studies poses challenges in establishing an optimal dose and administration duration that maximizes efficacy while minimizing toxicity. Investigating adjuvant treatment options following sclerotherapy could be a valuable approach to enhancing pregnancy rates (PR). For instance, higher doses of gonadotropins might be beneficial for women with preserved ovarian reserve. Furthermore, patient selection remains a critical factor in determining the most appropriate treatment approach. Sclerotherapy may serve as a suitable alternative for managing isolated endometriomas, whereas cases involving multiple endometriomas or severe endometriosis often require surgical intervention.^{1,3}

Sclerotherapy may be a realistic choice, especially in circumstances where more

invasive surgery is not an option, or for women who have ovarian tissue damage or are at risk of iatrogenic injuries. Future studies may investigate the use of liquid biopsy or microbial composition analysis to identify better candidates most likely to benefit from sclerotherapy.² These findings could play a significant role in personalising the therapy of patients with ovarian endometriomas by applying molecular techniques to uncover critical traits, allowing the selection of the most appropriate treatment strategy.^{3,5-12}

The primary limitation of this systematic review is the limited number of randomized trials directly comparing sclerotherapy with surgery. Additionally, some included studies involved small patient populations, and procedural heterogeneity may have increased the risk of bias and confounding factors. Furthermore, the term “sclerotherapy” encompasses a variety of techniques that differ in the choice of substance and method of administration, making it challenging to contextualize the findings. Despite these limitations, our results provide novel insights, suggesting that sclerotherapy may offer lower recurrence rates (RR) and improved pregnancy rates (PR) compared to surgical interventions.

CONCLUSION

Sclerotherapy offers a low incidence of postoperative complications and serves as a safe alternative for patients contraindicated for complex surgery, particularly those with diminished ovarian reserve or prioritizing fertility preservation. While surgical interventions generally show lower recurrence rates and more defined long-term outcomes, our analysis indicates that sclerotherapy achieves comparable recurrence and pregnancy rates when tailored to a patient's preoperative condition. To optimize treatment outcomes, future research should standardize ethanol dosage and retention time, explore adjuvant therapies, and develop biomarkers or imaging techniques for better patient selection. Long-term studies with larger cohorts and randomized trials are essential to refine clinical guidelines and expand treatment options for women with ovarian endometriomas.

DISCLOSURE

Author Statement

The authors declare that all the research and manuscript preparation was conducted with adherence to ethical standards and professional guidelines. The study does not involve direct intervention on human subjects, and all systematic review processes complied with PRISMA recommendations.

Funding

No specific funding was received for conducting this study. The authors carried out this work as part of their academic and professional commitments.

Conflict of Interest

The authors declare no conflict of interest related to the study, authorship, or publication of this manuscript.

Authors Contribution

The authors contributed as follows: I Gusti Ngurah Agung Trisnu Kamajaya, led the conceptualization, literature search, clinical studies, data acquisition, analysis, statistical work, and manuscript preparation. Anom Suardika contributed to conceptualization, design, manuscript editing, and review and acted as a guarantor. Putu Doster Mahayasa supported conceptualization, intellectual content, clinical studies, manuscript editing, and review and also acted as a guarantor. Nyoman Gede Budiana participated in clinical studies, intellectual content, and manuscript review. Gede Bagus Kantwa Abhimantra conducted the literature search, data acquisition, analysis, statistical work, and manuscript preparation.

REFERENCES

1. Hoyle AT, Puckett Y. Endometrioma. 2024.
2. Castellarnau Visus M, Ponce Sebastia J, Carreras Collado R, Cayuela Font E, Garcia Tejedor A. Preliminary Results: Ethanol Sclerotherapy After Ultrasound-Guided Fine Needle Aspiration Without Anesthesia in the Management of Simple Ovarian Cysts. *J Minim Invasive Gynecol.* 2015;22(3):475–82. Available from: <http://dx.doi.org/10.1016/j.jmig.2014.12.158>
3. Han K, Seo SK, Kim M-D, Kim GM, Kwon JH, Kim HJ, et al. Catheter-directed Sclerotherapy for Ovarian Endometrioma: Short-term Outcomes. *Radiology.* 2018;289(3):854–9.

Available from: <http://dx.doi.org/10.1148/radiol.2018180606>

4. Kim GH, Kim PH, Shin JH, Nam IC, Chu HH, Ko H-K. Ultrasound-guided sclerotherapy for the treatment of ovarian endometrioma: an updated systematic review and meta-analysis. *Eur Radiol.* 2021;32(3):1726–37. Available from: <http://dx.doi.org/10.1007/s00330-021-08270-5>
5. García-Tejedor A, Castellarnau M, Ponce J, Fernández M, Burdio F. Ethanol sclerotherapy of ovarian endometrioma: a safe and effective minimal invasive procedure. Preliminary results. *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2015;187:25–9. Available from: <http://dx.doi.org/10.1016/j.ejogrb.2015.02.004>
6. Begum MR, Ehsan M, Khan F, Ehsan N, Santa MSB, Sharmin F. Sclerotherapy with Ethanol: An Effective and Safe Alternative to Potentially Complex Surgical Treatment of Recurrent Ovarian Endometrioma. *Journal of South Asian Federation of Obstetrics and Gynaecology.* 2015;7(2):97–101. Available from: <http://dx.doi.org/10.5005/jp-journals-10006-1335>
7. Wang S, Cai H, Dong X, Fan Q, Wang L, Shao X, et al. 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. *Journal of Obstetrics and Gynaecology Research.* 2014;41(1):92–8. Available from: <http://dx.doi.org/10.1111/jog.12491>
8. Aflatoonian A, Tabibnejad N. Aspiration versus retention ultrasound-guided ethanol sclerotherapy for treating endometrioma: A retrospective cross-sectional study. *Int J Reprod Biomed.* 2020;18(11):935–42. Available from: <https://pubmed.ncbi.nlm.nih.gov/33349801>
9. 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–e0239846. Available from: <https://pubmed.ncbi.nlm.nih.gov/32986747>
10. Huang L, Chang M-Y, Shiau C-S, Hsieh T-T. Changes in anti-müllerian hormone after ultrasound guided aspiration and ethanol sclerotic therapy of ovarian cyst. *Taiwan J Obstet Gynecol.* 2021;60(3):509–12. Available from: <http://dx.doi.org/10.1016/j.tjog.2021.03.021>
11. 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. Available from: <http://dx.doi.org/10.1016/j.jmig.2021.08.018>
12. Meng B, Xu M. Pelvic Artificial Isolation with Ultrasound-Guided Fluid: A New Technique In Ovarian Endometriotic Cyst Transabdominal Sclerotherapy. *Med Sci Monit.* 2022;28:e937855–e937855. Available from: <https://pubmed.ncbi.nlm.nih.gov/36303417>



This work is licensed under a Creative Commons Attribution