

Ovarian reserve after endometrioma surgery

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Abstract

Objective. This study was designed to analyze the deleterious effect of endometriosis on ovarian reserve after surgery by studying anti-Müllerian hormone (AMH) levels. **Materials and method.** This is a systematic review that included observational studies and randomized clinical trials published in English between 2015 and 2019. We included 17 studies that reported AMH levels in patients undergoing laparoscopic surgery for endometrioma, measured preoperatively and postoperatively. **Results.** Seventeen studies met the inclusion criteria. A significant decrease in AMH levels was observed in the short-, medium- and long-term postoperative periods compared to baseline AMH levels. However, there were no differences between postoperatively immediately and one year after surgery. Postoperative AMH levels were significantly reduced in bilateral endometriomas compared to unilateral cases. Also, patients with endometriomas, compared to patients with other benign ovarian conditions, had a more important decline in AMH levels. The same was observed in cases of bilateral cystectomy compared to vaporization with bipolar energy or laser. A greater decrease in postsurgical AMH was also observed with bipolar energy hemostasis compared to suture and hemostatic agents. **Conclusions.** Endometrioma surgery has a negative effect on postoperative AMH levels. Bilateral endometriomas and those greater than 7 cm are associated with a significant decrease in AMH. The mechanical removal of healthy tissue and the destruction of the ovarian cortex may explain the reduction in ovarian reserve. **Keywords:** anti-Müllerian hormone, endometriosis, endometrioma, laparoscopic surgery, ovarian reserve

Submission date:
 15.05.2024
 Acceptance date:
 24.05.2024

Rezerva ovariană după chirurgia endometrioamelor

Suggested citation for this article: Costache CR, Mandi DM, Gorecki GP, Costache-Outas MC, Mitran M, Sima RM, Burcos T. Ovarian reserve after endometrioma surgery. *Ginecologia.ro*. 2024;44(2):24-34.

Rezumat

Obiectiv. Acest studiu a fost conceput pentru a analiza efectul dăunător al endometriozei asupra rezervei ovariene după intervenția chirurgicală, prin studierea nivelurilor hormonului antimüllerian (AMH). **Materiale și metodă.** Această revizuire sistematică include studii observaționale și studii clinice randomizate publicate în limba engleză între anii 2015 și 2019. Am inclus 17 studii care au raportat nivelurile AMH la pacienți care au suferit intervenții chirurgicale laparoscopice pentru endometriom, măsurate preoperatoriu și postoperatoriu. **Rezultate.** Șaptesprezece studii au îndeplinit criteriile de includere. S-a observat o scădere semnificativă a nivelurilor AMH în perioadele postoperatorii pe termen scurt, mediu și lung, comparativ cu nivelurile AMH de bază. Cu toate acestea, nu au existat diferențe între valorile imediate postoperatorii și cele la un an postchirurgical. Nivelurile postoperatorii de AMH au fost semnificativ reduse în endometrioamele bilaterale comparativ cu cazurile unilaterale. De asemenea, pacientele cu endometrioame, comparativ cu pacientele cu alte afecțiuni ovariene benigne, au avut o scădere mai importantă a nivelului AMH. Același lucru a fost observat în cazurile de chistectomie bilaterală, comparativ cu vaporizarea cu energie bipolară sau cu laser. S-a observat, de asemenea, o reducere mai mare a nivelului AMH postchirurgical la hemostaza de energie bipolară, comparativ cu agenții de sutură și hemostază. **Concluzii.** Chirurgia endometriozei are un efect negativ asupra nivelurilor postoperatorii de AMH. Endometrioamele bilaterale și cele mai mari de 7 cm sunt asociate cu o scădere semnificativă a nivelului AMH. Îndepărtarea mecanică a țesutului sănătos și distrugerea cortexului ovarian pot explica reducerea rezervei ovariene. **Cuvinte-cheie:** hormon antimüllerian, endometrioză, endometriom, chirurgie laparoscopică, rezervă ovariană

Introduction

Endometriosis is a benign, estrogen-dependent disease characterized by inflammation and the presence of stromal tissue and endometrial glands outside the uterine cavity. Endometriomas are cystic lesions that develop in the ovary, with a prevalence of around 10% in the general female population of reproductive age. However, endometrial implants can also be found throughout the abdomen, including the pelvic peritoneum, uterosacral ligaments, fallopian tubes, bowel, previous surgical incisions and, in rare cases, in distant locations such as the cerebellum. The clinical presentation varies, being independent of the lesions' extent. While 20-30% of patients remain asymptomatic, others may experience

hypogastric pain, dysmenorrhea, dyspareunia, chronic pelvic pain, menstrual disorders, and infertility. The preferred surgical techniques for endometriomas include laparoscopic decapsulation with suture or bipolar coagulation of the remaining tissue for bleeding control. Lately, many authors analyzed the deleterious effect of endometriomas surgery on ovarian reserve linked to the risk of premature ovarian failure secondary to destroying the ovarian tissue during the surgery^(1,2). Ovarian reserve is defined as the potential of conceiving a normal pregnancy⁽³⁾, and it is determined based on the levels of serum FSH, estradiol, inhibin B and anti-Müllerian hormone (AMH), along with the analysis of follicular count by ultrasound exam^(2,4). Endometriomas are preferred to

be reduced by laparoscopic cystectomy by many surgeons due to advantages such as a reduced recurrence rate and improved ovarian response to stimulation⁽⁵⁾. Literature indicates that factors like cyst size, recurrence, bilaterality, surgical techniques, surgeon expertise and hemostasis methods can influence the treatment results. Injury to and the residual presence of ovarian tissue near the endometriotic cyst wall are potential pre-surgical risks, particularly compounded in cases of bilateral endometriomas. The main complication associated with cystectomy is the damage to surrounding healthy ovarian tissue. This concern has led to a focus on developing surgical techniques that minimize the negative impacts on ovarian reserve. One mainly cause of this effect is the accidental destruction of healthy ovarian tissue surrounding the cyst's pseudocapsule during electrosurgical coagulation used for hemostasis^(6,7).

Ovarian reserve can be effectively indicated by anti-Müllerian hormone. Very low or undetectable levels of

serum AMH are associated with conditions such as early ovarian aging and premature ovarian failure, respectively⁽⁸⁾. Furthermore, AMH levels stay relatively stable throughout the menstrual cycle, unlike other ovarian hormones which fluctuate significantly. This stability indicates that anti-Müllerian hormone may be the most reliable single marker for monitoring ovarian aging. To maintain ovarian function and avoid follicular damage, new techniques for controlling bleeding are being introduced. These include suturing, plasma-jet vaporization, and the application of various hemostatic agents^(9,10). Recent research suggests that surgery for endometriosis adversely affects ovarian reserve, as shown by post-operative evaluations of AMH levels and antral follicle counts. However, there is still no consensus on whether the impact on ovarian reserve is caused by the disease itself, its severity, or surgery-related factors, including the type of surgical procedure and the hemostatic techniques employed^(4,11-13).

Table 1 Studies included in the review

Editor	Country	Years	Study	Participants	Grade
VIGNALI, 2015 ⁽¹¹⁾	ITALY	2009-2010	PROSPECTIVE COHORT	22	9
SAITO, 2018 ⁽²⁾	JAPAN	2011-2013	PROSPECTIVE COHORT	62	8
MUZII, 2019 ⁽¹⁴⁾	ITALY	2015-2016	PROSPECTIVE COHORT	52	8
SALIOGLU, 2016 ⁽⁴⁰⁾	TURKEY	2013-2014	PROSPECTIVE CASE CONTROL	67	7
KIM, 2017 ⁽¹⁰⁾	SOUTH KOREA	2011-2012	PROSPECTIVE COHORT	75	9
IWASE, 2016 ⁽¹²⁾	JAPAN	2008-2009	RANDOMIZED CLINICAL TRIAL	20	9
CHUN, 2016 ⁽¹⁶⁾	TAIWAN	2010-2013	PROSPECTIVE COHORT	65	8
ERGUN, 2015 ⁽¹⁷⁾	TURKEY	2011-2013	PROSPECTIVE COHORT	50	7
SHAO, 2016 ⁽¹⁸⁾	CHINA	2012-2013	PROSPECTIVE COHORT	80	8
MEHDIZADEH KASHI, 2017 ⁽¹⁹⁾	IRAN	2012-2013	PROSPECTIVE COHORT	70	8
KOVACEVIC, 2018 ⁽²⁰⁾	SERBIA	2013-2016	PROSPECTIVE COHORT	54	7
WANG, 2019 ⁽²¹⁾	CHINA	2014-2017	PROSPECTIVE COHORT	171	5
CANADIANI, 2018 ⁽²⁸⁾	ITALY	2017-2018	RANDOMIZED CLINICAL TRIAL	60	6
GIAMPAOLINO, 2015 ⁽²²⁾	ITALY	2012-2014	RANDOMIZED CLINICAL TRIAL	76	7
SONG, 2015 ⁽²⁴⁾	SOUTH KOREA	2011-2014	PROSPECTIVE COHORT	125	8
ZHANG, 2016 ⁽²⁵⁾	CHINA	2013	RANDOMIZED CLINICAL TRIAL	207	9
CHOI, 2018 ⁽²⁶⁾	SOUTH KOREA	2014-2016	RANDOMIZED CLINICAL TRIAL	80	9

This study aimed to evaluate the impact of endometrioma surgery on ovarian reserve by monitoring anti-Müllerian hormone levels at various intervals before and after the procedure. It also investigated the influence of laparoscopic cystectomy on ovarian reserve concerning the size and side of the lesions. Furthermore, the study compared the effects of laparoscopic surgery for endometrioma versus benign ovarian conditions on ovarian reserve, and it assessed the impact of different hemostatic techniques used during laparoscopic surgery for endometrioma on ovarian reserve.

Materials and method

This literature review did not involve human subject intervention; hence, it did not require approval from an Ethics Review Committee. This systematic review examined observational studies that assessed the impact of endometrioma surgery on ovarian reserve, as measured by AMH levels. We conducted searches across MEDLINE, SCOPUS, PubMed and Cochrane databases, spanning from 2015 to January 2019. Additionally, we reviewed references from relevant studies.

Table 2 Summary of results

Outcome		Mean Difference (95% CI)	Participants	Number of studies
Postoperative versus preoperative AMH	Short term	-2.16 (95% CI; -2.94 to -1.38)	90	3
	Medium term	-1.31 (-1.68 to -0.93)	34	1
	Long term	-2.16 (95% CI; -2.21 to -1.1)	90	3
	Short term versus long term	0.09 (95% CI; -0.08 to 0.30)	180	3
Postoperative AMH Endometrioma versus other benign ovarian pathology	Short term	-1.56 (95% CI; -2.45 to -0.67)	117	2
	Medium term	-1.77 (95% CI; -2.15 to -1.40)	187	3
Postoperative AMH Bilateral versus unilateral endometrioma	Short term	-1,4 (95% CI; -2.11 to -0.69)	34	1
	Medium term	0.14 (95% CI; -0.14 to 0.42)	109	2
	Long term	0.44 (95% CI; 0.06 to 0.83)	192	3
Postoperative AMH according to size	Endometrioma >7 cm versus <7 cm	-0.50 (95% CI; -0.65 to -0.35)	197	2
Postoperative AMH according to surgical technique	Bipolar ablation versus unilateral cystectomy	0.39 (95% CI; -1.62 to 2.4)	68	2
	Bipolar ablation versus bilateral cystectomy	0.4 (95% CI; -0.37 to 1.17)	26	1
	Laser ablation versus cystectomy	0.5 (95% CI; 0.01 to 0.99)	60	1
Postoperative AMH according to hemostatic technique	Suture versus bipolar energy	0.52 (95% CI; 0.35 to 0.68)	434	3
	Sealing agents versus bipolar energy	0.35 (95% CI; 0.18 to 0.52)	80	1
	Ultrasound versus bipolar energy	0.00 (-0.32 to 0.24)	138	2

Our search strategy utilized terms related to ovarian endometriosis, gynecological laparoscopy, endometriosis surgery and AMH, tailored to fit the specific syntax of each database used. The review encompassed retrospective and prospective observational studies, as well as randomized clinical trials that documented AMH levels before and after laparoscopic surgery for endometrioma. There were included in the study patients with benign ovarian disease and those who did not receive surgical treatment. The criteria for selecting these studies are detailed in Table 1.

The analysis focused solely on evaluating AMH levels, and excluded studies assessing different variables linked to ovarian reserve. Outcomes related to reproduction, such as spontaneous pregnancy rates or results from assisted reproductive technologies, were not considered. Additionally, patients who underwent laparoscopic surgery for other types of endometriosis, whether superficial or deep, were excluded from this study.

The outcomes were evaluated based on postoperative AMH levels in various contexts. AMH levels were measured in nanograms per milliliter, with standard deviation (SD) used for variability. Preoperative AMH levels served as the baseline. Short-term AMH was assessed within one month following surgery, medium-term AMH was measured between one and six months after surgery, and long-term AMH was measured at six months or more after the surgery.

Results

The initial search produced 66 articles. Of these, 49 were discarded during the title and abstract screening phase. Additional six articles were identified from the references of key publications. Ultimately, 17 studies satisfied the inclusion criteria, and were incorporated into the analysis. The results are summarized in Table 2.

Impact of laparoscopic cystectomy on ovarian reserve in cases of ovarian endometrioma: a comparison of postoperative AMH levels with baseline levels

Data from three studies compared the AMH levels before and short term after the surgery, with a total of 90 participants. Employing a random effects model, the analysis demonstrated a mean difference (MD) of -2.16 (95% CI; -2.94 to -1.38; $I^2 = 24%$) between short-term postoperative AMH levels and baseline levels (Figure 1).

The same studies, with 90 patients, compared the AMH levels before and long term after the surgery. It demonstrated a mean difference of -2.16 (95% CI; -2.21 to -1.1; $Q=77%$) between long-term postoperative AMH levels and baseline AMH levels (Figure 2).

Thus, we analyzed the selected studies, with 90 patients in the long-term postoperative AMH group and 90 patients in the short-term AMH group. A fixed effects analysis revealed a mean difference of 0.09 (95% CI; -0.08 to 0.30; $I^2 = 40%$) when comparing long-term to short-term postoperative AMH levels (Figure 3).

Table 3 Laparoscopic cystectomy – statistical data

Study or subgroup	Postop. short-term Mean	SD	Total	Preop. Mean	SD	Total	Weight	Mean Difference IV, random, 95% CI	Year
Vignal, 2015	1.67	1.56	22	3.98	3.27	22	23%	[-3.82, -0.80]	2015
Saito, 2017	0.5	0.5	34	3.1	1.7	34	42.38%	[-3.20, -2.00]	2017
Muzii, 2019	1.93	1.36	34	3.39	2.43	34	34.63%	[-2.40, -0.52]	2019

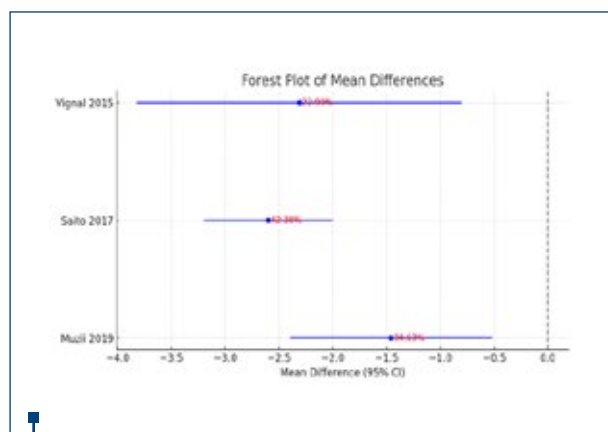


Figure 1. Comparison of short-term postoperative AMH to baseline AMH

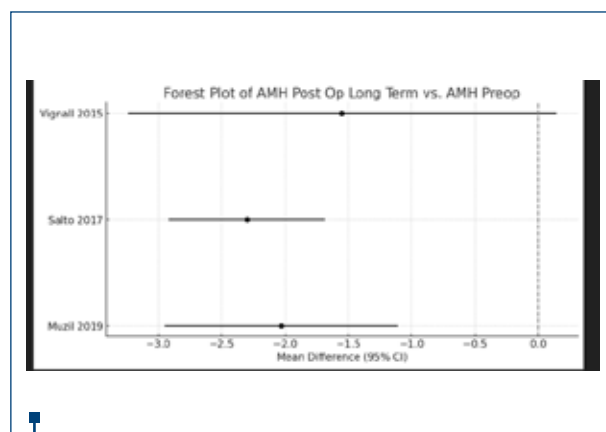


Figure 2. Comparison of long-term postoperative AMH to baseline AMH

Table 4 Comparison between baseline AMH levels and long-term AMH levels

Study	AMH postop. long term	SD	Total	AMH preop.	SD preop.	Weight (%)
Vignall, 2015	2.43	2.39	22	3.98	3.27	24.44%
Salto, 2017	0.8	0.7	34	3.1	1.7	37.78%
Muzii, 2019	1.36	1.27	34	3.39	2.43	37.78%

Table 5 Comparison between the AMH levels short term and long term after surgery

Study or subgroup	AMH long term Mean	SD	Total	AMH short term Mean	SD	Total	Recalculated weight	Mean Difference	95% CI	Year
Vignal, 2015	2.43	2.39	22	1.67	1.56	22	4.5%	0.76	[-0.43, 1.95]	2015
Salto, 2017	0.8	0.7	34	0.5	0.5	34	78.7%	0.30	[0.01, 0.59]	2017
Muzil, 2019	1.38	1.27	34	1.93	1.36	34	16.8%	-0.55	[-1.18, 0.08]	2019

1. Impact of laparoscopic cystectomy on ovarian reserve based on lesion laterality

There was only one study, with a total of 10 patients having bilateral endometriomas and 24 patients with unilateral endometriomas. The statistical analysis indicated that postoperative AMH levels were lower in patients with bilateral endometriomas compared to those with unilateral endometriomas immediately after surgery (MD -1.4; 95% CI; -2.11 to -0.69).

We found two studies, with a total of 43 patients having bilateral endometriomas and 66 patients with unilateral endometriomas. The statistical data indicated lower medium-term postoperative AMH levels in patients with bilateral endometriomas compared to those with unilateral endometriomas (MD 0.14; 95% CI; -0.14 to 0.42; $I^2 = 79.55\%$).

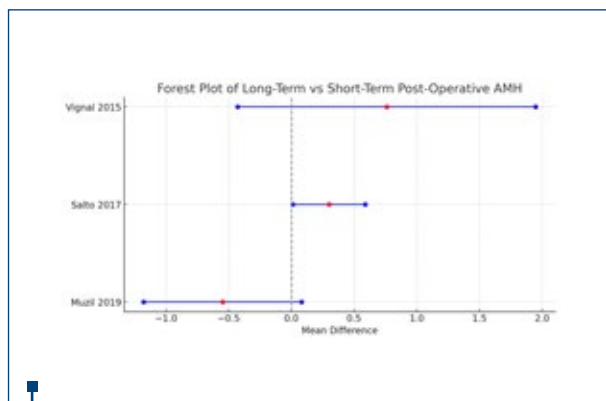


Figure 3. Long-term AMH levels compared to short-term postoperative AMH levels

Analyzing the AMH on the long term after surgery in patients with unilateral endometriomas compared to bilateral, we found that the AMH levels were lower in patients with bilateral endometriomas compared to those with unilateral endometriomas (MD 0.44; 95% CI; 0.06 to 0.83; $I^2 = 60.7\%$) – Figure 4. Three studies, totaling 74 patients with bilateral endometriomas and 118 patients with unilateral endometriomas, were found.

2. Endometriomas on ovarian reserve relative to benign ovarian conditions

We analyzed the AMH postsurgical levels on patients diagnosed with endometriosis compared to other benign ovarian conditions, and it was revealed that patients with endometriomas had lower postoperative AMH levels compared to those without endometriomas in the short term (Mean Difference -1.56; 95% CI; -2.45 to -0.67; $I^2 = 63\%$) – Figure 5. The two studies included 60 patients in the endometrioma group and 57 in the non-endometrioma group.

Three studies, comprising 119 patients with endometriomas and 68 without endometrioma, indicated lower medium-term AMH, defined as AMH levels at six months postoperative, in the endometrioma group (Mean Difference -1.77; 95% CI; -2.15 to -1.40; $I^2 = 50.44\%$) – Figure 6.

3. Influence of lesion size on ovarian reserve

Two studies, with 96 patients with endometriomas larger than 7 cm and 101 patients with endometriomas smaller than 7 cm, indicated lower postoperative AMH levels in the larger endometrioma group on the short term (Mean Difference -0.50; 95% CI; -0.65 to -0.35; $I^2 = 0\%$) – Figure 7.

Table 6 Bilateral versus unilateral endometriomas – statistical data

Study	Year	Bilateral Mean	Bilateral SD	Bilateral Total	Unilateral Mean	Unilateral SD	Unilateral Total	Weight (%)
Shao, 2016	2016	3.05	1.99	32	4.43	2.13	36	35.42
Kashi, 2017	2017	2.18	1.32	25	2.21	1.32	45	36.46
Kovacevic, 2018	2018	0.98	0.91	17	1.43	1.01	37	28.12

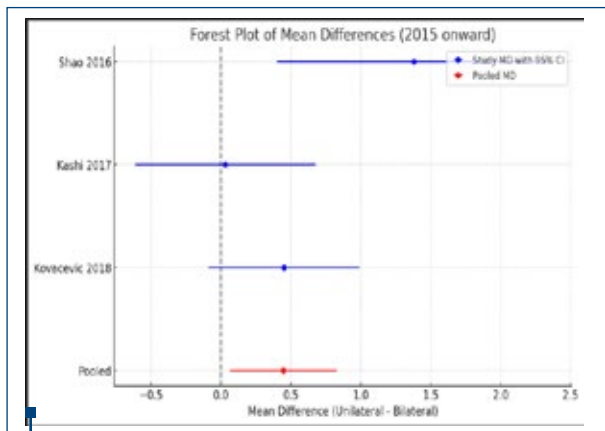


Figure 4. Long-term AMH in bilateral versus unilateral endometriomas

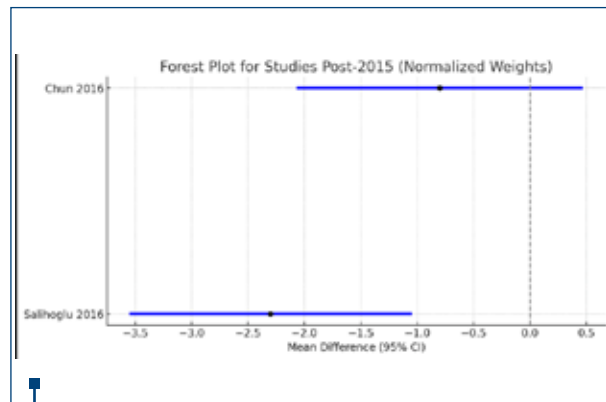


Figure 5. Postoperative AMH levels in endometriomas compared to those without endometrioma in the short term

Table 7 Endometriomas versus benign ovarian conditions – short-term AMH

Study or subgroup	Mean (endo-metrioma)	SD (endo-metrioma)	Total (endo-metrioma)	Mean (no endo-metrioma)	SD (no endo-metrioma)	Total (no endo-metrioma)	Weight (%)
Chun, 2016	3.59	1.83	26	4.39	2.64	24	49.18
Sallhoglu, 2016	2.5	1.6	34	4.8	3.3	33	50.82

Table 8 Endometriomas versus benign ovarian conditions – medium-term AMH

Study	Mean (endo-metrioma)	SD (endo-metrioma)	Total (endo-metrioma)	Mean (no endo-metrioma)	SD (no endo-metrioma)	Total (no endo-metrioma)	Mean Difference	95% CI	Recalculated weight (%)
Ergun, 2015	1.07	0.83	26	2.57	2.11	24	-1.50	[-2.40, -0.60]	28.50
Kim, 2017	2.8	0.2	59	4.9	1	16	-2.10	[-2.59, -1.61]	38.73
Muzii, 2019	1.38	1.27	34	2.63	1.6	28	-1.25	[-1.98, -0.52]	32.77

Table 9 AMH in cystectomy by lesion size

Study	Group size (n)	Mean AMH	SD	Mean Difference (95% CI)	Year
Ergun, 2015	>7 cm (9)	0.65	0.67	-0.65 [-1.24, -0.06]	2015
	<7 cm (17)	1.3	0.83		
Wang, 2019	>7 cm (87)	0.83	0.42	-0.49 [-0.65, -0.33]	2019
	<7 cm (84)	1.32	0.62		
Total	>7 cm (96)			-0.50 [-0.65, -0.35]	
	<7 cm (101)				

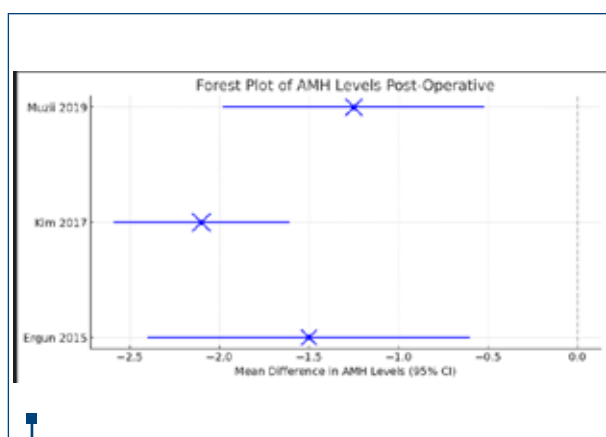


Figure 6. Medium-term postoperative AMH levels in endometrioma versus benign disease

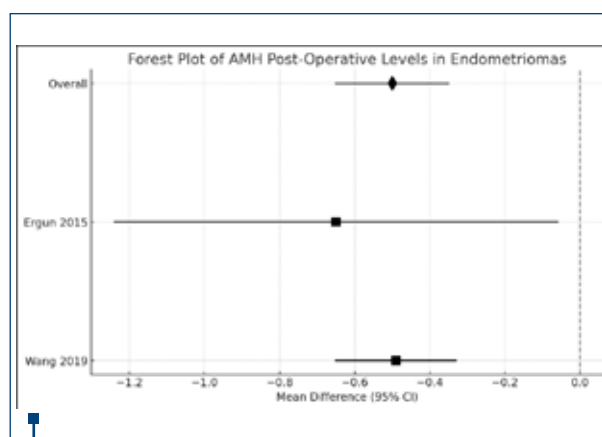


Figure 7. AMH in endometriomas larger than 7 cm versus smaller than 7 cm

Table 10 AMH levels after vaporization versus unilateral cystectomy

Study or subgroup	Vaporization Mean	Vaporization SD	Vaporization Total	Cystectomy Mean	Cystectomy SD	Cystectomy Total	Mean Difference (IV, Fixed, 95% CI)
Giampaolino, 2015	5.18	1.08	11	4.82	0.98	11	0.36 [-0.50, 1.22]
Salto, 2017	2.8	3.3	12	2.1	1.7	24	0.70 [-1.29, 2.69]

4. Surgical technique impact on ovarian reserve in patients with endometriomas

Two studies, involving a total of 33 patients treated with bipolar energy vaporization and 35 patients undergoing unilateral cystectomy, were analyzed. The analysis showed no differences in AMH levels post-procedure between the two groups (Mean Difference 0.39; 95% CI; -1.62 to 2.4; $I^2 = 0\%$) – Figure 8.

Sixteen patients treated with bipolar energy vaporization and ten patients undergoing bilateral cystectomy showed higher postoperative AMH levels in the bipolar energy group (Mean Difference 0.4; 95% CI; -0.37 to 1.17)^(2,27).

The AMH levels after laser vaporization versus cystectomy were analyzed in two studies having each group 30 patients, revealing higher postoperative AMH in the laser group (MD 0.5; 95% CI; 0.01 to 0.99)⁽²⁸⁾.

5. Hemostatic technique effect on ovarian reserve

Postoperative AMH based on sutured hemostasis versus bipolar energy hemostasis

Three studies, with a total of 225 patients benefiting of sutured hemostasis and 209 patients with bipolar energy hemostasis, revealed higher postoperative AMH levels after sutured hemostasis (MD 0.52; 95% CI; 0.35 to 0.68; $I^2 = 78.5\%$) – Figure 9.

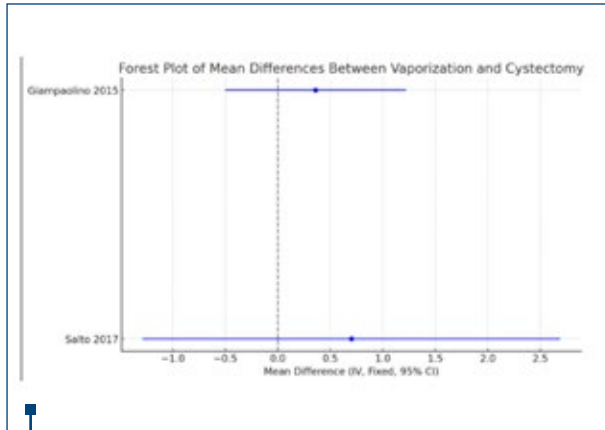


Figure 8. AMH levels following vaporization with bipolar energy versus unilateral cystectomy

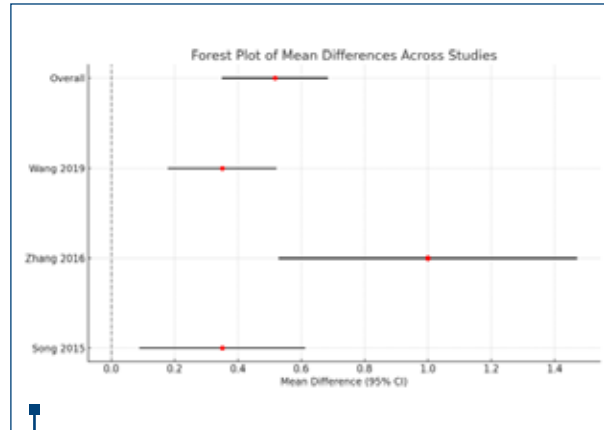


Figure 9. AMH levels after sutured hemostasis versus bipolar energy hemostasis

Table 11 AMH levels after suture versus bipolar energy hemostasis

Study or subgroup	Suture Mean	Suture SD	Suture Total	Bipolar coagulation Mean	Bipolar coagulation SD	Bipolar coagulation Total	Adjusted weight	Mean Difference IV, Random, 95% CI	Year
Song, 2015	2.32	0.83	63	1.97	0.615	62	35.5%	0.35 [0.09, 0.61]	2015
Zhang, 2016	3	1.8	69	2	0.9	69	25.6%	1.00 [0.53, 1.47]	2016
Wang, 2019	1.27	0.61	93	0.92	0.55	78	38.9%	0.35 [0.18, 0.52]	2019

The hemostatic agents are preferred to bipolar energy hemostasis, as showed by Choi (2018), in his study including 40 patients in each group.

A study with 69 patients having ultrasound hemostasis and another 69 patients having bipolar energy hemostasis revealed no significant differences in post-operative AMH levels between the groups (Mean Difference 0.00; 95% CI; -0.32 to 0.32)^(29,30).

Discussion

Main results

In this study, we conducted a systematic review of 17 studies, involving 1336 patients, to evaluate the impact of laparoscopic surgery for endometriomas on ovarian reserve. The findings indicated a notable reduction in AMH levels post-surgery across short-, medium- and long-term periods when compared to baseline anti-Müllerian hormone levels. However, no significant differences were observed between short- and long-term AMH levels, indicating a negligible recovery of anti-Müllerian hormone levels after one year. Additionally, laparoscopic cystectomy's impact on ovarian reserve varied with the laterality of the lesions, showing a more pronounced decrease in AMH levels in bilateral endometriomas compared to unilateral ones.

The study also highlighted that the decline in post-operative ovarian reserve was more severe in cases of

endometriomas than in other benign ovarian conditions, particularly noticeable in both the short and medium terms. This decline was even more significant in endometriomas larger than 7 cm⁽³¹⁾.

Regarding the specific surgical approaches, AMH levels post-surgery were significantly lower following bilateral cystectomy compared to treatments involving vaporization with bipolar energy. Similarly, laser vaporization led to lower AMH levels compared to cystectomy. No notable differences in AMH levels were found between unilateral cystectomy and bipolar energy vaporization^(25,32).

Furthermore, the use of bipolar energy for hemostasis resulted in a significant reduction in postoperative AMH levels compared to suturing and hemostatic agents, although this was not the case when compared to hemostasis achieved with ultrasound^(18,33).

Limitations

This study faced several limitations. Language barriers and incomplete data led to the exclusion of numerous studies, and it was often unfeasible to contact authors for access to their full datasets. The inclusion of several retrospective observational studies also posed challenges, particularly as the specific methods used for measuring AMH were not always clear.

Furthermore, while serum AMH levels are generally stable, they can decrease under the influence of

anovulatory drugs or GnRH analogues. Although this effect tends to reverse after discontinuation of these treatments, it remains a factor that must be considered when interpreting results.

Another complication arises from the variety of assay types used to measure AMH, which complicates comparisons across different studies due to variations in detection methods and their respective cut-off levels. This variability in measurement protocols can significantly impact the interpretation of AMH levels in clinical practice.

Lastly, the review exhibited considerable heterogeneity (as indicated by the I^2 statistic) in several key outcomes, which suggests that the overall precision of the meta-analysis might be moderate. This heterogeneity highlights the complexity and variability inherent in the studies analyzed.

Changes in ovarian reserve after endometrioma cystectomy

Numerous studies have documented the decline in ovarian reserve following endometrioma cystectomy, noting considerable variability in surgical methods, follow-up durations, and metrics for assessing ovarian reserve. Over the years, reductions in AMH indicative of diminished ovarian reserve have been reported consistently following such procedures^(11,34). However, some studies have noted that a subset of women may experience partial AMH recovery within three to 12 months post-cystectomy^(2,3).

A prospective study monitoring postoperative AMH levels at six and 12 months revealed recoveries of 36.4% and 72.2%, respectively, from baseline levels (Vignali et al., 2015). This aligns with a recent review that found some medium-term AMH recovery compared to short-term levels, irrespective of the lesion's bilateral presence (Younis et al., 2019). However, our study found no significant differences in AMH recovery when comparing short-term to long-term levels up to six months post-operation.

It is important to interpret these findings cautiously because of the significant heterogeneity across studies and the ongoing need for research with longer follow-up periods. Moreover, the influence of contraceptive use complicates these results; some contraceptives may temporarily reduce the anti-Müllerian hormone levels. Despite this, analyses have shown no significant differences when patients on contraceptives were excluded from the study groups.

Impact of lesion laterality on postoperative AMH levels

Our analysis further revealed that more substantial decreases in AMH occur following the removal of bilateral endometriomas compared to unilateral cases, as supported by some studies⁽³⁵⁾ and contested by others⁽³⁶⁾. These outcomes should be approached with skepticism, given the limited number of patients, the potential loss to follow-up, and the unassessed variance in surgical approaches. A recent review reported maximal reductions in postoperative AMH levels of 39.5% for unilateral

endometriomas and 57% for bilateral endometriomas⁽³⁵⁾, illustrating the significant impact of lesion laterality on ovarian reserve⁽³⁷⁾.

Impact of endometrioma on postoperative AMH levels

Ovarian endometriomas may inherently impact the ovarian reserve, and the surgical removal of these endometriomas can exacerbate this effect compared to surgeries for other benign cysts. A study noted that AMH levels post-surgery declined more significantly in patients with endometriomas than in those with benign ovarian cysts⁽¹⁴⁾. However, a recent meta-analysis suggested a comparable reduction in postoperative AMH across both conditions, estimated at about 38%⁽³⁸⁾.

Influence of endometrioma size on postoperative AMH levels

Research has indicated that the size of endometriomas correlates with the extent of AMH reduction post-surgery. Specifically, endometriomas larger than 5 cm are associated with a more notable decrease in AMH levels⁽²³⁾. In contrast, other studies have not found a significant link between the size of the endometrioma and the reduction in AMH, often due to small sample sizes and variations in the laterality of the lesions included in the analysis⁽³⁹⁾.

Impact of surgical technique on postoperative AMH levels

The debate continues over the specific impact of endometrioma decapsulation on ovarian reserve. One randomized clinical trial suggested that techniques such as vaporization of the cyst wall using bipolar energy might better preserve ovarian reserve compared to traditional cystectomy⁽⁴⁰⁾. Similarly, another study found that, although plasma energy ablation results in comparable initial decreases in AMH as cystectomy, it may allow for greater long-term recovery of ovarian reserve⁽⁴¹⁾.

Given these findings, vaporization using either bipolar or laser energy is increasingly viewed as the preferred surgical method for patients seeking to maintain their reproductive potential, offering a potentially less damaging alternative to cystectomy.

Impact of hemostatic techniques on postoperative AMH levels following endometrioma surgery

The most prevalent hemostatic techniques used in endometrioma surgeries include laser energy, bipolar energy, and suturing. A randomized clinical trial demonstrated significant reductions in postoperative AMH regardless of the hemostatic method used⁽²³⁾. This has spurred the development of new techniques aimed at mitigating ovarian damage. For instance, a recent prospective study found that suturing preserved ovarian reserve more effectively than bipolar coagulation, offering the benefits of lower cost and fewer biochemical complications, although it can also lead to ischemic damage and adhesions⁽⁸⁾.

Further investigations have revealed mixed results regarding the effectiveness of hemostatic suturing techniques, with some studies not observing significant decreases in postoperative AMH levels, suggesting that

meticulous surgical techniques can prevent reductions in ovarian reserve even without using bipolar energy. Conversely, other studies found no significant differences in ovarian reserve outcomes between hemostatic methods⁽⁴²⁾ which may be attributable to variations in surgical technique, surgeon experience, and AMH measurement methods.

One particular study comparing hemostatic sealants and bipolar coagulation noted that short-term ovarian damage was more severe with bipolar coagulation, though AMH levels three months post-surgery did not differ significantly between the two groups^(6,15). However, the small sample size in this study limits the strength of these conclusions. Another study indicated statistically significantly better outcomes with hemostatic sealants compared to bipolar energy at three months post-surgery^(6,23).

Systematic reviews and meta-analyses have suggested that non-thermal hemostatic techniques, such as suturing and sealing agents, may result in lesser declines in AMH compared to bipolar energy, emphasizing the need for larger sample sizes to enhance result precision and calling for long-term follow-up studies that primarily assess postoperative AMH only in the medium term⁽²⁾.

Interpretation and long-term implications

Many hypotheses have been proposed to elucidate the relationship between endometrioma excision and AMH reduction. Some researchers posit that the inherent difficulty in distinguishing between the cyst capsule and healthy ovarian parenchyma during surgery may lead to accidental mechanical damage to the ovarian cortex, resulting in follicle loss and diminished ovarian reserve. Additionally, the use of electrical hemostatic methods might inflict microvascular and inflammatory damage on residual ovarian tissue, potentially recoverable over the long term, due to revascularization and inflammation reduction.

Differences in AMH reductions post-cystectomy between unilateral and bilateral endometriomas may reflect the more extensive surgical interventions typically required for bilateral cases, which often involve more extensive use of sutures and hemostasis, and potentially greater removal of healthy ovarian tissue.

Comparatively, the impact of cystectomy on endometriomas appears to be more detrimental to ovarian reserve than that on other benign ovarian conditions, possibly due to the inflammatory nature of endometriomas and the adhesions they cause, which may increase the risk of accidental healthy tissue removal.

In conclusion, while the immediate postoperative decrease in AMH can be stark, the potential for long-term recovery and the efficacy of different surgical and hemostatic techniques continue to be areas ripe for further investigation to optimize outcomes for patients undergoing endometrioma surgery.

Surgical techniques and hemostasis impact on ovarian reserve during endometrioma surgery

During endometrioma surgery, ovarian damage may occur through two primary mechanisms: mechanical damage to growing follicles and electrical damage. Our

findings suggest that cystectomy tends to have a more significant negative impact on ovarian reserve compared to ablation techniques, likely due to mechanical damage and the removal of healthy tissue⁽²³⁾.

Furthermore, it has been hypothesized that different hemostatic techniques employed during cyst removal may compromise vascularization of the remaining ovarian tissue and induce inflammation, potentially explaining the observed recovery of AMH levels noted in various studies^(11,35). This recovery might be attributed to tissue revascularization and reduced inflammation enhancing ovarian reserve, although this was not conclusively demonstrated in our study, suggesting that extended monitoring might alter these findings.

Future directions

Endometriomas are commonly encountered in clinical settings, and they often necessitate surgical intervention. Our results confirm that laparoscopic surgery adversely affects ovarian reserve, with the size of the cyst and bilateral presence of endometriomas being particularly detrimental. However, factors such as surgeon experience and varying AMH measurement methods might also influence the extent of ovarian reserve reduction post-surgery.

The optimal management of endometriomas might vary by patient's subtype. While conservative management such as ablation is associated with less impact on ovarian reserve than cystectomy, it may not be as effective in achieving gestation and could lead to higher recurrence rates.

Patients should be fully informed about the different surgical options and the associated risks of decreased ovarian reserve and potential recurrence. Special considerations are necessary for infertile patients prior to undergoing *in vitro* fertilization (IVF) treatment, as not all studies correlate low AMH levels with reduced pregnancy rates⁽⁴³⁾.

Given that larger endometriomas are linked with significant reductions in AMH levels, and considering endometriosis's progressive nature, early detection and conservative management could prevent future reproductive issues. Older patients and those with severe endometriosis should be cautioned about the potential irreversible damage to ovarian function from surgery.

Future research directions

To mitigate the surgery's impact on anti-Müllerian hormone levels, new techniques are being developed, such as sclerotherapy guided by transvaginal ultrasound, using agents like tetracycline, methotrexate and ethanol to reduce the pathogenic potential of endometriomas⁽⁴¹⁾. Additionally, hormonal therapies are being explored as surgical alternatives.

Advancements such as orthotopic transplantation or cryopreservation of ovarian tissue should be considered for patients with poor reproductive prognoses. Future research should focus on conducting randomized clinical trials with robust methodologies to improve evidence quality and define the long-term impact of different management strategies on ovarian reserve.

Conclusions

Laparoscopic resection of endometriomas significantly affects the anti-Müllerian hormone levels in the short, medium and long term. While no differences are observed between short-term and long-term declines, the consistency of these results is affected by high heterogeneity among the studies. More severe reductions

in AMH are noted in bilateral endometriomas and in those larger than 7 cm compared to smaller or unilateral ones. Overall, cystectomy shows a more profound impact on anti-Müllerian hormone levels than benign ovarian conditions, with different hemostatic techniques also influencing the degree of AMH reduction post-surgery. ■

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CONFLICT OF INTERESTS: none declared.

FINANCIAL SUPPORT: none declared.



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