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Systematic review and meta-analysis of the effect of bipolar electrocoagulation during laparoscopic ovarian endometrioma stripping on ovarian reserve

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Synopsis: Bipolar electrocoagulation during laparoscopic ovarian endometrioma stripping is more detrimental to ovarian reserve than are hemostatic suturing and hemostatic matrix, and should be avoided.

ABSTRACT

Background: Laparoscopic stripping is the gold-standard treatment for ovarian endometriosis. The choice of hemostasis method might affect ovarian reserve.

Objectives: To determine whether bipolar electrocoagulation is more detrimental to ovarian reserve than non-thermal hemostasis methods.

Search strategy: Entry terms associated with the MeSH terms “endometrioma,” “laparoscopy,” and “ovarian reserve” were used to search databases for articles published up to April 3, 2017, in English, Spanish, Portuguese, French, and Italian.

Selection criteria: Randomized controlled trials comparing the 3-month postoperative serum anti-Müllerian hormone (AMH) level in premenopausal women undergoing laparoscopic stripping with bipolar hemostasis or non-thermal hemostasis methods were selected.

Data collection and analysis: Data were extracted by two independent reviewers and a meta-analysis was performed.

Main results: Three studies met the inclusion criteria; overall, 105 patients underwent surgery with bipolar electrocoagulation and 105 patients underwent surgery with an alternative hemostasis method. The AMH level 3 months after surgery was decreased in the bipolar electrocoagulation group (mean difference –0.79 ng/mL, 95% confidence interval –1.19 to –0.39).

Conclusions: Bipolar electrocoagulation negatively impacts ovarian reserve and should be avoided, especially for patients with reproductive goals.

1 INTRODUCTION

Endometriosis is a disease characterized by chronic pelvic pain secondary to the presence of growing endometriotic tissue outside the uterus. The ovaries and fallopian tubes are mainly affected, but other pelvic and abdominal organs or structures are also susceptible to endometriotic cell implantation. The disease has a fairly high prevalence, estimated at approximately 10% among fertile women [1]. The most prevalent form is ovarian endometrioma, accounting for up to half of cases [2,3].

Currently, laparoscopic surgery is the gold-standard treatment for endometriosis [4,5]. More specifically for ovarian endometriomas, laparoscopic stripping is considered to be the best therapeutic approach [6]. Among existing laparoscopic techniques, stripping is usually favored because of decreased symptom recurrence rates and increased pregnancy rates [7].

However, concern has arisen regarding the impact of ovarian cyst stripping on ovarian reserve. Ovarian reserve can generally be defined as the “reproductive potential at a certain point in time” [8] and is determined by a quantitative and qualitative analysis of the ovarian follicular pool [8,9]. A reduction of ovarian reserve after laparoscopic stripping might be attributable to irreversible damage caused by the use of bipolar electrocoagulation for hemostasis. This damage could be secondary to thermal effects on the ovarian stroma and vascularization, and/or to inadvertent excision of healthy ovarian follicles during cyst excision [10–12].

It is of utmost importance to better define the effect of bipolar electrocoagulation during laparoscopic endometrioma stripping on ovarian reserve, because this could alter surgical treatment approaches for patients with reproductive goals. Endometriosis itself causes diminished ovarian reserve [13,14], so any further reduction associated with laparoscopic endometrioma stripping would be a concern Pregnancy success rates and rates of premature ovarian failure could be increased among women who have undergone this type of surgery.

There have been few attempts to review existing data regarding the impact of bipolar energy during endometrioma stripping on the ovarian reserve. To our knowledge, no previous systematic reviews have exclusively considered randomized clinical trials (RCTs) in their meta-analysis. Because RCTs represent studies with the best level of clinical evidence, we wished to gather information based exclusively on this type of study. In doing so, the aim was to reduce statistical bias.

The main objective of the present study was to evaluate the impact of bipolar electrocoagulation on ovarian reserve by comparing the mean 3-month postoperative anti-Müllerian hormone (AMH) levels after laparoscopic endometrioma stripping with bipolar electrocoagulation versus non-thermal hemostasis methods. Serum AMH levels were used because of the independence of this ovarian marker from gonadotropic hormones, facilitating its measurement during any phase of the menstrual cycle both in clinical and in research scenarios [9].

2 MATERIALS AND METHODS

The present systematic review and meta-analysis was conducted in agreement with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting systematic reviews and meta-analyses of RCTs.

2.1 Literature search

A comprehensive search of the databases PubMed/Medline, Cochrane Library, Web of Science/Knowledge, Embase, and LILACS was conducted. The MeSH terms "endometriosis," "laparoscopy," and "ovarian reserve" were entered into the PubMed MeSH database to determine the entry terms associated with these MeSH terms. The entry terms (Appendix S1) were then used to search the mentioned databases. All articles published between database inception and April 3, 2017, were considered for examination.

2.2 Study selection

The present analysis included RCTs that measured the ovarian reserve in premenopausal women undergoing laparoscopic ovarian endometrioma stripping using preoperative and 3-month postoperative AMH levels. Studies were included if they compared the serum AMH level after bipolar hemostasis versus other hemostasis methods during laparoscopic surgery and had been fully completed at the time of writing the present review. Additionally, only articles written in English, Portuguese, Spanish, French, or Italian were selected.

Initially, studies were selected by thematic relevance based on the abstract and title. The selection was conducted by one independent researcher (PD) and reviewed by a second (CBdFM). Any discrepancy in opinion concerning article inclusion was solved by discussion until a consensus was reached. If no consensus was reached, a third researcher (SCR) was consulted.

2.3 Outcome measures

The outcome measure was the mean 3-month postoperative serum AMH level, along with the standard deviation of this level. The 3-month period was chosen because previous authors [15,16] had found no significant difference between AMH levels at 3 months and 12 months after surgery.

2.4 Assessment of risk of bias

Risk of bias in the selected RCTs was assessed by classifying the studies as having a “high,” “low,” or “unclear” risk of bias in six categories on the basis of the risk of bias tool in RevMan 5.3 (Nordic Cochrane Centre, Cochrane Collaboration, Copenhagen, Denmark). The categories included random sequence generation (selection bias), allocation concealment, masking of participants and personnel (performance bias), incomplete outcome data (attrition bias), incomplete outcome bias, and other sources of bias. Two researchers (PD and RdSS) independently evaluated each included study and agreed on risks.

2.5 Data extraction

RCTs selected for meta-analysis were read in full by PD, SCR, RdSS, and CBdFM. The outcome considered for meta-analysis was mean serum AMH level in ng/mL, including standard deviation, 3 months after laparoscopic ovarian endometrioma stripping. Data were considered up to the first decimal point and inserted into Rev Man 5.3 by PD and checked by RdSS. Mean preoperative AMH was also compared. The meta-analysis used the total number of patients submitted to treatment and did not use an intention-to-treat analysis.

2.6 Statistical analysis

A pooled meta-analysis of data from the selected RCTs was performed using RevMan 5.3. Calculations included standard deviation for AMH levels in ng/mL 3 months after laparoscopic endometrioma surgery, using varying hemostasis methods. The studies were weighted on the basis of the number of patients included in the studies. $P<0.05$ was considered statistically significant.

3 RESULTS

Of the initial 702 articles identified (519 after exclusion of duplicates), 12 were further assessed for inclusion in the meta-analysis (Figure 1). Among these 12 articles, one study [17] was rejected after review of the full paper because it included patients who underwent laparotomy. Another article was removed from the review because data collection for the study was still ongoing [18]. For a third article [19], the full paper could not be obtained. After the primary exclusion of articles, nine RCTs were eligible for analysis. Of these studies, six [15,17,20–23] were excluded because data on the absolute postoperative AMH level were missing, making a numerical comparison impossible. The remaining three RCTs [24–26] were selected for meta-analysis.

The total patient pool in the meta-analysis included 210 premenopausal women; 105 underwent surgery with the use of bipolar electrocoagulation for hemostasis and 105 underwent surgery with the use of an alternative (non-thermal) hemostasis method, which was either laparoscopic suturing or use of a hemostatic matrix. Patients for whom an ultrasonic scalpel was used in the study conducted by Zhang et al. [26] were not included in analysis. The risk of bias in the three studies was generally low (Table 1). However, it is noteworthy that one of the selected RCTs [24] did not use computerized random group allocation. The baseline characteristics in the selected studies were similar (Table 2).

In two of the included RCTs [24,25], the impact on ovarian reserve of the two hemostasis methods being compared was not significantly different (Figure 2). By contrast, the third RCT [26] found a significant difference, to the disadvantage of bipolar hemostasis during laparoscopic endometrioma stripping. In the pooled analysis, the 3-month postoperative AMH level was significantly lower in the bipolar electrocoagulation group than when an alternative hemostasis method was used (mean difference –0.79 ng/mL, 95% confidence interval –1.19 to –0.39).

There was considerable heterogeneity between the studies (I^2=74%, P=0.02).

4 DISCUSSION

The present meta-analysis showed a greater reduction in postoperative ovarian reserve with bipolar electrocoagulation than with non-thermal hemostatic methods (suture or hemostatic polymer). However, of the three RCTs included in the analysis, only one study [26] found a significant difference between the hemostasis methods, favoring suturing over bipolar electrocoagulation. In the other two studies [24,25], the difference between the hemostasis methods was not significant. These findings are in agreement with previous comparative studies [17,20], an RCT [22], and two meta-analyses [27,28], pointing to a detrimental effect of bipolar hemostasis on the ovarian reserve, as indicated by a greater decrease of AMH in the bipolar hemostasis group.

It has been conjectured that the reduction in postoperative AMH levels might be transient, because some authors [16,29] have demonstrated a recovery of AMH levels in the long term. However, the potential recovery of AMH levels remains controversial. Other authors [15,16] found no significant difference between AMH levels at 3 months and at 12 months after surgery, which reinforces our suggestion that AMH should be measured 3 months after laparoscopic endometrioma resection.

Hemostatic methods aside, endometrioma stripping alone may be responsible for the decline in ovarian reserve after surgery, owing to inadvertent tissue removal and consequent follicle loss [30]. However, Muzii et al. [31] considered endometrioma stripping to be a safe, tissue-sparing technique. To date, no consensus has been reached as to the effect of endometrioma stripping per se on the ovarian reserve.

Other factors could also affect the ovarian reserve, such as cyst size [32], laterality of the endometriomas [33], and surgical skill of the physician performing cyst stripping [34]. However, scientific data regarding these factors are contradictory and the mentioned variables might not have any tangible influence [35–37]. The present study did not take these factors into account.

With respect to cyst laterality, differences in AMH decline after unilateral versus bilateral endometrioma stripping might be attributable to differences in the timepoint after surgery when AMH was measured. Ledger [38] reported that postoperative AMH levels tend to be lower in patients undergoing surgery for bilateral endometriomas but that ovarian function in these patients tends to recover when given time. Another prospective study [37] found no significant differences in ovarian reserve with varying endometrioma sizes; this result was also explained by a recovery of ovarian function.

The present finding that bipolar hemostasis is more detrimental to ovarian reserve than other types of hemostasis is supported by previous results. Ata et al. [28] demonstrated in a systematic review and meta-analysis that bipolar electrocoagulation has a more negative impact on the ovarian reserve than do alternative hemostasis methods: the mean reduction in serum AMH at 3 months after surgery was 7.0% (95% confidence interval [CI] –3.0% to –0.9%, *P*=0.02) smaller with alternative methods than with bipolar electrocoagulation. The present study differs from the study by Ata et al. [28] because the present analysis included RCTs only. Given that RCTs are considered to provide the best level of evidence, the exclusion of other types of study could have increased the statistical accuracy of the present meta-analysis. Additionally, although the total number of patients included in the two meta-analyses was similar (n=210 in the present study vs n=213 in the study by Ata et al. [28]), the two study populations were not the same. Therefore, the fact that the two studies had similar results reinforces the notion that bipolar hemostasis is more detrimental to ovarian reserve than are non-thermal hemostasis methods.

Also consistent with the present findings are two RCTs [20,22] that were not included in the present meta-analysis. These RCTs were excluded because they evaluated the impact on ovarian reserve on the basis of the rate of AMH decline, rather than by comparing preoperative and postoperative AMH levels. One of these trials [20] favored laparoscopic suturing over bipolar electrocoagulation, whereas the other, conducted by Song et al. [22], favored the use of a hemostatic sealant over bipolar hemostasis. In both studies, the use of bipolar energy had a more damaging effect on the ovarian reserve than did other hemostasis methods. Another study by Song et al. [17] also supports the claim that laparoscopic suturing is less prejudicial to ovarian reserve decline than the use of bipolar energy.

Other previous findings [15,27] are in disagreement with the present results. In a systematic review [27], AMH analysis showed no significant difference between the bipolar coagulation and the suture groups at 3 months (weighted mean difference [WMD] –0.75 ng/mL, 95% CI –1.82 to 0.31), 6 months (WMD –1.45 ng/mL, 95% CI –2.43 to –0.47), and 12 months (WMD –1.01 ng/mL; 95% CI –1.85 to –0.17) after surgery. However, the AMH levels tended to be lower in the hemostasis groups, and the antral follicle count was significantly decreased with bipolar coagulation compared with hemostatic suture (WMD –2.53, 95% CI –4.94 to –0.12). In an RCT [15] that included 100 patients with bilateral endometriomas undergoing laparoscopic ovarian stripping with hemostasis either by laparoscopic suturing or by bipolar coagulation, there was no difference in AMH levels after surgery. Furthermore, this RCT failed to detect any differences in terms of pregnancy rate, time to conception, and rate of endometrioma recurrence between the two hemostasis groups.

The present study has a few limitations. First, the total number of women included in the meta-analysis (n=210) was fairly small. Second, the fact that the RCT by Zhang et al. [26] was given a larger weight in the analysis than the other two included RCTs could have led to an overestimation of the negative impact of bipolar hemostasis. Third, there was potential selection bias because of a lack of proper randomized allocation concealment in one of the included RCTs [24]. Finally, the heterogeneity between the included studies was substantial (I^2=74%), although it could be argued that this is a characteristic inherent to most meta-analyses.

In conclusion, the present findings indicate a reduction in ovarian reserve caused by the use of bipolar hemostasis during laparoscopic ovarian endometrioma stripping. Consequently, alternative hemostasis methods such as laparoscopic suturing and/or hemostatic matrix should be used to preserve the ovarian reserve, especially in infertile women with endometriosis who have reproductive goals. The use of bipolar electrocoagulation should be kept to a minimum; this technique should only be used after failure of alternative hemostasis methods. Further RCTs with long-term postoperative follow-up are needed to better define the impact of different hemostasis techniques on the ovarian reserve.

Author contributions

PD was the main author of the manuscript; she also participated in the conception and design of the study, the study selection and acquisition, the risk of bias evaluation, and the data interpretation. SCR participated in the conception of the study, the selection and acquisition of studies, the data interpretation, and the writing and revision of the manuscript. RdSS contributed to the statistical analysis and data interpretation, the risk of bias evaluation, and the writing of the manuscript. CBdFM contributed to the conception and design of the study, the selection and acquisition of the studies included in the meta-analysis, and the writing of the manuscript. ECB contributed to the conception of the study, the data interpretation, and the writing and revision of the manuscript.

Conflicts of interest

The authors have no conflicts of interest.

References

[1] Viganò P, Parazzini F, Somigliana E, Vercellini P. Endometriosis: epidemiology and aetiological factors Best Pract Res Clin Obstet Gynaecol. 2004;18:177-200.

[2] No authors listed. Italian Endometriosis Study Group (Gruppo italiano per lo studio dell'endometriosi) Endometriosis: prevalence and anatomical distribution of endometriosis in women with selected gynecological conditions; results from a multicentric Italian study. Hum Reprod. 1994;9:1158-1162.

[3] Jenkins S, Olive DL, Haney AF. Endometriosis: pathogenetic implications of the anatomic distribution. Obstet Gynecol. 1986;67:335-338.

[4] Busacca M, Vignali M. Endometrioma excision and ovarian reserve: a dangerous relation. J Minim Invasive Gynecol. 2009;16:142-148

[5] Yuen PM, Yu KM, Yip SK, Lau WC, Rogers MS, Chang A. A randomized prospective study of laparoscopy and laparotomy in the management of benign ovarian masses. Am J Obstet Gynecol. 1997;177:109-114.

[6] Muzii L, Bellati F, Palaia I, et al.. Laparoscopic stripping of endometriomas: a randomized trial on different surgical techniques. Part I: Clinical results. *Hum Reprod* 2005; 20: 1981-1986

[7] Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P. Randomized clinical trial of two laparoscopic treatments of endometriomas: cystectomy versus drainage and coagulation. Fertil Steril. 1998;70:1176-1180.

[8] Alammari R, Lightfoot M, Hur HC. J. Impact of Cystectomy on Ovarian Reserve: A Review of the Literature. Eur J Obstet Gynecol Reprod Biol. 2015;194:64-67

[9] Practice Committee of the American Society for Reproductive Medicine. American Society for Reproductive Medicine, Birmingham, Alabama. Testing and interpreting

measures of ovarian reserve: a committee opinion.
https://www.asrm.org/uploadedFiles/ASRM_Content/News_and_Publications/Practice_Guidelines/Committee_Opinions/Testing_and_interpreting_measures_of_ovarian_reserve-pdfmembers.pdf. Accessed March 09, 2017.

[10] Raffi F, Metwally M, Amer S. The impact of excision of ovarian endometrioma on ovarian reserve: a systematic review and meta-analysis J Clin Endocrinol Metab. 2012;97:3146-3154

[11] Mohamed ML, Nouh AA, El-Behery MM, Mansour SA. Effect on ovarian reserve of laparoscopic bipolar electrocoagulation versus laparotomic hemostatic sutures during unilateral ovarian cystectomy. Int J Gynecol Obstet. 2011;114:69–72.

[12] Celik HG, Dogan E, Okyay E, et al. Effect of laparoscopic excision of endometriomas on ovarian reserve: serial changes in the serum antimullerian hormone levels. Fertil Steril. 2012;97:1472-1478

[13] Kitajima M, Defrere S, Dolmans MM, et al. Endometriomas as a possible cause of reduced ovarian reserve in women with endometriosis. Fertil Steril. 2011;96:685-691

[14] Uncu G, Kasapoglu I, Ozerkan K, Seyhan A, Oral Yilmaztepe A, Ata B. Prospective assessment of the impact of endometriomas and their removal onf ovarian reserve and determinants of the rate of decline in ovarian reserve. Hum Reprod. 2013;28:2140-2145.

[15] Ferrero S, Venturini PL, Gillott DJ, Remorgida V, Leone Roberti Maggiore U. Hemostasis by bipolar coagulation versus suture after surgical stripping of bilateral ovarian endometriomas: a randomized controlled trial. J Minim Invasive Gynecol. 2012;19:722-730

[16] Chang HJ, Han SH, Lee JR, Jee BC, Lee BI, Suh CS, Kim SH. Impact of laparoscopic cystectomy on ovarian reserve: serial changes of serum anti-Müllerian hormone levels. Fertil Steril. 2010;94:343-349

[17] Song T, Kim WY, Lee KW, Kim KH. Effect on ovarian reserve of hemostasis by bipolar coagulation versus suture during laparoendoscopic single-site cystectomy for ovarian endometriomas J Minim Invasive Gynecol. 2015;22:415-420

[18] Detorakis S, Protopapas A, Louradour D, Giannoulis G, Hatzipapas I, Loutradis D. Bipolar energy for ovarian hemostasis in endometrioma surgery: During, after or not at all? Presentation of 3 different cystectomy techniques compared in an ongoing rct; Gynaecological Surgery 2014 11:1(1) 54-55

[19] Chenn CC, Falcone T. Endoscopic management of endometriosis, Minerva Ginecol. 2006; 58: 347-360.

[20] Asgari Z, Hosseini R et al. Comparing ovarian reserve after laparoscopic excision of endometriotic cysts and hemostasis achieved either by bipolar coagulation or suturing: a randomized clinical trial. Arch Gynecol Obstet. 2016;293:1015-1022

[21] Kang JH, Kim YS, Lee SH, Kim KW. Comparison of hemostatic sealants on ovarian reserve during laparoscopic ovarian cystectomy. Eur J Obstet Gynecol Reprod Biol. 2015;194:64-67

[22] Song T, Lee SH, Kim WY. Additional benefit of hemostatic sealant in preservation of ovarian reserve during laparoscopic ovarian cystectomy: a mutli-center, randomized controlled trial. Hum Reprod. 2014;29:1659-1665

[23] Kumakiri J, Kikuchi I, Kitade M, Jinushi M, Takeda S. Effects on Ovarian Reserve of Laparoscopic Cystectomy for Ovarian Endometrioma That Performs Hemostatic Suturing after Stripping and Electrocoagulation after Stripping by Vasopressin Injection. Journal of Minimally Invasive Gynecology 2012; 19: S49.

[24] Tanprasertkul C, Ekarattanawong S, Sreshthaputra O, Vutyavanich T. Impact of hemostasis methods, electrocoagulation versus suture, in laparoscopic endometriotic

cystectomy on the ovarian reserve: a randomized controlled trial. J Med Assoc Thai. 2014 ;97:S95-101.

[25] Sönmezer M, Taşkın S, Gemici A, et al. Can ovarian damage be reduced using hemostatic matrix during laparoscopic endometrioma surgery? A prospective, randomized study. Arch Gynecol Obstet. 2013;287:1251-1257

[26] Zhang CH, Wu L, Li PQ. Clinical study of the impact on ovarian reserve by different hemostasis methods in laparoscopic cystectomy for ovarian endometrioma. Taiwan J Obstet Gynecol. 2016;55:507-511

[27] Ding W, Li M, Teng Y. The impact on ovarian reserve of haemostasis by bipolar coagulation versus suture following surgical stripping of ovarian endometrioma: a meta-analysis. Reprod Biomed Online. 2015;30:635-642

[28] Ata B, Turkgeldi E, Seyhan A, Urman B. Effect of hemostatic method on ovarian reserve following laparoscopic endometrioma excision; comparison of suture, hemostatic sealant, and bipolar dessication. A systematic review and meta-analysis. J Minim Invasive Gynecol. 2015;22:363-372

[29] Vignali M, Mabrouk M, Ciocca E, et al. Surgical excision of ovarian endometriomas: Does it truly impair ovarian reserve? Long term anti-Müllerian hormone (AMH) changes after surgery. J Obstet Gynaecol Res. 2015;41:1773-1778.

[30] Aytac PC, Parlakgumus HA, Bolat FA, Cok T, Haydardedeoglu B, Kilicdag EB. Pathological assessment of follicular loss in laparoscopic endometrioma excision: effects of cyst size and surgeon's experience. J Obstet Gynaecol Res. 2015;41:264-268

[31] Muzii L, Bianchi A, Crocè C, Manci N, Panici PB. Laparoscopic excision of ovarian cysts: is the stripping technique a tissue-sparing procedure? Fertil Steril. 2002;77:609-614.

[32] Mehdizadeh Kashi A, Chaichian S, Ariana S, et al. The impact of laparoscopic cystectomy on ovarian reserve in patients with unilateral and bilateral endometrioma. Int J Gynecol Obstet. 2017;136:200–204.

[33] Hwu YM, Wu FS, Li SH, Sun FJ, Lin MH, Lee RK. The impact of endometrioma and laparoscopic cystectomy on serum anti-Mullerian hormone level. Reprod Biol Endocrinol. 2011;9:80

[34] Yu HT, Huang HY, Soong YK, Lee CL, Chao A, Wang CJ. Laparoscopic ovarian cystectomy of endometriomas: surgeons' experience may affect ovarian reserve and live-born rate in infertile patients with in vitro fertilization-intracytoplasmic sperm injection. Eur J Obstet Gynecol Reprod Biol. 2010;152:172-175

[35] Ercan CM, Sakinci M, Duru NK, Alanbay I, Karasahin KE, Baser I. Antimullerian hormone levels after laparoscopic endometrioma stripping surgery. Gynecol Endocrinol. 2010;26:468-472

[36] Biacchiardi C, Piane LD, Camanni M, et al. Laparoscopic stripping of endometriomas negatively affects ovarian folicular reserve even if performed by experienced surgeons. Reprod Biomed Online. 2011;23:740-746.

[37] Alborzi S, Keramati P, Younesi M, Samsami A, Dadras N. The impact of laparoscopic cystectomy on ovarian reserve in patients with unilateral and bilateral endometriomas. Fertil Steril. 2014;101(2):427-434.

[38] Ledger WL. Measurement of antimüllerian hormone: not as straightforward as it seems. Fertil Steril 2014;101:339.

Figure legends

Figure 1 Flow chart of study selection process. Abbreviations: RCT, randomized controlled trial; AMN, anti-Müllerian hormone.

Figure 2 Meta-analysis comparing the 3-month postoperative anti-Müllerian hormone level by hemostasis method. Abbreviations: BE, bipolar electrocoagulation; CI, confidence interval.

Supporting information legend

Appendix S1 List of entry terms used in the database searches.

Table 1 Risk of bias assessment.

Bias category	**Tanprasertkul et al. 2014 [24]**	**Sönmezer et al. 2013 [25]**	**Zhang et al. 2016 [26]**
Random sequence generation (selection bias)	High risk [a]	Low risk	Low risk
Allocation concealment (selection bias)	Low risk	Low risk	Low risk
Masking of participants and personnel (performance bias)	Low risk	Low risk	Low risk
Incomplete outcome assessment (detection bias)	Low risk	Low risk	Low risk
Selective reporting (reporting bias)	Low risk	Low risk	Low risk
Other bias	Unclear risk	Unclear risk	Unclear risk

[a] A table of random numbers was used, as well as opaque and sealed envelopes.

Table 2 Characteristics of the studies included in the meta-analysis.[a]

Study	Hemostasis methods compared	Patient age, y [b]			Laterality of ovarian endometrioma	Endometrioma diameter, cm [b]		Time of postoperative follow-up [c]	Outcome
		Total	BE	Non-thermal hemostasis		BE	Non-thermal hemostasis		
Tanprasertkul et al. 2014 [24]	BE (n=15) vs suture (n=13)	18–45	33.6 ± 5.2	33.6 ± 6.6	Unilateral and bilateral	5.4 ± 2.0	5.0 ± 1.6	1 mo, 3 mo	At 1 mo, AMH was significantly lower in the BE group; at 3 mo, AMH levels were similar in both hemostasis groups
Sönmezer et al. 2013 [25]	BE (n=25) vs hemostatic matrix (n=25)	19–35	27.1 (19–38)	27.9 (25–40)	Unilateral	5.5 (4–10)	5.0 (4–7)	1 wk, 1 mo, 3 mo, 6 mo	No significant difference in AMH between the two hemostasis groups; in both groups, AMH was significantly decreased from the first postoperative week until the sixth month
Zhang et al. 2016 [26]	BE (n=65) vs suture vs ultrasonic scalpel (n=67)	31.8 ± 8.2 (18–45)	30.9 ± 8.2	Ultrasonic scalpel: 31.4 ± 8.5; Suture: 33.1 ± 7.2	Unilateral and bilateral [d]	5.2 ± 2.6	Ultrasonic scalpel: 4.9 ± 2.9 Suture: 5.3 ± 2.7	1 mo, 3 mo, 6 mo, 12 mo	AMH was significantly lower in the BE and ultrasound groups than in the suture group at all time points

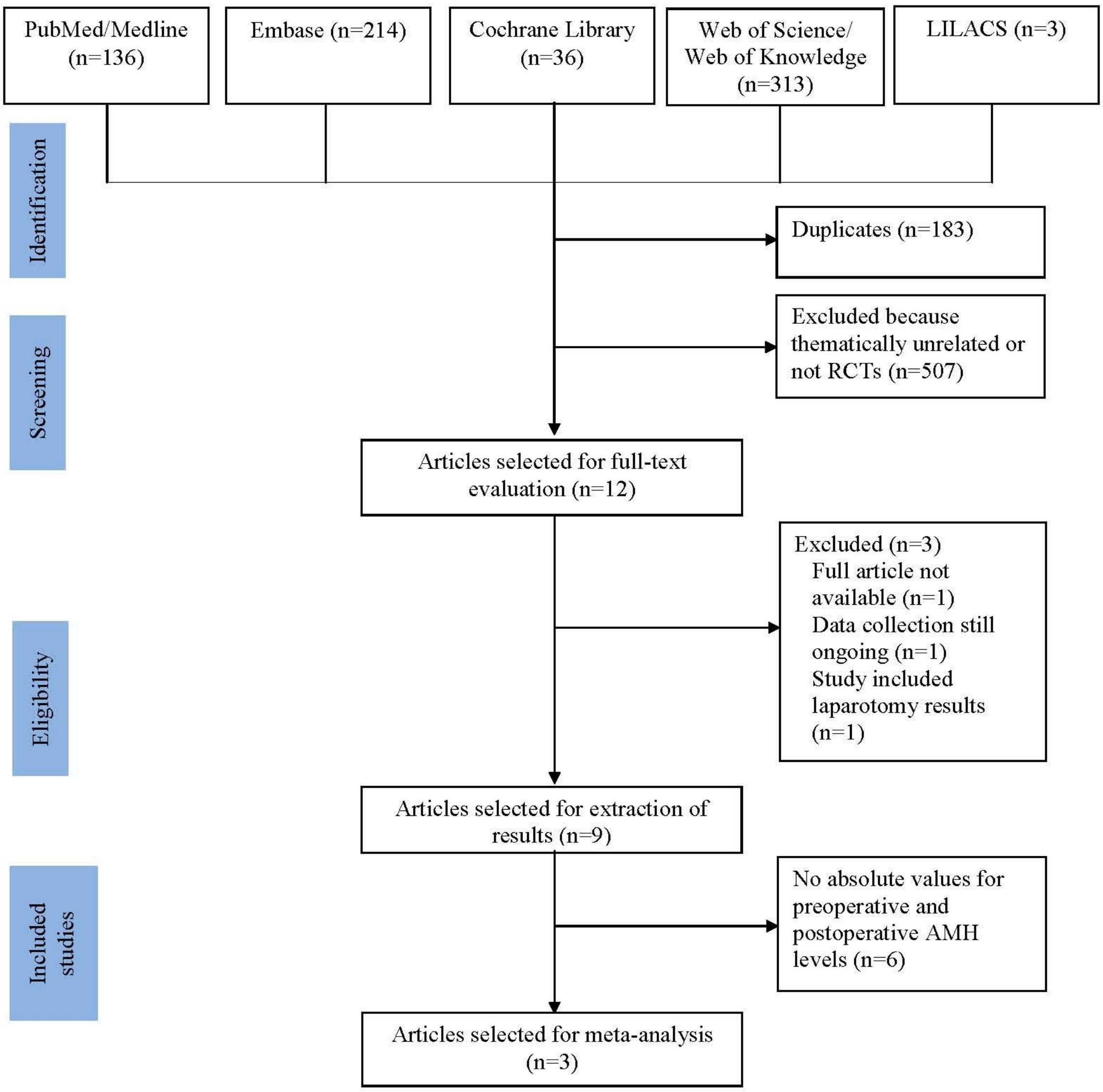
Abbreviations: BE, bipolar electrocoagulation; AMH, anti-Müllerian hormone.

[a] Total number of patients might differ from original study; number of patients actually submitted to treatment considered here (i.e. not intention-to-treat).

[b] Values are given as range, mean ± SD, median (range), or mean ± SD (range).

[c] Measurement of AMH.

[d] Not distinguished in the analysis.


PubMed/Medline (n=136)
Embase (n=214)
Cochrane Library (n=36)
Web of Science/ Web of Knowledge (n=313)
LILACS (n=3)
Identification
Duplicates (n=183)
Screening
Excluded because thematically unrelated or not RCTs (n=507)
Articles selected for full-text evaluation (n=12)
Eligibility
Excluded (n=3)
Full article not available (n=1)
Data collection still ongoing (n=1)
Study included laparotomy results (n=1)
Articles selected for extraction of results (n=9)
Included studies
No absolute values for preoperative and postoperative AMH levels (n=6)
Articles selected for meta-analysis (n=3)

	BE			Non thermal-hemostasis				Mean difference in AMH (ng/ml)
Study or Subgroup	Mean AMH (ng/ml)	SD	Total	Mean AMH (ng/ml)	SD	Total	Weight	IV, Fixed, 95% CI
Sönmezer M. et al. 2013	2.84	1.12	15	3.07	1.43	13	17.1%	-0.23 [-1.19, 0.73]
Tanprasertkul C. et al. 2014	2.09	1.66	25	1.96	1.68	25	18.4%	0.13 [-0.80, 1.06]
Zhang C.H. et al. 2016	1.8	1	65	3	1.8	67	64.5%	-1.20 [-1.69, -0.71]
Total (95% CI)			**105**			**105**	**100.0%**	**-0.79 [-1.19, -0.39]**

Heterogeneity X^2 =7.73, *df* 2 (P = 0.02); I^2 = 74%
Test for overall effect: Z = 3.89 (P < 0.0001)