LIST OF PUBLICATIONS

1) Tanprasertkul C, Manusook S, Somprasit C, Ekarattanawong S, Sreshthaputra O, Vutyavanich T. Antimullerian hormone changes after laparoscopic ovarian cystectomy for endometrioma compared with the non-ovarian conditions. Minim Invasive Surg 2014;2014:654856.

2) 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 Suppl 8:S95-101.

3) Tanprasertkul C, Manusook S, Somprasit C, Sreshthaputra O, Patumanond J, Vutyavanich T. Recurrence of Endometrioma Following Conservative Ovarian Endometrioma Cystectomy: Laparoscopy versus Laparotomy. J Med Assoc Thai 2015; 98 Suppl 3:S96-100.

Appendices

Appendix A

Philosophical context of clinical epidemiology design in this thesis

Philosophical context of clinical epidemiology design in this thesis

Research questions

1. How does AMH level change after laparoscopic cystectomy of ovarian endometrioma compared with other non-ovarian pelvic surgery?
2. Does bipolar coagulation for hemostasis during laparoscopic cystectomy of endometrioma have the same effect on ovarian reserve as suturing?
3. Is there a difference in the recurrence rate of endometrioma after its removal via the laparoscopy or laparotomy approach?

Research titles for publication

Study I

Anti-Mullerian hormone changes after laparoscopic ovarian cystectomy for endometrioma compared with the non-ovarian conditions

Study II

The impact of hemostasis methods, electrocoagulation versus suture, in laparoscopic endometriotic cystectomy on the ovarian reserve : a randomized controlled trial

Study III

Recurrence of endometrioma following conservative ovarian endometrioma cystectomy; laparoscopy versus laparotomy

1. Theoretical design

1.1 To compare the difference in the levels of serum anti-mullerian hormone in patients who underwent laparoscopic ovarian cystectomy (LOC) versus other non-ovarian pelvic surgery (NOS).

Study Design : A prospective cohort study

Occurrence relationship:

Changes of AMH level = f [surgical intervention in LOC or NOS/ age, BMI, pathological conditions, severity, size, duration of surgery, blood loss]

Study domain: Reproductive women who underwent laparoscopic ovarian cystectomy or laparoscopic non- ovarian pelvic surgery

Research type: Therapeutic research

1.2 To compare the changes in ovarian reserve between two methods of hemostasis during laparoscopic excision of ovarian endometrioma; bipolar coagulation versus suturing.

Study design: A randomized controlled trial

Occurrence relationship:

Changes of AMH level = f [methods of hemostasis during laparoscopic ovarian cystectectomy/ age, BMI, endometriotic stage, size, bilaterality]

Research type: Therapeutic research

Study domain: Women who underwent laparoscopic ovarian cystectomy for endometrioma

1.3 To compare the recurrence rate and the time to recurrence of endometrioma after its excision via the laparoscopy or laparotomy approach

Study Design: A retrospective cohort study

Occurrence relationship:

Time to recurrence of endometrioma = f [Surgical approach (laparoscopy or laparotomy)/ age, tumor size, staging, other adjunct treatments]

Research type: Therapeutic research, explanatory model

Study domain: Reproductive women who underwent laparoscopic ovarian cystectomy

2. Data collection design

Study setting and study period

All of the studies in this thesis were conducted at the department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand. This is a tertiary-care hospital in the northern area of Bangkok, with a capacity of 800 beds. The clinical trial was registered with the ClinicalTrials.gov, as Thammasat University Protocol Record MTU-OB-3-096/56, Identifier: NCT02500342.

Study domain

Study I

Patients in study I were reproductive women, who underwent laparoscopic ovarian cystectomy or laparoscopic non- ovarian pelvic surgery

The exclusion criteria were

- patients who had polycystic ovarian syndrome according to the Rotterdam criteria[1]
- patients with a pathological report showing a malignant disease
- those who required an open-laparotomy

Study II

Patients in study II were reproductive women, aged 18- 45 years, who underwent laparoscopic ovarian cystectomy

The exclusion criteria were

- polycystic ovarian syndrome according to the Rotterdam criteria
- pathological diagnosis of excised ovarian tissue did not confirm an endometriotic cyst
- conversion to laparotomy

Study III

Patients in study III were reproductive women, aged 18- 45 years, who underwent ovarian endometriotic cystectomy via a laparoscopy or laparotomy approach at the department of Obstetrics and Gynecology, Thammasat University, Pathumthani, Thailand.

The exclusion criteria were

- pathological diagnosis of excised ovarian tissue did not confirm an endometriotic cyst
- missing data on important baseline clinical covariates

3. Study design

Study I

- A therapeutic research
- The design was a prospective cohort study

Study II

- A therapeutic research
- The design was a randomized control trial

Study III

- A therapeutic causal research
- The design was a retrospective cohort study, with data collection on time to recurrence of ovarian endometrioma

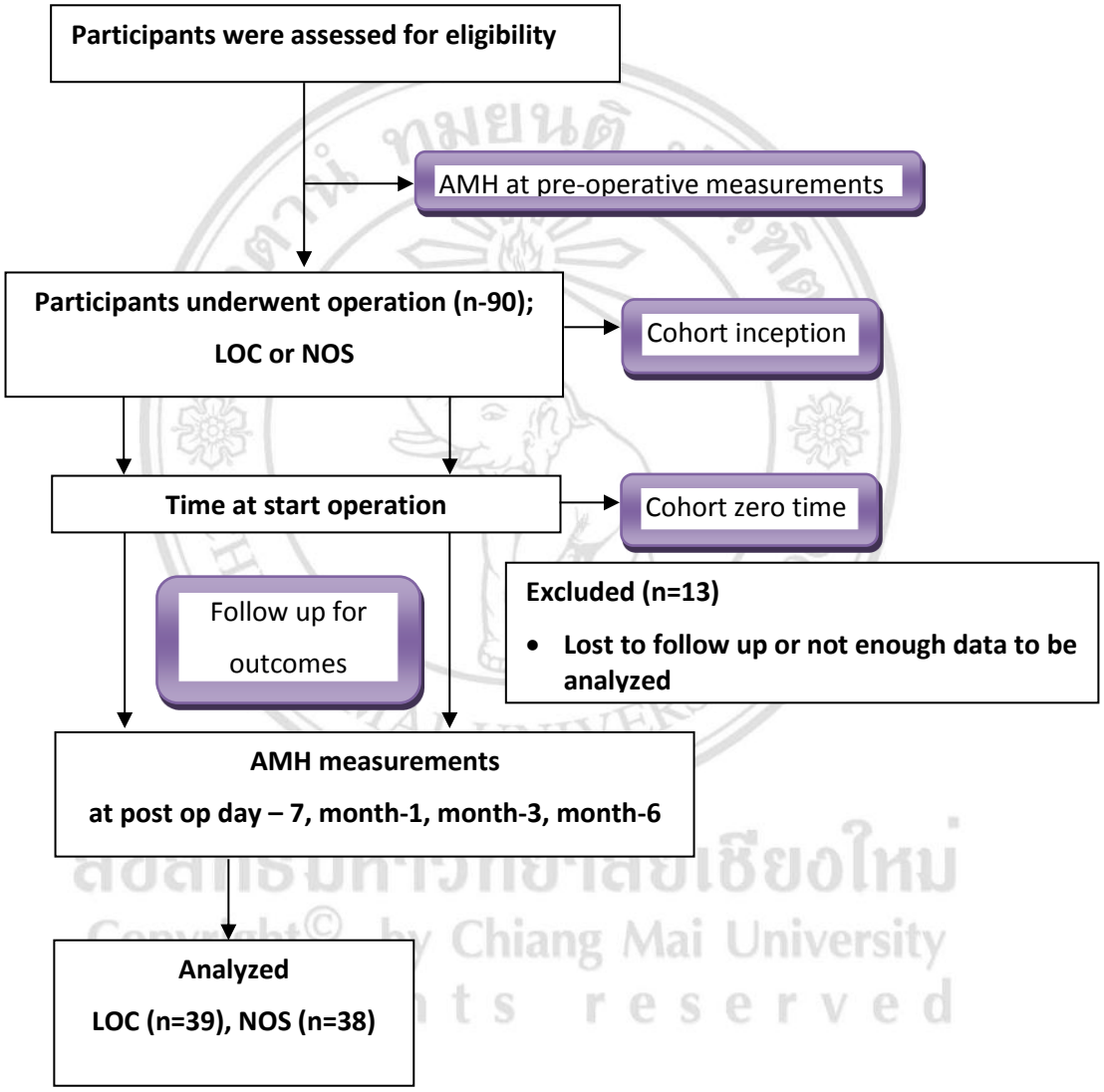
4. Data collection process

- Standardization of data collectors

Medical files were reviewed and extracted by staff working full time at the study site. Hypothesis of all studies were disclosed. We collected a broad range of variables, using a case record form specifically designed for each study. Data collectors were standardized by discussion and clarification of each variable with the research team. Unofficial meetings were also held to facilitate problem solving during the data collection period. This process was performed to minimize information error. We also controlled the quality of data by doing a quality audit.

Study flow

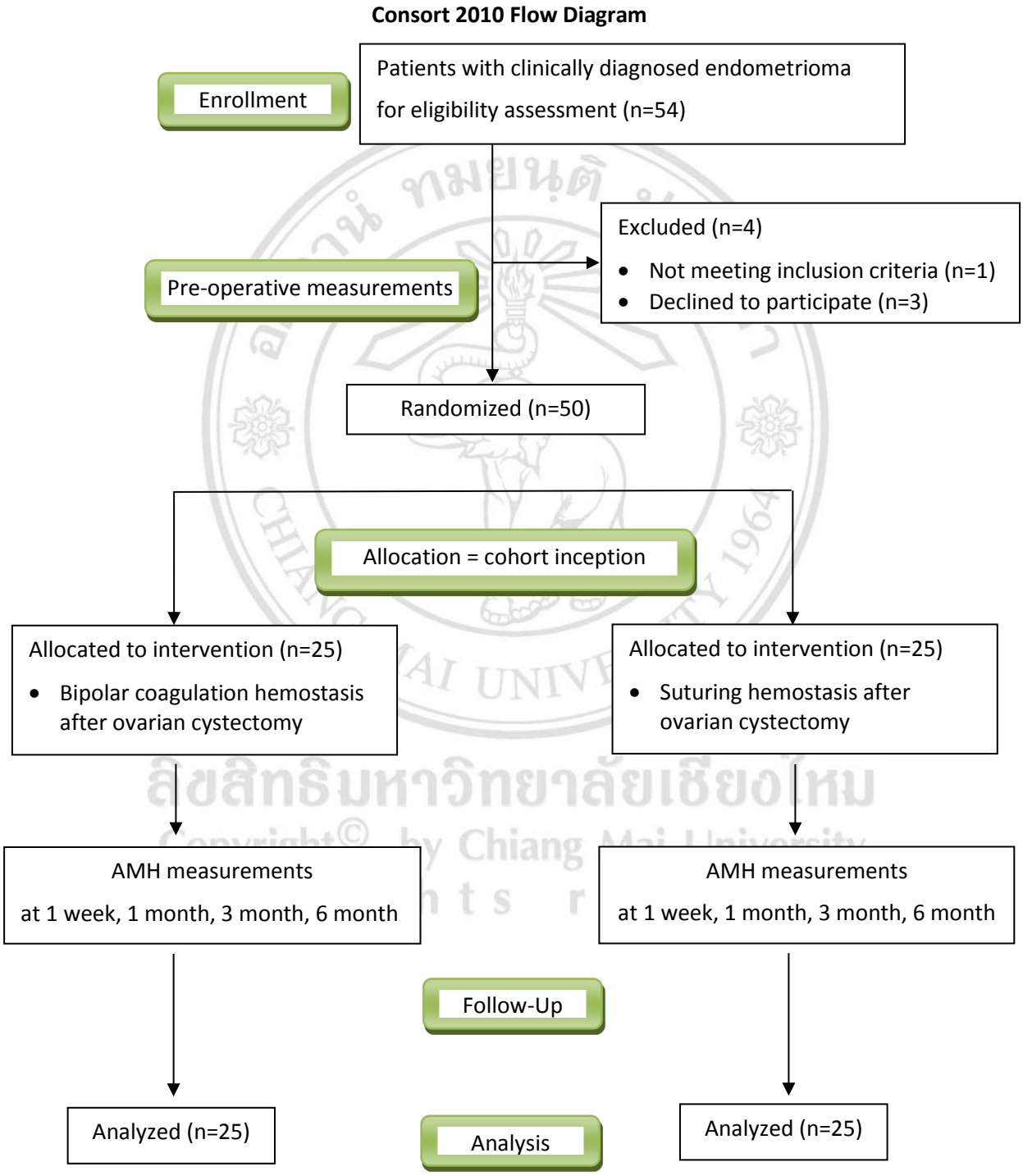
Study I. Anti-Mullerian hormone changes after laparoscopic ovarian cystectomy (LOC) for endometrioma compared with other non-ovarian surgeries(NOS)



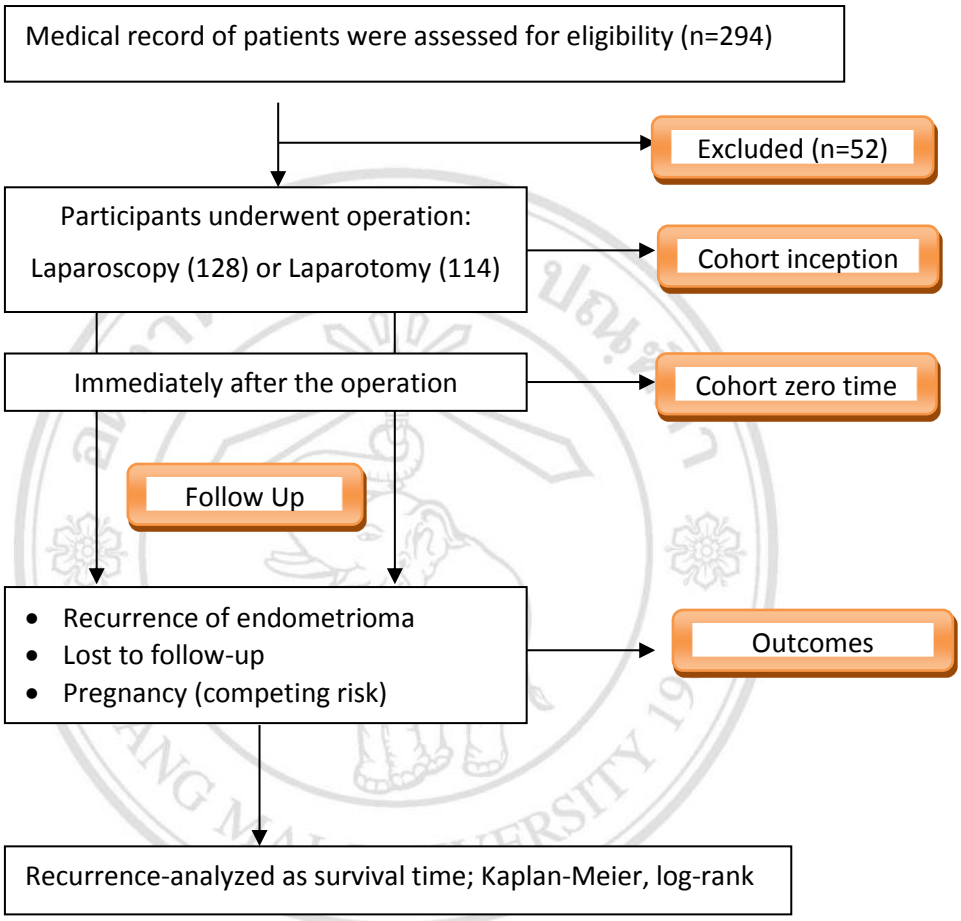
Laparoscopic ovarian cystectomy; LOC

Non-ovarian surgeries; NOS

Study II. The impact of hemostasis methods, electrocoagulation versus, in laparoscopic endometriotic cystectomy on the ovarian reserve : a randomized controlled trial



Study III. Recurrence of endometrioma following conservative ovarian endometrima Cystectomy ; laparoscopy versus laparotomy



5.Data analysis design

5.1 Study I : a therapeutic research

: primary outcome was the difference in AMH levels between the two groups

: unpaired t-test was used for comparing continuous data between two groups

5.2 Study II : a therapeutic research

: primary outcome was the difference in AMH levels between the two groups

: unpaired t-test was used for comparing continuous data between two groups

5.3 Study III: an explanatory research

: primary outcome was the time to events of disease recurrence

: a multi-stage analysis was done, as followings ;

Step 1: Unpaired t-test or rank sum test was used for comparing continuous data between two groups and Fisher's exact test was used for comparing categorical data between both groups.

Step 2: Propensity score was used as a covariate to control for confounding by group assignment (laparoscopy or laparotomy approach).

Step 3: Multivariable cox proportional hazard regression analysis, stratified by clinical variables and propensity score

Propensity score[2, 3] is useful when the chance of receiving treatment in each group is unequal. In a non-randomized trial, the confounders between the exposed and non-exposed participants are not balanced. The outcomes of these studies are likely to be bias and less reliable. The propensity score is proposed to control such confounders, by balancing them between the two groups. The score minimizes the confounding by indication, and also the confounding by contraindication, producing an unbiased estimate of the treatment effect and create balanced covariates between the two groups.

An equation model to predict the probability for the chance of receiving treatment (laparoscopy vs. laparotomy) has been demonstrated as:

Propensity Score = Pr (Treated | background info)

To estimate the propensity score, a logistic regression model was created in which treatment status (laparoscopic vs. laparotomy approach) was regressed on the baseline characteristics that might affect the treatment selection and outcomes (age, body weight, height, body mass index, disease stage, bilaterality, and size of the endometrioma). Each data were transformed as an assignment (propensity) score, which informed the probability of the chance of receiving treatment based on their baseline characteristics. Patients were matched on the logit of the propensity score, using calipers of width equal to 0.2 of the standard deviation of the logit of the estimated propensity score (Figure 6-1 left). The groups of data with similar scores are expected to have the nearest values of all confounders. Using the entire

study sample, quintiles of the estimated propensity score were calculated. All patients in the study were stratified into five approximately equal-size groups, using the quintiles of the estimated propensity score to assess whether the propensity score model had been adequately specified, as shown in Figure 6-1 right.

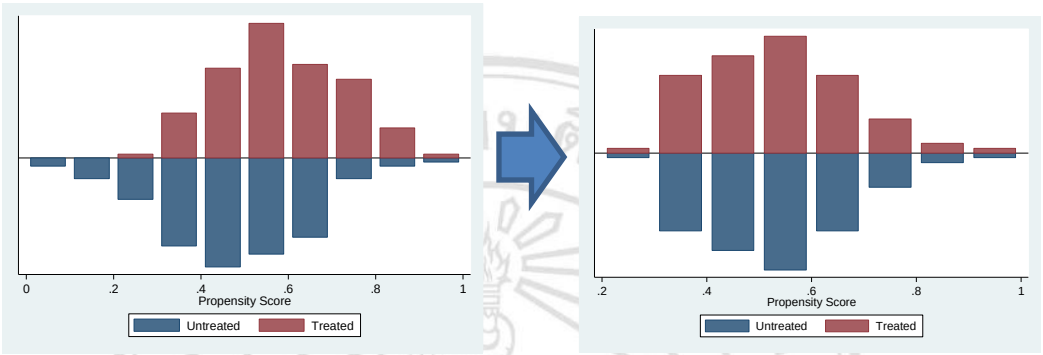


Figure 6-1 Propensity score matching for 1-to-1 analysis (Laparoscopy group was shown in "Treat" and laparotomy group was shown in " Untreated").

The calculated propensity score was then used as a covariate to control for confounding for group assignment to either the laparoscopy or laparotomy approach in the final model. In this study a Cox proportional hazard model was used to estimate the effect of the operative approach, which was the main study factor, on the time to recurrence of endometrioma after adjusting for other confounding variables.

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Appendix B

Tanprasertkul C, Manusook S, Somprasit C, Ekarattanawong S, Sreshthaputra O, Vutyavanich T. Antimullerian hormone changes after laparoscopic ovarian cystectomy for endometrioma compared with the nonovarian conditions. Minim Invasive Surg 2014;2014:654856.

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Research Article

Antimullerian Hormone Changes after Laparoscopic Ovarian Cystectomy for Endometrioma Compared with the Nonovarian Conditions

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Laparoscopic ovarian cystectomy is recommended for surgical procedure of endometrioma. The negative impact on ovarian reserve following removal had been documented. Little evidence had been reported for nonovarian originated effects. *Objective.* To evaluate the impact of laparoscopic ovarian cystectomy for endometrioma on ovarian reserve, measured by serum antimullerian hormone (AMH), compared to nonovarian pelvic surgery. *Materials and Methods.* A prospective study was conducted. Women who underwent laparoscopic ovarian cystectomy (LOC) and laparoscopic nonovarian pelvic surgery (NOS) were recruited and followed up through 6 months. Clinical baseline data and AMH were evaluated. *Results.* 39 and 38 participants were enrolled in LOC and NOS groups, respectively. Baseline characteristics (age, weight, BMI, and height) and preoperative AMH level between 2 groups were not statistically different. After surgery, AMH of both groups decreased since the first week, at 1 month and at 3 months. However, as compared to the LOC group at 6 months after operation, the mean AMH of the NOS group had regained its value with a highly significant difference. *Conclusion.* This study demonstrated the negative impact of nonovarian or indirect effects of laparoscopic surgery to ovarian reserve. The possible mechanisms are necessary for more investigations.

1. Introduction

Endometriosis, the presence of endometrial tissue outside the lining of the uterine cavity, is one of the most common pelvic diseases in women. It is generally acknowledged that an estimated 6–10% of all women during their reproductive years are affected by this condition. In group of infertility women, 38 percent (20–50%) of them have endometriosis. If the patients have a history of chronic pelvic pain, the prevalence could be as high as 71–87 percent [1–4].

The ovarian endometriosis was recognized by the common term, namely, endometriotic cyst or endometrioma. The surgical intervention, laparoscopy, is the most useful option for further evaluation, treatment, and pathological removal [5]. Moreover, laparoscopic surgery is currently accepted as the procedure of choice for both diagnostic and therapeutic modalities. The systematic reviews showed that the excisional surgery or laparoscopic ovarian cystectomy for endometrioma provided more favorable outcomes than drainage and ablation surgery with regard to the recurrence of the endometrioma, recurrence of pain symptoms [6]. However, there were some reports that showed the negative impact on ovarian reserve, measured by serum antimullerian hormone (AMH) levels following ovarian cystectomy [7–11]. AMH levels represent the ovarian follicular pool and could be a useful marker of ovarian reserve. The clinical application of AMH measurement had been proposed in the prediction of quantitative and qualitative aspects in assisted reproductive technologies (ART). AMH seemed to be a better marker in predicting ovarian response to control ovarian stimulation

Table 1: Characteristics of the participants between the laparoscopic ovarian cystectomy (LOC) and nonovarian surgery (NOS) group.

	LOC ($n = 39$)	NOS ($n = 38$)*	P value
Age (yrs)	32.74 ± 6.98	34.74 ± 5.2	0.16
Weight (kg)	52.51 ± 9.42	53.79 ± 6.93	0.49
Height (cm)	159.28 ± 4.63	156.86 ± 6.11	0.05
Duration of surgery (min)	67.05 ± 29.73	92.26 ± 34.20	0.001
Blood loss (mL)	61.15 ± 42.36	105.79 ± 57.50	0.002
Size of ovarian cyst (cm)	5.46 ± 1.70		
Bilateral	6 (15.38%)		
Stage of disease/rASRM score			
III	24 (61.54%)		
IV	15 (38.46%)		

rASRM: the revised American Society for Reproductive Medicine score.
*Laparoscopic NOS: 19 hysterectomies (without adnexectomy), 16 myomectomies, and 3 adenomyomectomies.

than the patient's age, FSH (follicular stimulating hormone), estradiol, and inhibin B [12].

This negative effect had been explained by injury of adjacent ovarian follicles during the cyst wall excision. Also, the comparative study group of the most previous trials was benign, nonendometrioma ovarian cyst. To the best of our knowledge, there were a very few data which explored the possible effects of laparoscopic surgery and anesthesia on AMH in the nonovarian disease. The aim of current study was to evaluate the impact of laparoscopic ovarian cystectomy for endometrioma on ovarian reserve as measured by serum AMH, compared to nonovarian pelvic surgery.

2. Materials and Methods

This was a prospective cohort study which was conducted at Department of Obstetrics and Gynaecology in Thammasat University Hospital, Thailand. After approval from Ethical Institute Committee, the patients were enrolled with the following criteria; having 18–45 years; having regular menstrual cycles (21–35 days) at the time of operation; having no evidence of any other endocrine disorders such as diabetes mellitus, thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia, Cushing's syndrome, or adrenal insufficiency; undergoing laparoscopic ovarian cystectomy or laparoscopic nonovarian pelvic surgery for benign pelvic disease; having no previous history of adnexal surgery; having no suspicious findings of malignant ovarian diseases, never taking any medication such as oral pill and hormonal drugs within 3 months before the enrollment, pathological diagnosis of excised ovarian tissue confirmed it to be an endometriotic cyst in the study group and to consist of other benign pelvic diseases in control group. The participants were excluded if they had one of the following: polycystic ovarian syndrome according to the Rotterdam criteria [13] or operation conversion to exploratory laparotomy or pathological report as the malignant diseases.

All patients underwent the standard surgical procedures under general anesthesia. Each patient was appointed to visit the hospital on the seventh day and 1st, 3rd, and sixth months after laparoscopic ovarian cystectomy or nonovarian pelvic surgery. On each visit and preoperative day, blood samples would be obtained from the patients by venipuncture to measure the levels of AMH. The patient's sera were obtained from blood samples by centrifuge at 1400 ×g for 10 minutes to separate cellular contents and debris. The serum was transferred to sterile polypropylene tubes and stored at −70°C until assayed. Serum AMH levels were measured by enzyme-linked immunosorbent assay (ELISA, Diagnostic Systems Laboratories, Webster, TX, USA).

The sample size was calculated based on the determination of difference in means including confidence interval approach. The difference in means of serum AMH from previous studies was used for sample size calculation. From the study of Ercan et al. [11], mean preoperative AMH levels of the study and the control cases were 1.62 ± 1.09 and 2.06 ± 0.51 ng/mL, respectively. According to these values, the sample size was calculated by STATA program. The estimated number of women in each group was 40. In data and statistical analysis, descriptive statistics was used to describe study subjects' characteristics. Concentrations of serum AMH were interpreted between each sampling point (preoperative, postoperative first week, for 1st, 3rd and 6th months). The P value of less than 0.05 was considered as statistically significant.

3. Results

In this study, 90 women were enrolled. There were thirty-nine and 38 women in laparoscopic ovarian cystectomy (LOC) and laparoscopic nonovarian pelvic surgery (NOS), respectively, who had adequate complete data to analyze (Table 1). The mean age, weight, and height were not different between both groups. Duration of surgery and blood loss in LOC group were statistically significant in their differences from those of the NOS group. The mean diameter of endometrioma was 5.46 cm and ranged from 3 cm to 10 cm. Most of cases were unilateral but more so on the left side(58.97%). Bilateral disease was found to be only 15.38 percent. NOS group is composed of 19, 16, and 3 cases of laparoscopic hysterectomy (without adnexectomy), myomectomy, and adenomyomectomy, respectively.

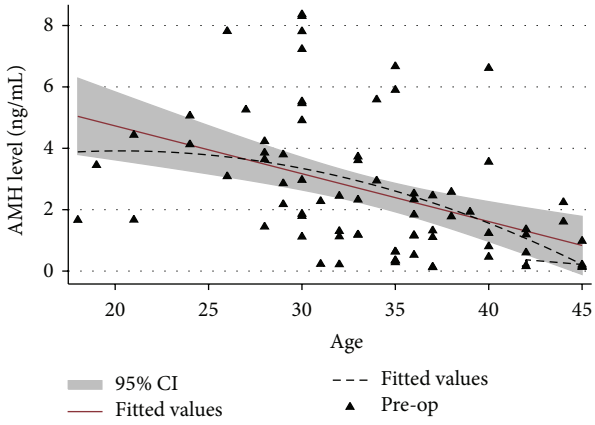

Figure 1: The correlation of serum AMH and age in participants. (AMH: antimullerian hormone).

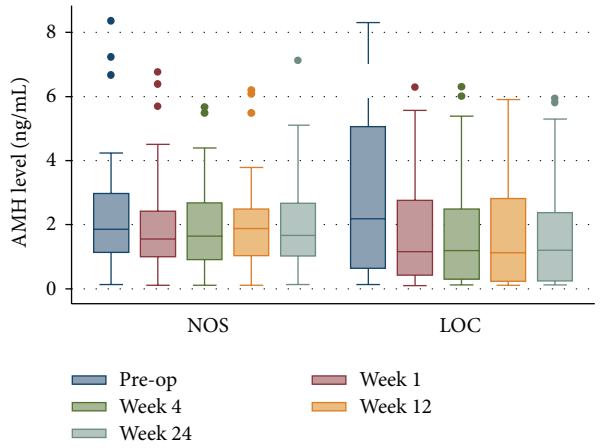

Figure 2: The changes in the serum AMH level at preoperative, post-op over periods of first week, 1, 3 and 6 months in the LOC and NOS groups. (AMH: antimullerian hormone, LOC: laparoscopic ovarian cystectomy, and NOS: nonovarian laparoscopic pelvic surgery).

As shown in Figure 1, the distribution of serum AMH levels was inversely correlated to the patients' age. After age of 40, the rate of declination was accelerated.

When comparing the serum AMH of LOC to NOS group, there was no statistically significant difference between groups at preoperative level, first visit on 7th day, second visit on first month, and third visit on 3rd month. However, there was statistically significant difference between groups at 6th month of operation. This negative change also occurred in the unilateral LOC group but there was no statistical difference.

4. Discussion

As shown in Figure 1, the AMH level was decreased with the advance of women age. This result demonstrated that ovarian reserve was declined throughout reproductive age. However, the cut-off value for serum AMH level for approving diminished ovarian reserve is still not determined. Previous research suggested that AMH was a promising marker [9]. But availability was limited because it was of high cost.

This study found that laparoscopic ovarian cystectomy in cases of endometrioma had negative effect on the ovarian capacity. Similar to previous studies which had been shown, the ovarian cystectomy can be harmful to ovarian reserve [7–10]. The present study showed that this adverse effect occurred immediately after operation and affected the patient for medium term, at least 6 months. In 9–12 months, we also investigated some patients; this diminished ovarian reserve effects still persist in most of them (data not available).

The results demonstrated that there is a strong negative impact of ovarian cystectomy on ovarian reserve; the guideline for management of ovarian cyst or endometrioma might be adjusted and reconsidered. Busacca et al. [14] reported that patients who underwent surgical operation for bilateral endometrioma had a prevalence of 2.4% ovarian failure immediately after surgery. This was consistent with Somigliana et al. [15] that in vitro fertilization (IVF) outcome and ovarian reserve were severely impaired in women who underwent operation for bilateral ovarian endometriomas. Similar to these findings, bilaterality is the major risk factor. Therefore, before ovarian surgery, not only morphological assessment but also careful ovarian function evaluation was needed. In case of low ovarian reserve, the surgical technique might be tailored and adjusted. The other alternative treatment may be a better option.

Most previous studies compared women who had ovarian cystectomy to the patients who had no history of surgery, for example, infertile women. Moreover, the study was cross-sectional design which did not have ability to demonstrate the causal relationship. The flaws of these were the uncertain causes of decline in ovarian reserve. Not only loss of follicles during stripping the endometriotic cyst but also blood loss in operative field could be another explainable reason. Atabekoğlu et al. [16] had reported the additional effect of total abdominal hysterectomy on serum AMH, 30% more loss of ovarian reserve. The surgery, hysterectomy, could reduce ovarian blood supply and resulted in temporary decline in ovarian reserve. In this study, we compared LOC to the NOS group in which laparoscopic surgery does not directly involve the ovaries, for example, hysterectomy and myomectomy. The postulated mechanism of decline in AMH especially in first 3 months might be due to the effect of blood loss and anaesthesia. This could be rescued by revascularisation of the ovaries.

As shown in Table 2 and Figure 2, AMH level of both groups had declined immediately after laparoscopic surgery. In LOC group the serum AMH level had declined until six months at least. However, this effect lasts only for short term, three months in NOS group. This might demonstrate that the effect of blood volume depletion includes the aesthetic impact during surgery. But it was only short term and temporary adverse effect.

There were some limitations of the study. Firstly, the ovarian reserve was measured by only single marker. Antral follicle count (AFC) is another useful marker for ovarian

Table 2: Comparison of serum AMH level (ng/mL) between LOC and NOS group.

Serum AMH	LOC			NOS	Diff.	*P* value		
	Uni* ($n = 33$)	Bi* ($n = 6$)	All* ($n = 39$)	($n = 38$)	All/NOS	All/NOS	Uni/NOS	Bi/NOS
Preoperative	2.94 ± 2.47	2.01 ± 1.02	2.84 ± 2.47	2.33 ± 1.91	0.51	0.31	0.22	0.69
Postoperative								
7 days	1.71 ± 1.41	1.48 ± 1.07	1.76 ± 1.52	1.97 ± 1.64	−0.21	0.57	0.48	0.48
1 month	1.79 ± 1.74	1.41 ± 0.77	1.80 ± 1.70	2.24 ± 1.40	−0.44	0.22	0.23	0.16
3 months	1.86 ± 1.60	0.98 ± 0.42	1.72 ± 1.55	2.28 ± 1.46	−0.56	0.11	0.25	0.03
6 months	2.03 ± 1.74	0.94 ± 0.46	1.69 ± 1.63	2.44 ± 1.59	−0.75	0.04§	0.30	0.02§

Uni: unilateral, Bi: bilateral, and *mean ± standard deviation.
§Statistically significant, Diff.: mean difference, and NOS: nonovarian laparoscopic pelvic surgery.
AMH: antimullerian hormone and LOC: laparoscopic ovarian cystectomy.

reserve. Sugita et al. [17] postulated the balancing effect of a healthy ovary which may compensate for a reduced ovarian reserve in the contralateral, affected ovary. Therefore, AFC may be a more accurate marker than AMH. However, this study did not have enough AFC data for analysis. Also, the measurement of AFC is subjective and evaluator-dependent. Secondly, the operations in the NOS group varied and were non-unique. Moreover, laparoscopic surgeons use a variety of techniques to operate on a case by case basis. Thirdly, there were some dropout participants, caused by loss follow-up and becoming pregnant.

5. Conclusion

Laparoscopic ovarian cystectomy in case of endometrioma had negative impact on the ovarian reserve, measured by serum AMH. This effect was sustained at least 6 months after operation. The negative impact occurred in patients who had nonovarian pelvic surgery but this adverse effect was only mild and temporary. This study showed the negative impact of nonovarian or indirect effects of laparoscopic surgery on ovarian reserve; however, the exact mechanisms were still unknown and needed to be explored more.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Appendix C

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 Suppl 8:S95-101.

Impact of Hemostasis Methods, Electrocoagulation versus Suture, in Laparoscopic Endometriotic Cystectomy on the Ovarian Reserve: A Randomized Controlled Trial

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Objective: *To evaluate the impact on ovarian reserve between two different methods of hemostasis after laparoscopic ovarian endometrioma excision.*

Material and Method: *A randomized controlled study was conducted from January to December 2013 in Thammasat University Hospital, Thailand. Reproductive women, age 18-45 years who underwent laparoscopic ovarian cystectomy were randomized in electrocoagulation and suture groups. Clinical baseline data and ovarian reserve outcome (anti-Mullerian hormone (AMH)) were evaluated.*

Results: *Fifty participants were recruited and randomized in two groups. Electrocoagulation and suture groups consisted of 25 participants. Baseline characteristics between 2 groups (age, weight, BMI, height, cyst diameter, duration and estimated blood loss) were not statistically different. There were no significant difference of AMH between electrocoagulation and suture group at pre-operative (2.90±2.26 vs. 2.52±2.37 ng/ml), 1 week (1.78±1.51 vs. 1.99±1.71 ng/ml), 1 month (1.76±1.50 vs. 2.09±1.62 ng/ml), 3 months (2.09±1.66 vs. 1.96±1.68 ng/ml) and 6 months (2.11±1.84 vs 1.72±1.68 ng/ml), respectively. However, mean AMH of both groups significantly decreased since first week of operation. Effect of laparoscopic ovarian surgery had significantly declined and sustained AMH level until 6 months.*

Conclusion: *Laparoscopic cystectomy of ovarian endometrioma has negative impact to ovarian reserve. Either electrocoagulation or suture method had no different effects.*

Keywords: *Laparoscopic ovarian cystectomy, Anti-Mullerian hormone, Endometrioma*

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Ovarian endometrioma is one of the most common manifestations of endometriosis[1]. Laparoscopic ovarian cystectomy is currently considered the procedure of choice in women with endometrioma and benign ovarian cysts[2]. The systematic review and meta-analysis demonstrated that excisional surgery for endometrioma provides for a more favorable outcome than drainage and ablation with regard to the recurrence of the endometrioma, recurrence of pain symptoms including women who were previously sub-fertile[3]. This approach has been gaining increasing acceptance among gynecologic surgeons. However, there are some studies which demonstrated the negative impact of laparoscopic ovarian endometrioma excision on ovarian reserve[4-8]. The ovarian reserve testing comprises hormonal markers such as basal follicle stimulating hormone (FSH), estradiol, inhibin-B, anti-Mullerian hormone (AMH) and ultrasonographic markers (ovarian volume and antral follicle counts (AFC)). These markers have limitations in terms of which test(s) should be used to predict reliably ovarian reserve with regard to accuracy, invasiveness, cost, convenience and utility[9].

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Anti-Mullerian hormone (AMH) levels represent the ovarian follicular pool and could be a prediction of quantitative and qualitative aspects in assisted reproductive technologies (ART). AMH seems to be a better marker in predicting ovarian response to controlled ovarian stimulation than age of the patient, FSH, estradiol, inhibin B and antral follicle count (AFC)[10-13].

Hemostasis technique in laparoscopic excision of ovarian cysts has been questioned to be a part major of compromising ovarian reserve. Basically, electrocoagulation with bipolar has been used to secure bleeding after laparoscopic excision of ovarian cysts. But few studies reported the type of hemostasis associated with a significant reduction in ovarian reserve[14-16]. According to the questionable and inconclusive results on the impact of these hemostasis techniques in laparoscopic cystectomy on ovarian reserve in cases of endometrioma, objective of the current study was to evaluate the impact of two different methods of hemostasis after laparoscopic excision of ovarian endometriomas on ovarian reserve.

Material and Method

The present study, randomized controlled trial was conducted at department of Obstetrics and Gynecology in Thammasat University Hospital, Thailand during January and December 2013 after approval from ethical institute committee. We enrolled the patients with endometrioma who underwent laparoscopic ovarian cystectomy. They met all the following eligibility criteria: ages of 18-45, completely understand the process of this study with written informed consent, having regular menstrual cycles, never taking any medication such as oral pill and hormonal drugs during the 3 months before the enrollment, no previous history of adnexal surgery, no evidence of any other endocrine disorders such as diabetes mellitus, thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia, Cushing's syndrome, or adrenal insufficiency, pathological diagnosis of excised ovarian tissue confirmed as endometriotic cyst. They were excluded if they had polycystic ovarian syndrome according to the Rotterdam criteria[17], pathological diagnosis of excised ovarian tissue was confirmed as non-endometriotic cyst and converted to laparotomy.

Eligible patients who provided written informed consent underwent randomization. In order to achieve comparable groups, a table of random numbers was used. Randomization was carried out using opaque and sealed envelopes that were consecutively numbered. The details of randomization were kept in safe and confidential. Subjects withdrawn from the trial retain their identification codes (e.g. randomization number). New subjects received a new identification code. Allocation concealment was maintained until the time when hemostasis was started. All patients were blinded for the study intervention. Blinding of the surgeon and people in the operating was not feasible. The assessors of serum AMH were blinded to patients' allocated treatment group for postoperative evaluation.

The sample size was calculated based on the determination for difference in means with repeated measures includes confidence interval approach. The means of serum AMH from previous studies was used for sample size calculation. From the study of Ercan et al[6], mean pre-operative AMH levels of the study group was 1.62 ± 1.09 ng/ml. If estimation of the difference and power were 20% and 80%, respectively, the significance level was 0.05 by two-sided. By calculation, sample size for means with repeated measures, the number of women in each group was 25; hence the number of patients in the present study was 50.

For the operation techniques for laparoscopic cystectomy, all patients underwent the surgical procedure under general anesthesia. Laparoscopic pneumoperitoneum had been created by CO_2 in sufflation via Verres needle that was passed through a 5-mm umbilical incision until the intra-abdominal pressure reached 12 mmHg. Following pneumoperitoneum, umbilical 5-mm trocar and telescope entries were made. Then, two of 5-mm trocars were inserted from suprainguinal region or suprapubic area under direct laparoscopic observation. Successful removal of a cyst consisted of incisions of the ovarian cyst with scissors, identifying the cystic wall and removing it from the ovarian cortex by traction with grasping forceps. If the cystic content leaked, suction with irrigation of spillage content as much as possible was preferred.

In bipolar coagulation group, hemostasis was achieved with 25-30 W bipolar current forceps applied on the ovarian parenchyma. To reduce the possible damage of normal ovarian tissues, hemostatic procedure was minimally performed, as necessary. In suture group, the operated ovary was sutured for approximation of the ovarian edges and bleeding control. A single polydioxa non-suture (2-0 Vicryl) on a CT curved needle holder would be used to re-approximate the edges and achieve satisfactory

hemostasis. The suture was performed with intra-ovarian knots and the knots were not detectable on the ovarian surface. Bleeding from ovarian hilus was resolved only by suturing, as well. All procedures were performed by one or two gynecologic laparoscopists who had experience in laparoscopic ovarian cystectomy more than a hundred cases.

After the removal of ovarian cyst, specimens were assessed by visual inspection for any evidence of malignancy such as vegetation. Histo-pathological examination of removed specimens was always done. The patients were kept under observation in the in-patient room for 24 to 48 hours after the operation to avoid any complications associated with surgery or anesthesia and then discharged.

Each patients were asked to visit the hospital on the seventh day of postoperative status, 1 month, 3 months and month 6 after laparoscopic ovarian cystectomy. At each visit and pre-operative day, blood samples would be obtained from the patients by venipuncture to measure the levels of AMH. The patient's sera were obtained from blood samples in 5-milliliter tube and centrifuged at 1,400 x g for 10 minutes to separate cellular contents and debris. The sera were transferred to sterile polypropylene tubes and stored at -70°C until assayed. Serum AMH levels were measured by enzyme-linked immunosorbent assay (ELISA, Diagnostic Systems Laboratories, Webster, TX, USA).

Statistical methods were used to assess the quality of data, homogeneity of treatment groups, endpoints and safety of the both groups. The confirmatory analysis was performed on the basis of an intention-to-treat (ITT) population and with respect to ITT principles. Categorical data were summarized by means of absolute and relative frequencies (count and percent). Continuous data were presented by means of the following summary statistics: the number of observations, median, minimum and maximum. Concentrations of serum AMH were compared between each sampling point using unpaired t-test. A *p*-value of less than 0 .05 was considered as statistically significant.

Results

Of the 50 participants recruited, there were 25 patients in each group, bipolar coagulation and suture, respectively. Most patients were nulliparous and never had prior lower abdominal surgery. There were no major complications related to the surgery in both groups. The postoperative courses were uneventful. Baseline characteristics between 2 groups such as age, weight, height, size of endometrioma, duration of surgery and blood loss were not statistically different (Table 1). The stage of disease and the bilateral of endometrioma presenting were also comparable. Mean of the revised American Society for Reproductive Medicine (rASRM) scores between bipolarcoagulation and suture groups were not statistically different (48.76±22.83 vs. 43.52±16.86, $p = 0.36$).

There were no significant differences in AMH of electrocoagulation and suture group at pre-operative (2.90±2.26 vs. 2.52±2.37 ng/ml), 1 week (1.78±1.51 vs. 1.99±1.71 ng/ml), 1 month (1.76±1.50 vs. 2.09±1.62 ng/ml), 3 months (2.09±1.66 vs. 1.96±1.68 ng/ml) and 6 months (2.11±1.84 vs. 1.72±1.68 ng/ml), respectively. However, mean AMH of both groups significantly decreased since first week of operation. Mean AMH of all participants at pre-operative and 6 months after

Table 1. Baseline clinical profiles of the patients

Clinical profiles	Coagulation (n = 25)	Suturing (n = 25)	*p*-value
Age (years)	33.6±5.2	33.6±6.6	0.96
Body weight (kg)	50.3±6.5	53.7±7.9	0.10
Height (cm)	158.5±4.5	158.9±4.6	0.76
BMI (kg/m^2)	20.1±2.8	21.3±3.5	0.17
Duration of surgery (min)	81.4±30.8	80.6±34.9	0.93
Blood loss (cc)	88.8±66.3	79.6±41.8	0.56
Stage of disease (%)			1.00
III	12 (48)	13 (52)	
IV	13 (52)	12 (48)	
Bilaterality (%)	6 (25)	5 (20)	1.00
Size of endometrioma (cm)	5.4±2.0	5.0±1.6	0.54

Numbers are mean ± SD, or n (%)

surgery were (2.62±2.27 ng/ml) and (1.91±1.75 ng/ml), respectively (p<0.001). Effect of laparoscopic ovarian surgery had significantly declined and sustained AMH level until 6 months.

The concentration of AMH was decreasing with the patients age. The distribution of some values were out of 95% confidence interval. The changes of serum AMH level at first week post-operation had much significantly decreased in coagulation group (67% vs. 31%, p<0.001) from pre-operative level. However, this significant decline was not apparent at one month, 3 months and 6 months.

Discussion

In the present study, the authors findings supported previous studies that the laparoscopic ovarian cystectomy or stripping technique for endometrioma had significant negative effect on ovarian reserve[5,6,8]. Several markers such as antral follicle count (AFC), FSH or AMH could be commonly utilized to assess ovarian reserve. Serum AMH level was selectively applied in the present study because it is the most sensitive and practical marker compared with the others. AMH level is not affected by gonadotropin, GnRH agonist, pregnancy or sex hormones. Moreover, the level is stable throughout menstrual cycle[18-20].

The reduction of AMH level in this study was significantly apparent from the first week after operation. The adverse effect had been maintained for at least six months after surgery. Mechanisms underlying the reduction of ovarian reserve in an operated ovary could be explained in the following explanations. Firstly, this damage could have occurred before surgery. Since the cyst per se can negatively affect the surrounding ovarian tissue. Secondly, in performing the cystectomy, some healthy follicles in adjacent ovarian tissue were removed during excision, stripping the capsule. Hirokawa et al[21] also reported that pre-operative AMH was correlated with the number of follicles in the cystectomy specimen. To avoid abundant effect, surgeon has to identify carefully the location of healthy follicles before starting remove the cyst wall. Bilaterality of endometrioma was determined as one of the major risk factors[22]. However, the authors failed to demonstrate the effect of bilateral endometrioma because only one-fifth of our patients were in this group.

The effects of hemostasis technique had showed precisely only at the first week. The AMH level in bipolar coagulation group was significantly diminished and much more decreased from prior baseline level than the suture group, on whom had been used only the suturing technique to stop bleeding. The electrical coagulation was presumed to be an important role in terms of damage to ovarian stroma and vascularization. This finding was consistent to the study of Zoitoun et al[23]. In their study, the only suturing for hemostasis was performed in cases of laparotomy. Most of gynaecologists prefer to stop bleeding by suturing in open laparotomy. Because hemostasis for the active bleeding in laparoscopic field needs much more time and expertise, endoscopic suturing and knotting are among the highest skills used in laparoscopic surgery.

The recovery of ovarian reserve was reported by Suksompong et al[24]. The mechanisms of the event are still not exactly understood. Vascular vasculature and rescue from atretric follicles could be the most possible explanations. Our findings also found this effect after 3 months post-operation. But there was no statistically significance between the different haemostatic methods (Fig. 1).

European Society of Human Reproduction and Embryology recommended the ovarian cystectomy when the size of cyst more than 3 cm to histologically confirm[2]. However, clinicians must outweigh the risk

Table 2. Serum anti-Mullerian hormone (AMH) level (ng/ml) in patients undergoing coagulation or suturing, difference and 95% confidence interval

Time	Coagulation (n = 25)	Suturing (n = 25)	Difference	95% CI	p-value
Preoperative	2.90±2.26	2.52±2.37	0.38	-0.93, 1.70	0.56
Day 7	1.78±1.51	1.99±1.71	-0.21	-1.13, 0.71	0.65
Month 1	1.76±1.50	2.09±1.62	-0.33	-1.35, 0.69	0.50
Month 3	2.09±1.66	1.96±1.68	0.13	-0.91, 1.18	0.52
Month 6	2.11±1.84	1.72±1.68	0.39	-0.66, 1.44	0.47

Numbers are mean ± SD

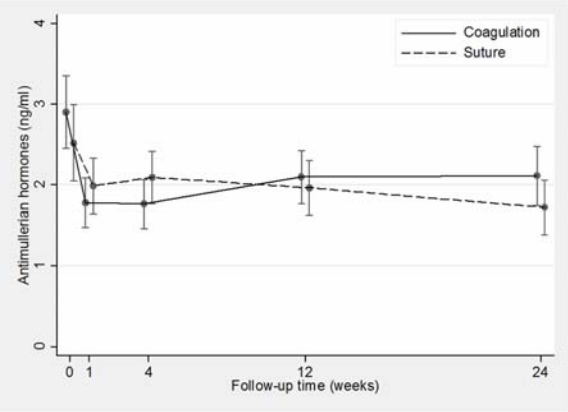

Fig. 1 The changes of serum AMH level at preoperative, post op day 7, month 1, month 3 and month 6 in coagulation group versus suturing group.

of the reduced ovarian function and possible loss of the ovary after surgery, especially in infertile patients.

There are several limitations of this study. Firstly, only one marker of ovarian reserve was used. Application of more ovarian reserve markers, associated with numerous of confounders, would be carefully interpreted. Secondly, although only two surgeons were involved in the study, the variation of techniques and the operating field in case by case are still the key factor which cannot be accurately controlled. Thirdly, the study was only prospectively investigated for 6 months. Long-term outcomes assessment such as response to infertility treatment, pregnancy outcomes could be the best end points.

Conclusion

The laparoscopic ovarian cystectomy for endometrioma had significant adverse effect on ovarian reserve, assessed by AMH level. The suturing technique for hemostasis has had a tendency to lessen this effect rather than the electrical coagulation by bipolar cauterization. However, this had only been shown in the short term, the first week visit. In the intermediate term, 6 months follow-up, the effects of hemostasis technique were showed to be insignificantly different.

What is already know in this topic ?

Excisional surgery for endometrioma provides for a more favorable outcomes than drainage and ablation with regard to the recurrence of the endometrioma, recurrence of pain symptoms including women who were previously sub-fertile.

There are some studies which demonstrated the negative impact of laparoscopic ovarian endometrioma excision on ovarian reserve.

What this study add ?

Laparoscopic cystectomy of ovarian endometrioma has negative impact on ovarian reserve.

To stop bleeding during surgery, neither electrocoagulation nor the suture method had different effects on ovarian reserve.

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Potential conflict of interests

None.

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ผลของวิธีหยุดเลือด ระหว่างการจี้ไฟฟ้าห้ามเลือดและการเย็บผูก ในการผ่าตัดส่องกล้องเลาะถุงน้ำรังไข่ชนิดเอนโดเมทริโอมาต่อการทำงานของรังไข่: การศึกษาแบบทดลองสุ่ม

ชำนาญ แท่นประเสริฐกุล, โสภาพรรณ เอกรัตนวงศ์, โอภาส เศรษฐบุตร, ธีระพร วุฒยวนิช

วัตถุประสงค์: เพื่อประเมินผลของวิธีหยุดเลือด ระหว่างการจี้ไฟฟ้าห้ามเลือดและการเย็บผูก ในการผ่าตัดส่องกล้องเลาะถุงน้ำรังไข่ชนิดเอนโดเมทริโอมาต่อการทำงานของรังไข่

วัสดุและวิธีการ: ได้ทำการศึกษาโดยวิธีทดลองสุ่มในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติระหว่าง เดือนมกราคม ถึง เดือนธันวาคม พ.ศ. 2556 โดยเลือกผู้ป่วยสตรีอายุระหว่าง 18-45 ปี ที่ได้มาทำผ่าตัดส่องกล้องเลาะถุงน้ำรังไข่ชนิดเอนโดเมทริโอมา และสุ่มเลือกวิธีการหยุดเลือดระหว่างการผ่าตัดโดยวิธี จี้ไฟฟ้าห้ามเลือดและการเย็บผูก เก็บรวมรวมข้อมูลพื้นฐานและประเมินผลต่อการทำงานของรังไข่โดยการใช้ระดับของฮอร์โมนแอนติมูลเลอเรียน

ผลการศึกษา: ได้ผู้เข้าร่วมวิจัย 50 ราย โดยสุ่มเป็น 2 กลุ่ม คือ 25 ราย ในกลุ่มจี้ไฟฟ้าห้ามเลือด และ 25 ราย ในกลุ่มเย็บผูกเพื่อห้ามเลือด ข้อมูลพื้นฐานทั้งสองกลุ่ม ได้แก่ อายุ น้ำหนัก ส่วนสูง ดัชนีมวลกาย ขนาดของก้อน เวลาการผ่าตัดและปริมาณการเสียเลือดระหว่างการผ่าตัด ไม่แตกต่างกัน ระดับของฮอร์โมน แอนติมูลเลอเรียนก่อนผ่าตัด ไม่มีความแตกต่างกันระหว่างสองกลุ่ม (2.90±2.26 และ 2.52±2.37 นาโนกรัมต่อมิลลิลิตร) และไม่พบว่ามีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติระหว่างสองกลุ่ม หลังการผ่าตัดที่ 1 สัปดาห์ (1.78±1.51 และ 1.99±1.71 นาโนกรัมต่อมิลลิลิตร) ที่ 1 เดือน (1.76±1.50 และ 2.09±1.62 นาโนกรัมต่อมิลลิลิตร) ที่ 3 เดือน (2.09±1.66 และ 1.96±1.68 นาโนกรัมต่อมิลลิลิตร) และที่ 6 เดือน (2.11±1.84 และ 1.72±1.68 นาโนกรัมต่อมิลลิลิตร) ตามลำดับ อย่างไรก็ตามระดับเฉลี่ยของฮอร์โมนแอนติมูลเลอเรียน ลดลงอย่างมีนัยสำคัญทางสถิติภายหลังการผ่าตัดที่ 1 สัปดาห์ และผลการลดลงนี้คงอยู่อย่างต่อเนื่องจนกระทั่ง 6 เดือน

สรุป: การผ่าตัดส่องกล้องเลาะถุงน้ำรังไข่ชนิดเอนโดเมทริโอมามีผลเสียต่อการทำงานของรังไข่ โดยที่วิธีการหยุดเลือดระหว่างการจี้ไฟฟ้าห้ามเลือดและการเย็บผูกไม่มีผลต่างกัน

Appendix D

Tanprasertkul C , Manusook S , Somprasit C, Sreshthaputra O, Patumanond J , Vutyavanich T. Recurrence of Endometrioma Following Conservative Ovarian Endometrioma Cystectomy: Laparoscopy versus Laparotomy. Med Assoc Thai 2015 ;98 Suppl 3:S96-100.

Recurrence of Endometrioma Following Conservative Ovarian Endometrioma Cystectomy: Laparoscopy versus Laparotomy

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Objective: *To investigate the recurrence rate and disease-free interval between laparoscopy versus laparotomy for the conservative surgery of endometrioma.*

Material and Method: *A retrospective cohort study was conducted. The medical records of reproductive women who underwent conservative ovarian cystectomy surgery (laparoscopy or laparotomy) for endometrioma at Thammasat University Hospital were retrieved. The patients were followed through 24 months to evaluate the recurrence of endometrioma. Propensity scoring was used to adjust for confounding by indication and confounding by contraindication. Model for competing time to event was used in analysis.*

Results: *One hundred and twenty-eight and 114 patients were enrolled in laparoscopy and laparotomy groups, respectively. Mean age and body weight in laparotomy group were statistically higher than those in the other group were. Mean height and body mass index were, however, not statistically different in either groups. In addition, the stage of disease and bilaterality in both groups were comparable. Diameter of endometrioma in laparotomy group was significantly larger than that in laparoscopy group (7.0±2.5 vs. 6.2±1.8 cm, respectively; p = 0.004). After adjusting for propensity scoring, the endometrioma recurrence rate was significantly higher in laparoscopy group as compared to laparotomy group (27.3% vs. 14.9%, respectively; p = 0.02). However, the cumulative rate of pregnancy after surgery was not statistically different (4.7% vs. 4.4%, respectively; p = 1.0).*

Conclusion: *The present study has demonstrated that the surgical technique has a strong impact on the recurrence or disease-free interval. Laparoscopy might not eradicate the disease pathology as effectively as open laparotomy in some situations, such as in cases with complexity of disease.*

Keywords: *Recurrence of endometrioma, Ovarian cystectomy, Laparoscopy, Laparotomy*

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Endometriosis is a common gynecologic condition. It is a complex, benign and chronic disease. Ovarian endometriosis or endometrioma, is one of the most common manifestations among reproductive women with endometriosis. European Society of Human Reproduction and Embryology (ESHRE) recommends that histology should be obtained to exclude malignancy when the diameter of ovarian endometriosis is more than 3 cm[1]. Among types of endometriosis-linked ovarian cancer, endometrioid and clear-cell are the commonest[2,3].

Although definite treatment of endometriosis is a hysterectomy with removal of the both ovaries, conservative surgery is preferred as the treatment of endometriosis and ovarian cyst when fertility still needs to be preserved. However, one of most concerned issues after conservative surgery is the recurrence of endometrioma. In general, the recurrence rate for endometriosis is 20-30.4% in the first two years after

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surgery[4].

To date, most surgical procedures have been performed by laparoscopy, which offers more short-term advantages than laparotomy does. In some circumstances, it could have limitations in the operative field and might increase the complication rate. Moreover, when the disease is complex, there are reports that the operation might not eradicate all the disease pathology.

Nowadays, laparotomy surgery is still warranted in some situations, such as the places with low resources, no expertise, difficulty to operate cases and also when the availability of the endoscopy is not easy to access. The present study's objective was to compare the recurrence rates of endometrioma by laparoscopy to laparotomy.

Material and Method

Research design was a retrospective cohort study. The study was approved by the ethic committees of Faculty of Medicine at Thammasat University and of Thammasat University Hospital. The data from medical records of reproductive women, aged 18-45 years who underwent ovarian endometrioma cystectomy either laparoscopy or laparotomy approach the Department of Obstetrics and Gynecology, Thammasat University Hospital during October 2005-December 2012, were retrieved. The pathological diagnosis of excised ovarian tissue was confirmed as endometrioma. Findings of malignant ovarian diseases were excluded. The recurrence of ovarian endometrioma was defined as having typical cysts, as detected by transvaginal ultrasonography, of more than 2 cm in diameter within two years of surgery. The recurrence was diagnosed only when the cyst had not disappeared following several consecutive menstrual cycles when it was impossible to distinguish the cyst from a transient corpus luteum cyst or an intraovarian hematoma[5].

The sample size was calculated based the determination for survival-time event. Recurrent rate in two years was 30.4%[5]. Power was set at 80%, and significance level at $p<0.05$ (two-sided). By calculation, the total number of women required was 288. Demographic data of patients, namely age, height, weight, BMI and clinical characteristics; revised American Society of Reproductive Medicine (rASRM) score; operation type; size of ovarian cyst; bilaterality; duration of surgery and complications were recorded. For data and statistic analysis, descriptive statistics was used to describe study subjects' characteristics, count with percentages for categorical variables and mean with standard deviation for continuous variables. Fisher's exact test and independent t-test were used for comparing categorical variables and continuous variables, respectively.

As a retrospective study, the two contrast groups were not assigned to treatments at random. Confounding by indication and confounding by contraindication for the two treatment modalities were likely to interfere with the true association between treatments and recurrence of endometrioma. A propensity score analysis was therefore used to handle this problem. The propensity score was estimated as a surrogate of the likelihood or the probability of being assigned to each treatment arm. It was calculated in the form of logit as a function of factors most likely to influence the likelihood of being assigned to each treatment arm (age, body weight, height, body mass index, disease stage, bilaterality, and size of endometrioma). The calculated propensity was then used as a covariate to control for confounding by indication and confounding by contraindication in the final model.

The effect of each treatment on the recurrence of endometrioma was analyzed by time-to-event, considering pregnancy during the follow-up time as a competing risk and presented with competing risk adjusted failure curves.

Results

Two hundred ninety-four women underwent endometrioma ovarian cystectomy during the studied period. Only 242 records had complete data to analyze. As shown in Table 1, 114 and 128 medical records were in the laparotomy and laparoscopy groups, respectively. The mean age and body weight of laparotomy patients were significant higher than those of the laparoscopy group (33.9$\pm$5.9 years vs. 30.9$\pm$5.4 years, respectively, $p<0.001$; 53.7$\pm$7.9 kg vs. 51.6$\pm$6.3 kg, respectively, $p = 0.02$). However, the mean of height and BMI (body mass index) were not statistically different. In addition, the stage of disease and bilaterality in both groups were comparable. All of the patients were in the advanced stage of disease; about one-third of which was in stage IV. Diameter of endometrioma in the laparotomy group was significantly larger than that in the laparoscopy group (7.0$\pm$2.5 cm vs. 6.2$\pm$1.8 cm, respectively; $p = 0.004$).

The operative time of both groups was not different. Furthermore, the proportions as percentages of pre and post-operative treatment were comparable. The recurrence rate of disease in the laparotomy group

was about one half lower than that in the laparoscopic patients (14.9% vs. 27.3%, respectively; p = 0.02). However, the cumulative rate of pregnancy after surgery was not different (4.4% vs. 4.7%, respectively; p = 1.0).

The recurrence of disease and competing-risks regression were analyzed in the form of survival curve. The cumulative incidences of both groups were presented in Fig. 1. The recurrent incidence of laparoscopic group began higher than that of the other 12 months of conservative surgery follow-up.

Discussion

Laparoscopic surgery for endometrioma has been reported in a bunch of literature as the standard operative technique[6]. Compared to the open laparotomy, laparoscopic approach has much better short-term health benefits, such as rapid recovery, less pain, and early return to work[7]. However, open laparotomy technique still has role and been used in many circumstances.

Comparing baseline demographic data between both groups, the laparoscopic patients were younger and had less body weight than the other. In addition, the diameter of endometrioma seemed to be smaller. Despite stage of disease, bilaterality and duration of surgery were not different. This could be explained by the preference of surgeons. In leaner and younger patients whose operations are likely to be easier, the way to explore the pelvic pathology tends to be laparoscopic approach. This fact results in bias and confounding by indication, which is an important limitation of the present study. Hence, we used the

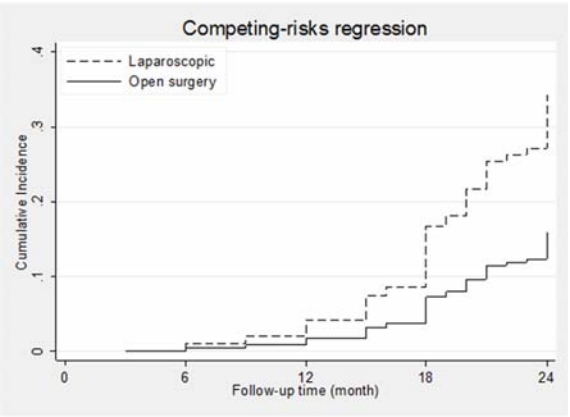

Fig. 1 Survival curve of recurrent endometrioma between the laparotomy and laparoscopic groups by competing risks regression analysis.

Table 1. Characteristics of reproductive-aged endometriosis women

Characteristics	Laparotomy (n = 114)	Laparoscopy (n = 128)	p-value
Age (year)*	33.9±5.9	30.9±5.4	<0.001
Body weight (kg)*	53.7±7.9	51.6±6.3	0.020
Height (cm)*	157.6±5.7	157.4±5.3	0.730
Stage of disease/rASRM score**			0.780
III	75 (65.8)	87 (68)	
IV	39 (34.2)	41 (32)	
Bilateral**	12 (10.5)	13 (10.2)	1.000
Size of ovarian cyst (cm)*	7.0±2.5	6.2±1.8	0.004
Duration of surgery (minute)*	71.6±33.4	69.8±32.8	0.680
Pre-operative hormonal treatment**	6 (5.3)	7 (5.5)	1.000
Post-operative hormonal treatment**	35 (30.7)	36 (28.1)	0.674
Last status			
No disease/loss**	92 (80.7)	87 (68)	<0.001
Disease recurrence**	17 (14.9)	35 (27.3)	0.020
Pregnancy**	5 (4.4)	6 (4.7)	1.000
Follow time (month)*	19.3±5.7	19.0±5.6	0.730

rASRM = revised American Society of Reproductive Medicine
* Mean ± standard deviation, ** Number (%)

propensity score to correct this bias. With the propensity scoring, the distribution of baseline covariates was similar between the compared groups. In the present study, the logistic regression model was used.

After 1 year of conservative surgery, the recurrence rates were still comparable. The difference in the rate of recurrence, however, was substantially high at 18 and 24 months after operation. The laparotomy group had a significantly lower recurrence rate than the laparoscopy group. This finding was similar to previous reports[4,8] that the recurrent rate was increased by an average of 10-15% each year. The important clinical risk factors of recurrence, such as higher diameter of endometrioma, advanced stage and presence of pelvic adhesion should always be considered[9-11].

The present study defined the criteria of the recurrent case based on transvaginal ultrasonogram. The diagnosis of recurrence was made only when a typical imaging of cyst was seen at the diameter larger than 2 cm. Tandoi et al and Sesti et al had defined the recurred case by clinical recurrence of pain[8,9]. However, we disagreed to use the pain criteria because the presenting symptoms of the patients in the study were not only pain symptom but also infertility and pelvic mass. The explanations of high recurrent rate in the present report must be described. Firstly, we included the recurred cyst of both sides, previous affected side or unaffected side. In addition, other investigators had defined recurred cases by larger size. Secondly, the recruited patients had high rASRM score and advanced stage. Thirdly, we enrolled operative cases of all gynecologists in our center who had a variety of surgical skills. Lastly, transvaginal ultrasonography itself, which was the means of diagnosis of endometrioma in the present study, was an imaging study. The final diagnosis must be the histo-pathological confirmation.

Open laparotomy technique could be the better way than laproscopy to eradicate pathology in some situations[12,13]. Most surgeons feel more comfortable excising the cyst wall completely, eradicating all residual disease and using the suturing technique when they do exploratory laparotomy. In other words, the laparoscopic approach has been suboptimal in many circumstances. This mainly and directly relies on the skill and experience of laparoscopists. The short-term benefits of laparoscopy have to outweigh the long-term adverse effect-the possibility of higher recurrence.

Conclusion

The present study has demonstrated that surgical technique has a strong impact on the recurrence or disease-free survival. Laparoscopy might not eradicate the disease pathology like open laparotomy does in some situations, such as cases with complexity of disease.

Potential conflicts of interests

None.

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การกลับเป็นซ้ำของภาวะถุงน้ำเอนโดเมทริโอมา ภายหลังการผ่าตัดเลาะถุงน้ำรังไข่แบบอนุรักษ์ โดยการส่องกล้องเปรียบเทียบกับการผ่าตัดเปิดหน้าท้อง

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วัตถุประสงค์: *เพื่อศึกษาอัตราการกลับเป็นซ้ำของภาวะถุงน้ำเอนโดเมทริโอมาและระยะเวลาโรคสงบภายหลังการผ่าตัดแบบอนุรักษ์ โดยการส่องกล้องเปรียบเทียบกับการผ่าตัดเปิดหน้าท้อง*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังแบบติดตามกลุ่มผู้ป่วยโดยรวบรวมข้อมูลจากแฟ้มประวัติและบันทึกการผ่าตัด ผู้ป่วยที่ได้รับการวินิจฉัยเป็นภาวะถุงน้ำเอนโดเมทริโอมาที่ได้รับการผ่าตัดแบบอนุรักษ์โดยการส่องกล้องหรือผ่าตัดเปิดหน้าท้อง ที่โรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ โดยติดตามหลังผ่าตัดเป็นเวลา 24 เดือนเพื่อประเมินการกลับเป็นซ้ำของถุงน้ำเอนโดเมทริโอมาการวิเคราะห์ใช้คะแนน propensity เพื่อปรับปัจจัยที่เกิดจากข้อบ่งชี้ของการรักษาด้วยวิธีทั้งสอง และวิเคราะห์ด้วย competing time to event*

ผลการศึกษา: *รวบรวมข้อมูลได้เป็นกลุ่มที่ได้รับการผ่าตัดโดยการส่องกล้อง 128 ราย และผ่าตัดเปิดหน้าท้อง 114 รายตามลำดับพบว่าอายุและน้ำหนักเฉลี่ยในกลุ่มผ่าตัดเปิดหน้าท้องสูงกว่าอย่างมีนัยสำคัญแต่ส่วนสูงและดัชนีมวลกายของทั้งสองกลุ่ม ไม่มีความแตกต่างกันรวมทั้งไม่พบความแตกต่างของระยะของโรค และการเป็นทั้งสองข้าง อย่างไรก็ตามพบว่าขนาดเฉลี่ยของถุงน้ำในกลุ่มที่ได้รับการผ่าตัดเปิดหน้าท้องมากกว่า กลุ่มที่ได้รับการผ่าตัดโดยการส่องกล้องอย่างมีนัยสำคัญทางสถิติ (7.0±2.5 และ 6.2±1.8 เซนติเมตร, ตามลำดับ; p = 0.004) เมื่อเปรียบเทียบการกลับเป็นซ้ำของภาวะถุงน้ำเอนโดเมทริโอมาหลังการปรับปัจจัยรบกวนโดยใช้คะแนน propensity พบว่าอัตราการกลับเป็นซ้ำสูงกว่าในกลุ่มที่ผ่าตัดผ่านกล้อง เมื่อเปรียบเทียบกับกลุ่มที่ผ่าตัดเปิดหน้าท้องอย่างมีนัยสำคัญทางสถิติ (ร้อยละ 27.3 และ 14.91 ตามลำดับ; p = 0.02) อย่างไรก็ตามพบว่าอัตราการตั้งครรภ์ สะสมโดยรวมไม่แตกต่างกัน (ร้อยละ 4.7 และ 4.4 ตามลำดับ; p = 1.0)*

สรุป: *ผลการศึกษาบ่งชี้ว่าเทคนิคการผ่าตัดเป็นปัจจัยสำคัญที่มีผลต่อการกลับเป็นซ้ำของภาวะถุงน้ำเอนโดเมทริโอมา การผ่าตัดแบบอนุรักษ์โดยการส่องกล้องอาจไม่สามารถขจัดรอยโรคได้ดีเท่าการผ่าตัดแบบเปิดหน้าท้องในบางกรณี โดยเฉพาะในรายที่มีระยะของโรคสูงหรือพยาธิสภาพของโรคซับซ้อน*

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Publications;

1. *Tanprasertkul C* ,Manusook S ,Somprasit C,Sreshthaputra O,Patumanond J ,Vutyavanich T.Recurrence of Endometrioma Following Conservative Ovarian Endometrioma Cystectomy: Laparoscopy versus Laparotomy. Med Assoc Thai 2015 ;98 Suppl 3:S96-100.
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Presentation;

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