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Original Research

Comparison of impact on ovarian reserve between laparoscopic and laparotomy ovarian cystectomy

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Summary

Objective: To compare the effects of laparoscopy and laparotomy in unilateral ovarian cystectomy on ovarian reserve by measuring serum anti-Müllerian hormone (AMH) levels. *Design:* Prospective cohort single-blind study. *Setting:* Tertiary care university hospital. *Materials and Methods:* Fifty-two patients with unilateral benign ovarian cysts were prospectively recruited from March to December 2016. Twenty-six patients underwent laparoscopic ovarian cystectomy and the other 26 underwent laparotomic ovarian cystectomy. Serum samples were obtained from all the study population preoperatively and two months postoperatively for AMH measurement. The number of follicles attached to the removed cyst wall were counted and recorded by a gynecological pathologist. *Results:* A statistically significant decrease in ovarian reserve at two months postoperatively was found in the laparotomy group when compared to the laparoscopy group. There was no difference in the number of follicles retained in the removed ovarian cyst walls between groups. No major operative complications occurred in either group. *Conclusion:* Patients undergoing ovarian cystectomy using a laparoscopic approach had better postoperative ovarian preservation when compared to conventional laparotomy.

Key words: Ovarian cysts; Ovarian cystectomy; Ovarian reserve.

Introduction

Ovarian cysts are a frequent gynecological finding [1]. They are often divided into two groups: functional ovarian cysts, derived from normal changes to ovarian follicles corresponding to the menstrual cycle, and ovarian cystic neoplasm. In the latter case, the cysts do not collapse if left untreated. In many cases, ovarian cysts are asymptomatic and are found incidentally on routine pelvic examination. In other cases, patients present with various symptoms such as pelvic pain, palpable masses, gastrointestinal symptoms, or infertility [2].

Ovarian cystectomy is the treatment of choice for benign ovarian cysts, particularly among young women and those who have indications for surgery and desire to preserve their future fertility. This surgical procedure can be carried out by either laparotomy or laparoscopy. In the past, laparotomy was the gold standard for gynecologic surgery. Nowadays, the laparoscopic approach has become increasingly popular. Laparoscopy has gained popularity compared to laparotomy due to procedure-related advantages including fewer cases of operative morbidity, lower postoperative pain, and shorter length of hospital stay [3, 4].

In terms of ovarian function preservation, several studies have consistently suggested that ovarian cystectomy had a negative impact on ovarian reserve [5-9]. This damage is secondary to an inadvertent removal of healthy ovarian tissue during cystectomy and thermal destruction of ovarian follicles during surgery. Ovarian cystectomy performed via either laparotomy or laparoscopy approaches reduces ovarian preservation. However, the impact of surgical approach type on the severity of this reduction remains inconclusive. [10-15].

In Thailand, ovarian cystectomy using both laparoscopic and laparotomic approaches is widespread. Nevertheless, no study has been conducted to compare the impact of these techniques on ovarian reserve. Accordingly, this study was conducted to compare the effects of laparoscopy and laparotomy in unilateral ovarian cystectomy on ovarian reserve by measuring serum anti-Müllerian hormone (AMH) levels.

Materials and Methods

This was a prospective cohort single-blind study conducted in Srinagarind Hospital, a tertiary care university hospital in Thailand. The study was approved by the institutional review board of The Khon Kaen University Ethics Committee in Human Research (HE581388). A written informed consent was obtained from all participants before enrollment. The identities of participants were kept confidential and the assigned participant numbers were used for identification.

Fifty-two women with unilateral ovarian cysts aged between 20 and 40 years who visited Khon Kaen University's Srinagarind Hospital between March and December 2016 were enrolled in this study. Serum samples were obtained from the study population preoperatively and two months postoperatively for AMH measurement. Moreover, the ovarian cyst tissues were evaluated by a

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Table 1. — *Demographic parameters and clinical characteristics of study populations.*

Characteristics	Laparoscopy group (n=26) (mean±SD)	Laparotomy group (n=26) (mean±SD)	*p* value
Age (years)	31 (5.9)	31.92 (5.2)	0.553
BMI[1] (kg/m^2)	21.88 (2.6)	22.52 (3.7)	0.478
Size of cyst (cm)	5.35 (0.4)	5.56 (0.7)	0.391
Parity (%)			
Nullipara	22 (84.6)	20 (76.9)	0.486
Multipara	4 (15.4)	6 (23.1)	
Detailed final pathology (%)			
Endometrioma (78.8)	21 (80.8)	20 (76.9)	0.474
Mature cystic teratoma (15.4)	3 (11.5)	5 (19.2)	
Serous cystadenoma (3.8)	1 (3.8)	1 (3.8)	
Mucinous cystadenoma (1.9)	1 (3.8)	0 (0)	
rAFS[2] stage of endometriosis (%)			
Moderate	15 (71.4)	11 (55)	0.275
Severe	6 (28.6)	9 (45)	

[1]*Body mass index.* [2]*Revised American Fertility Score.*

gynecological pathologist after they were removed. The inclusion criteria were as follows: consent to be included in the study, age between 20 and 40 years, presence of a unilateral ovarian cyst 5-8 cm in size, no clinical signs or ultrasound evidence of ovarian malignancy, no evidence of endocrinologic disorders, no history of hormonal use within three months before enrollment, and a regular menstrual cycle for at least three months before enrollment. Women who met any of the following criteria were excluded: previous history of adnexal surgery, histopathologic diagnosis of malignant ovarian cysts, cardiopulmonary disease, cardiac arrythmia, or other underlying diseases which contraindicated for surgery.

Ovarian reserve defines a woman's reproductive potential as a function of the number and quality of her remaining oocytes [16, 17]. Available tests of ovarian reserve include examination of biochemical markers (i.e., FSH, estradiol, AMH, and inhibin B) and ovarian ultrasound imaging (i.e., antral follicle count and ovarian volume). In this study, the authors used serum AMH levels to reflect the ovarian reserve of the study population.

AMH is a glycoprotein hormone of the transforming growth factor beta superfamily, produced by granulosa cells of primordial, preantral, and small antral follicles [18]. Serum AMH tests are the most accurate way to evaluate ovarian reserve, as serum AMH remains consistent within and between menstrual cycles in both normal young ovulating women and in women with infertility [16]. As the number of ovarian follicles declines with age, AMH concentrations also decline.

The serum samples were collected from each patient once preoperation on the day before surgery and again at two months after surgery. Serum AMH concentration was measured using an electrochemiluminescence immunoassay. The assay has a range of detection between 0.01 and 23 ng/ml and intermediate imprecision of 2.9-4.4% [19, 20]. Both samples (preoperative and two months after surgery) from a given patient were analyzed in a single assay.

Laparoscopic ovarian cystectomy was conducted by creating three abdominal incisions: 5 mm at the umbilicus and two lateral sites. A Veress needle was used for creating the initial pneumoperitoneum and the primary trocar was introduced via umbilical incision. Following this, a 0-degree angle telescope was inserted in order to identify the pelvic organs. The other two incisions were created at the lateral sites, and accessory trocars were inserted under visual control.

Enucleation of the cyst was preceded by aspiration of the cyst contents. After this step, the cyst capsule was incised using scissors. Two atraumatic grasping forceps were used to exert traction and countertraction on the incision margin in order to discriminate proper cleavage plane. The ovarian cyst capsule was then detached from the ovarian parenchyma using a stripping technique. However, in cases with suspected mature cystic teratoma, enucleation of the cyst was done with intact ovarian cyst capsule. Hemostasis of the ovarian bed was obtained using a bipolar coagulation electrode at a power of 30 W for three seconds. The ovarian margins were left to heal by primary intention.

Laparotomic ovarian cystectomy was conducted using Pfannenstiel incision. Ovarian cyst removal was then carried out using the same technique that was used in the laparoscopy group. After removal of the cyst, hemostatic suturing was meticulously conducted using absorbable Vicryl 2-0 with running mattress technique. The ovarian surface was then neatly reapproximated with a subcortical running suture. Both laparoscopies and laparotomies were performed by the same team of surgeons and the same technique of surgery.

Formalin fixed tissue specimens were sent to the department of pathology. The reports were assessed by an expert gynecologic pathologist. The gross specimens were examined and submitted in paraffin block every 3 mm in thickness. After that, H&E slides were taken of each paraffin block. The follicles were measured by microscopic exam and counted.

This study was a single-blinded control trial study, as patient information about abdominal entry approach was concealed from both pathologists and medical laboratory scientists. The data were recorded by a research assistant.

All statistical analyses were performed using SPSS Statistical Package Version 16.0. A p value less than 0.05 was accepted as statistically significant. Results are expressed as mean ± SD or percentages, as appropriate. For baseline characteristics of the population in laparoscopic and laparotomy group; categorical variables were compared using the chi-square test or Fisher's exact test when appropriate. Continuous variables were compared using Student t-test. Median levels of preoperative and postoperative serum AMH were compared by Mann-Whitney U test. Median levels of declining in serum AMH after operation and number of follicles presence in pathological specimens between the two comparison groups were compared using Mann-Whitney U test.

Table 2. — *Preoperative and postoperative levels of anti-Müllerian hormone and number of ovarian follicles in specimens.*

Time of measurement	Laparoscopy group (n=26) (median (IQR)	Laparotomy group (n=26) (median (IQR)	*p* value
Preoperatively AMH (ng/mL)	2.38 (1.50-2.80)	2.38 (1.05-4.10)	0.522
Postoperatively AMH (ng/mL)	1.88 (1.00-2.73)	1.71 (0.84-2.68)	0.869
Median difference of AMH [1] (ng/mL)	0.27 (0.07-0.68)	0.63 (0.20-1.51)	0.040
Number of follicles in ovarian specimens	0.5 (0-14)	3.5 (0-11)	0.450

IQR; (interquartile range). Data analyzed by Mann-Whitney U test. [1]Anti-Müllerian hormone.

Table 3. — *Pain score and complications.*

Complications	Laparoscopy group (n=26) (mean±SD)	Laparotomy group (n=26) (mean±SD)	*p* value
Pain score	2.07 (0.70)	3.13 (0.76)	< 0.01
Urinary tract injury	0 (0)	0 (0)	1.000
Bowel injury	0 (0)	0 (0)	1.000
Ovarian cyst recurrence	0 (0)	1 (3.84)	0.317
Febrile morbidity	0 (0)	0 (0)	1.000

Data analyzed by Independent-samples t-test.

Results

Fifty-two women who met the eligibility criteria were enrolled in the study from March to December 2016. Twenty-six underwent laparoscopic ovarian cystectomy and the remaining 26 underwent laparotomic ovarian cystectomy. The clinical characteristics of the studied populations are presented in Table 1.

All baseline characteristics were similar between the two groups. The mean ages of the study participants were 31 ± 5.9 years in the laparoscopy group and 31.92 ± 5.18 years in the laparotomy group. The mean BMIs in the laparoscopy and laparotomy groups were 21.88 ± 2.58 kg/m^2 and 22.52 ± 3.7 kg/m^2, respectively. The mean diameters of ovarian cysts were 5.35 ± 0.44 cm and 5.56 ± 0.69 cm in the laparoscopy group and laparotomy group, respectively. The majority of the study population were nulliparity.

The most common kind of ovarian cyst discovered from the final histopathological diagnosis was endometriotic cyst (78.8%). Other cysts were diagnosed as mature cystic teratoma, serous cystadenoma, and mucinous cystadenoma at 15.4%, 3.8 %, and 1.9%, respectively. No changes in malignancy were detected. No statistically significant difference was noticed between the groups regarding detailed final histopathology. The revised American Fertility Score (rAFS) system was use to define the severity of endometriosis, and this scoring did not differ between groups, as shown in Table 1.

Table 2 demonstrates the baseline level of preoperative serum AMH between laparoscopic and laparotomy group which were not statistically significant different with median value of 2.38 ng/mL (IQR; 1.50-2.80) and 2.38 ng/mL (IQR; 1.05-4.10), respectively. After operation, median levels of AMH had declined by 0.27 ng/ml (IQR; 0.07-0.68) in the laparoscopy group compared to 0.63 ng/ml (IQR; 0.20-1.51) in the laparotomy group. This median difference of postoperative decline in AMH reached statistical significance ($p = 0.04$) as analyzed using a Mann-Whitney U test.

Numbers of ovarian follicles seen during pathological examination of excised ovarian specimens were 0.5 (IQR;0-14) follicles in laparoscopy group and 3.5 (IQR; 0-11) follicles in laparotomy group. This difference, however, was not statistically significantly ($p = 0.45$).

A numerical pain scale was used to evaluate the pain scores. The pain scores were recorded every four hours in the first 24 hours postoperatively. Pain scores differed significantly between the laparoscopy and laparotomy groups. Mean pain scores were 2.07 ± 0.70 and 3.13 ± 0.76 in the laparoscopy group and laparotomy group, respectively. There were no major or minor complications, including urinary tract injury, bowel injury, or febrile morbidity, in either group, as shown in Table 3. There was only one case in the laparotomy group in which the patient had endometrioma 3 cm in diameter in the opposite site ten weeks after the first operation. This case had severe endometriosis as determined by rAFS score. The difficulty of surgery might lead to incomplete operation.

Discussion

Benign ovarian cysts are common in female populations. In cases in which surgery is indicated and the patient wishes to preserve fertility, ovarian cystectomy is the treatment of choice. Surgical intervention may be performed using either a laparoscopic or laparotomic approach. Laparoscopic surgery is superior to laparotomy in that it tends to result in less postoperative pain and fewer complications. However, there is no definite consensus regarding which approach is more preferable in terms of ovarian reserve.

A total of 52 participants were prospectively recruited from March 2016 to December 2016. The result revealed

that preoperative and postoperative serum AMH levels did not differ between the two groups. However, postoperative decline of AMH levels differed significantly between the laparoscopy and laparotomy groups. The median postoperative declines in AMH were 0.27 ng /ml and 0.63 ng /ml in the laparoscopy and laparotomy group, respectively.

Declining of ovarian reserve following surgery has been demonstrated in many previous studies [5-9, 21]. Inadvertent removal of normal ovarian tissue during cyst wall stripping, thermal damage from bipolar electrocauterization, postsurgical inflammation, and ischemia have been proposed as a potential causes of the reduction of ovarian reserve after ovarian cystectomy.

The present authors found a difference in the level of decline of ovarian reserve between the laparoscopy and the laparotomy group, and that this decline following surgery was higher in the laparotomy group. This is in contrast to previously reported findings. For example, by measuring the changes of AMH, AFC, and peak systolic velocity of the ovarian stromal vasculature, Mohamed *et al.* [12] demonstrated that laparoscopic ovarian cystectomy was associated with a significant reduction in ovarian reserve compared with laparotomy. In addition, Moustafa *et al.* [13] reported a statistically significant decrease in ovarian reserve as measured by AMH and FSH among women undergoing laparoscopic ovarian cystectomy compared to those who underwent laparotomy. However, both studies used 40W bipolar energy for four seconds for hemostasis, while the present study which used only 30W for three seconds. The greater decline in ovarian reserve in the laparoscopy group in their study might be due to the higher energy levels leading to more electrical burn. Moreover, due to the magnification of laparoscopic surgery, surgeons could identify the lesions and plane of cystectomy also lysis of adhesion easier than in laparotomy. Additionally, precise hemostasis by bipolar coagulation in laparoscopy group only at point of bleeding might be better for ovarian tissue than suturing in laparotomy. Ovarian suturing may deteriorate blood supply of ovary and induce postoperative inflammation and adhesion. These may have led to better preservation of healthy ovarian tissue in situ in laparoscopy in our study.

The ovarian cyst wall specimen from each patient was submitted in paraffin block every 3 mm in thickness. By counting the number of primordial follicles on all slides of removed cyst walls, it could be seen that a slightly higher number of follicles were attached to the cyst walls in the laparotomy group (3.5 ± 11 *vs.* 0.5 ± 14). However, this did not reach statistical significance, suggesting that the amounts of follicles inadvertently removed during the cystectomy procedure were comparable between the two groups. The present authors were unable to find any other studies that compared the numbers of follicles on removed specimens between these two methods of abdominal entry. This may be due to the difficulty to evaluate a large amount of pathological slides from each specimen. Some studies have analyzed follicle numbers retained in cystectomy specimens between endometrioma and non-endometrioma groups [8, 22]. However, the present authors did not analyze this aspect, due to the small number of patients in the study population that had non-endometriotic cysts.

As expected, pain scores after surgery as measured by a numerical pain scale were significantly lower in the laparoscopy group compared with laparotomy group. No differences between the two groups were found in terms of intraoperative and postoperative complications involving urinary tract injury, bowel injury, or febrile morbidity. However, complications between the two groups may be different if there had been a larger study population.

The present authors evaluated AMH, a standard surrogate indicator for ovarian reserve, which is not influenced by the menstrual cycle. The present study also has some limitations. First, this is not a randomized controlled trial study and, thus, effects of some confounders may be inevitable. Second, it would have been more scientific to use the same hemostatic technique in the same way for both abdominal entry approaches. However, laparoscopic ovarian stripping using bipolar electrocoagulation and open laparotomy using hemostatic suture are the routinely used techniques at the present center. And lastly, the authors recruited both endometriotic and non-endometriotic ovarian cysts which have different effects to surgical difficulty. In the future study, the authors suggest evaluating the effect of surgery in endometriotic or non-endometriotic cysts independently and following long term impact after operation.

Conclusion

Patients undergoing ovarian cystectomy using the laparoscopic approach with 30W bipolar electrocoagulation had better postoperative ovarian preservation than laparotomy with hemostatic suturing. Laparoscopic unilateral ovarian cystectomy does have an advantage over conventional laparotomic ovarian cystectomy in terms of ovarian preservation as determined by serum AMH levels.

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