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# Impacts of endometrioma type and two-different techniques of laparoscopic cystectomy on ovarian reserve by measuring anti-mullerian hormone concentration



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## ABSTRACT

**Introduction:** Endometriosis caused chronic inflammation reaction, fibrosis, and adhesion resulting in anatomic distortion of pelvic organ commonly suffered by young woman. This study aims to understand the impact of the type of endometrioma and two different laparoscopic cystectomy excision techniques ("stripping" or complete excision vs. partial excision) on the ovarian reserve by measuring the anti-mullerian hormone (AMH) levels in patients with endometrioma.

**Method:** This is an experimental study in the form of pre-test and post-test group design. The subjects were patients with >3 cm endometrioma detected via transvaginal USG which were classified into two different groups, i.e., the "stripping" laparoscopic cystectomy group as control and partial excision laparoscopic cystectomy as an intervention group. Cystectomy techniques were chosen based on "formulated block sampling." The AMH levels measurements were performed before the operation (pre-test), and post-operation levels were measured at one and three months after the procedures on both groups. The study was conducted in Bali Royal Hospital (BROS), Denpasar, Indonesia, between January 2012 and January 2018. Independent sample t-test was used to analyze the collected data.

**Results:** There was no significant difference in the age and length of marriage between the two groups ( $p > 0.05$ ). Unilateral endometrioma had higher concentration of AMH compared to bilateral endometrioma before the laparoscopy ( $2.09 \pm 1.33$  vs  $1.99 \pm 1.25$  ng/ml;  $p = 0.768$ ), 1 month after the laparoscopy ( $1.20 \pm 0.59$  vs  $1.12 \pm 0.72$  ng/ml;  $p = 0.647$ ), as well as 3 months after the laparoscopy ( $1.79 \pm 0.97$  vs  $1.44 \pm 0.87$  ng/ml;  $p = 0.148$ ), but they were not statistically significant ( $p > 0.05$ ). Based on the laparoscopy techniques, there's no significant difference in AMH concentration before laparoscopy ( $1.87 \pm 1.23$  vs  $2.36 \pm 1.13$ ;  $p = 0.119$ ) in both groups. Otherwise, AMH level in partial excision laparoscopic cystectomy was significantly higher ( $p < 0.05$ ) than in the stripping laparoscopic cystectomy, one month after ( $1.33 \pm 0.62$  vs  $0.98 \pm 0.67$  ng/ml;  $p = 0.038$ ), as well as three months ( $1.88 \pm 0.97$  vs  $1.29 \pm 0.77$ ;  $p = 0.011$ ) after the surgery.

**Conclusion:** Unilateral and bilateral endometriomas have no significant difference in AMH levels. There's also no significant difference of AMH levels before operation in both different cystectomy technique. Thus, it was found that the effect of partial excision laparoscopic cystectomy on AMH concentration was significantly lesser effect than in stripping laparoscopic cystectomy.

**Keyword:** Endometrioma, stripping excision, AMH

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## INTRODUCTION

Endometriosis is a condition when functional endometrium tissues, such as the gland and stroma, grown outside the uterine cavity. Endometriosis caused chronic inflammation reaction, fibrosis, and adhesion resulting in anatomic distortion of pelvic organ.<sup>1,2</sup> Endometriosis is commonly suffered by young woman, but the incidence is not related to any ethnic or social groups. Patients with endometriosis will complain of pelvic pain, painful menstruation and pain during intercourse, these complaints will usually hurt their physical, mental, and social health.<sup>1</sup> Based on epidemiology, the incidence of endometriosis is 6 to 10% in the general female population. In women with pelvic pain or infertility or both, the number is about 35-50%. Approximately, 25-50% of infertile

women have endometriosis, and more than 30-50% of women with endometriosis are infertile. Pelvic endometriosis, particularly those involving the ovaries, forms a cyst called endometrioma.

The presence of space occupying effect will decrease the number of follicles by inhibiting follicular development causing atresia, and the presence of local inflammatory reactions due to the high concentration of iron associated with the presence of cytotoxic oxidative stress, or both, will decrease the number of functional ovarian tissues resulting in reduced ovarian reserve.<sup>3</sup> The treatment for endometriosis involves medical and surgical procedures. Study by Dunselman et al. (2014) in the ESHRE Guideline article: management of women with endometriosis stated that conservative

surgery with laparoscopy is the standard of care to remove endometrioma.<sup>4</sup> However, laparoscopic surgery is associated with functional ovarian tissue damage. The extent of this damage depended on whether the laparoscopic cystectomy technique, be it “stripping” excision (complete cyst excision) or partial cyst excision. Stripping laparoscopic cystectomy excision may result in a greater loss of ovarian cortex tissue compared with partial excision. Additionally, stripping cystectomy will lead to reduced ovarian arterial blood flow.<sup>5</sup>

Impaired ovarian function due to surgical techniques, either with stripping or partial excision cystectomy, can be evaluated by measuring ovarian reserve. Several methods had been reported to assess ovarian reserve, such as FSH serum level on the third day of the menstrual cycle seemed to be the best predictor, but have a significant variability from one cycle to another. Recently anti-mullerian hormone (AMH) appeared as a novel ovarian test marker reflecting ovarian reserves.<sup>6</sup> AMH is excreted by the preantral follicle or early antral follicle in the ovary and plays an important role in folliculogenesis, acting on the modulation of follicular recruitment in the granulosa cells to limit the number of recruited oocytes and to regulate the number of growing follicles and their selection for ovulation.<sup>17</sup> Some researchers have described that AMH levels are low in women with endometrioma either before or after surgery.<sup>5</sup> Therefore, this study intends to evaluate the impact of endometrioma and two different techniques of laparoscopic cystectomy on the ovarian reserve based on the measurement of AMH levels.

## METHOD

### Design and Subjects

The study design of this study is an experimental study in the form of pre-test – post-test group design, conducted at Bali Royal Hospital (BROS), Denpasar, Bali between January 2014 and January 2018. The measurement of AMH concentration was performed in Prodia Laboratory, Denpasar, Bali.

Suspected endometriosis patients who come to the Fertility Endocrinology and Reproduction (FER) outpatient clinic at BROS were investigated using Siemens transvaginal ultrasound type sonoline G 20 to diagnose the presence or absence of endometrioma in one or both of the ovaries. When an endometrioma of larger than 3 cm size was discovered, the AMH concentration of the patients was measured and documented as the pre-test group. This pre-test group was then divided into two groups: “stripping” laparoscopic cystectomy group and partial excision laparoscopic cystectomy

group. All procedures were performed using Olympus®. Selection of surgical technique is made by formulated block sampling. The second and third measurement of AMH levels was at one month and three months after the surgery, respectively. All the laparoscopic surgery are performed by an expert in laparoscopic surgery team and consultant in endocrinology fertility and reproduction. These AMH concentrations were marked as the outcome of this study. Patients who had a history of treatment or surgery for endometriosis were not included in the study.

### Laparoscopic Surgery Protocol

1. Stripping excision cystectomy is a laparoscopic surgery to remove cystic contents by slowly pulling out the cyst wall (pseudocyst) and maintaining the ovary tissue beneath it with the atraumatic forceps so that the entire cyst wall is removed.
2. Partial excision cystectomy is a laparoscopic surgery to remove the contents of the cyst by excision along the “endometrial - cortical junction.”

### Data analysis

The data were presented descriptively, then analyzed with Kolmogorov-Smirnov normality test and with Levene’s test of homogeneity. Comparability test of AMH data before and after treatment was performed with an independent t-test. The p-value <0.05 was considered statistically significant.

## RESULT

The total sample in this study is 60 patients with endometriosis, which was divided into 30 subjects per group, there was no drop out sample in this study, all the 60 patients complete the follow up within three months of AMH evaluation. It was found that the lowest age of endometrioma patients was 21 years old and the oldest was 48 years old with mean age of  $33.50 \pm 5.96$  years. Based on marital duration, the longest duration of marriage was 15 years, and the shortest marital duration was one year with the mean age of marriage of  $5.89 \pm 4.13$  years-old. Based on the level of education, one of the patients only completed junior high school education (2.5%), 20 subjects had high school education (50%) people, and as many as 19 (47.5%) people had university degree. Of 40 patients with endometrioma, 22 (55%) subjects were infertile; 4 (10%) subjects had menstrual disorders, and 14 (35%) subjects complained of menstrual pain. Comparison of subject characteristics, including age and duration of marriage, were presented in [table 1](#).

Based on table 1, shows that with independent t-test on both variables, p-value of greater than 0.05 was obtained. Therefore, no significant differences were found in the mean age and marital duration between the stripping and partial excision groups.

Comparison of AMH levels between the unilateral and bilateral type endometrioma using independent sample t-test is presented in table 2.

Based on table 2, shows that no significant differences in the AMH level between bilateral endometrioma and unilateral endometrioma before, after one month, and after three months of surgery ( $p > 0.05$ ), even though the AMH levels in the unilateral endometrioma group were higher compared to the bilateral endometrioma group.

Comparison of AMH levels between the two groups after surgical action is performed. Analysis with independent sample t-test is presented in table 3.

Based on table 3, shows that before operation there's no significant difference in the mean AMH level between both groups. But the mean AMH levels in the partial excision laparoscopic

cystectomy group were significantly higher ( $p < 0.05$ ) than the stripping excision laparoscopic group, in one month and three months after the surgical action was performed.

## DISCUSSION

The results of this study showed that patients with both unilateral and bilateral endometrioma had lower AMH levels than the normal values. Although AMH levels before surgery did not differ significantly between the two types of endometrioma, the AMH levels in bilateral endometrioma were lower than in unilateral endometrioma. Research by Hwu *et al.* (2017) reported similar results in which the AMH levels of patients in bilateral endometrioma were significantly lower than in unilateral endometrioma.<sup>7</sup> In our study, the lower AMH levels in bilateral endometriomas than in unilateral endometrioma were statistically insignificant. Differences in size and number of tumors provide a pattern of different AMH levels, in this study the size of the tumors in the bilateral endometrioma group tends to be smaller compared to the unilateral endometrioma group so this may underlie the absence of difference in AMH levels between unilateral and bilateral endometrioma. Thus we concluded that the different types of endometrioma have no significant impact on AMH levels.

Treatment of endometrioma is still controversial, several modalities of endometrioma treatment include medical and surgical handling. Surgical treatment can be done through aspiration with ultrasound guidance, aspiration plus sclerotherapy, conservative stripping laparoscopic cystectomy method, drainage, and coagulation. Radical surgery can be done by ovariectomy.<sup>8</sup> Vaginal ultrasonography drainage without surgery seems to be ineffective. Five studies showed a high recurrence rate that ranges from 28 - 100% using drainage only technique. Some researchers combined aspiration with tetracycline, ethanol, or methotrexate as sclerotic substances. A study by Akamatsu *et al.* (1988) reported a decrease in recurrence rate from 0-9% using ethanol.<sup>9</sup> ESHRE guidelines on endometrioma surgical management recommend cystectomy as treatment. Research by Jadoul *et al.* (2012) reported several reasons for performing cystectomy surgery on endometrioma such as (1) reduction in menstrual pain, (2) increase fertility, where the pregnancy rate reaches 50% after one-year endometrioma removal, (3) reducing the risk of ovarian cancer.<sup>10</sup> Reported in the study that the reasons for not performing surgery include: (1) that surgery may decrease the chances of conceiving because of decreased ovarian reserves

**Table 1 Comparison of research subjects characteristics**

Variables	Surgical techniques		p-value
	Stripping excision (Control Group) (n=30)	Partial excision (Intervention Group) (n=30)	
Age (year-old)	33.30 ± 5.55	33.70 ± 6.51	0.799
Marital duration (years)	6.18 ± 4.28	5.73 ± 3.76	0.667

**Table 2 Mean AMH concentration based on type of endometrioma**

Variable	Type of Endometrioma		p-value
	Bilateral (n=35)	Unilateral (n=25)	
Before operation	2.07 ± 1.18	2.17 ± 1.24	0.766
One month after operation	1.12 ± 0.72	1.20 ± 0.59	0.647
Three months after operation	1.44 ± 0.87	1.79 ± 0.97	0.148

**Table 3 Mean AMH levels based on laparoscopic cystectomy techniques**

Variables	Surgical techniques		p-value
	Stripping excision (Control group) (n=30)	Partial excision (Intervention group) (n=30)	
Before operation	1.87±1.23	2.36±1.13	0.119
One month after operation	0.98±0.67	1.33±0.62	0.038
Three months after operation	1.29±0.77	1.88±0.97	0.011

and occasional premature ovarian failure. These situations can happen if stripping was done on the wall of the endometrioma. It is said that about 6% of the normal ovarian cortex and about 50% of normal ovarian tissue will be removed during the process. Electrocoagulation will also cause damage to the normal ovarian tissue, (2) that the success rate of in vitro fertilization (IVF) after the removal of endometrioma did not increase. This is due to the small number of oocytes obtained and the declining rate of implantation after surgery, (3) bleeding may cause premature ovarian failure and reduced ovarian reserve. Despite the controversy over endometrioma treatment, the ESRHE recommends laparoscopic cystectomy as the standard of care in endometrioma. The standard cystectomy technique for endometrioma is stripping by gently pulling the walls of the pseudocyst and retain the underlying tissue of the ovary with atraumatic forceps. Hemostasis is done using pinpoint bipolar electrocautery. This technique is estimated to decrease ovarian reserves by 13% and a decrease in ovarian response to stimulation by about 50% but decreased ovarian response will not occur in the non-operated ovary. In accordance to reduce the effects of stripping cystectomy, various alternative surgical techniques have been performed including endometrioma fenestration and drainage followed by bipolar coagulation. In this study, we used stripping excision cystectomy and partial excision cystectomy technique by excision along the endometrial cortical junction. Both of these techniques can damage the functional ovaries tissue.

In this study, it was found that in the partial excision group, the AMH concentration was significantly higher than in the stripping excision group. This finding was supported by another study by Celik et al. (2012) in which there was a significant decrease of 61% in AMH levels six months post stripping excision surgery.<sup>11</sup> Another similar study by Hwu et al. (2011) reported that there was a decrease in AMH levels before three months after a stripping cystectomy.<sup>7</sup> It was further stated that three months after surgery, the levels of AMH decreased by 49.11%. The results were also supported based on research conducted by Somigliana et al. (2012) which states that a decline in AMH levels was recorded after 3 and six months after stripping surgical excision.<sup>12</sup> Furthermore, it was stated that in the case of bilateral endometrioma, there was also a significant decrease in the AMH levels. Hwu et al. study (2011) also state that AMH levels in bilateral endometriomas are lower than those in unilateral endometriomas.<sup>7</sup> These results are consistent with the results of our study in which lower AMH levels were also obtained in the bilateral endometriomas group.

Similar results were also reported by Tiarna et al. (2011) which suggested that there was a decrease in AMH levels following laparoscopic cystectomy surgery of bilateral endometriomas.<sup>13</sup> The decreased postoperative AMH levels after stripping laparoscopic cystectomy was caused by damage to the functional network of the ovary due to space occupying effect and the removal of the follicle by stripping. In partial excision techniques, smaller decrease in AMH concentration is because of the partial loss of space occupying effect and the lower number of removed follicles due to the excision is performed only at the endometrial cortical junction. Although there was a decrease in AMH levels after stripping laparoscopic cystectomy, the pregnancy rate was reported to be about 50% after one year of surgery.<sup>14</sup> The rate of pregnancy after partial excision cystectomy have not been widely reported. Only research by Donnez et al. (2010) reported that out of 52 endometrioma patients who performed partial excision cystectomy the cumulative pregnancy rate obtained was 32%.<sup>15</sup>

Similar research conducted by Abdelmgid et al. (2013) in his study concluded that partial excision cystectomy gave better pregnancy rates than excision of stripping cystectomy.<sup>16</sup> Partial excision cystectomy was associated with a higher rate of endometrioma recurrence, but Donnez et al. (2010) reported that the recurrence rate with partial excision was only about 2% and in our study, the recurrence rate of endometrioma is only 5%.

The limitation in this study is that this study only provides an overview of different AMH levels in different surgical techniques and different tumor sites, but does not provide a causal pattern of the role of AMH as an ovarian reserve and the relationship between AMH with different tumor sites

## CONCLUSION

Unilateral and bilateral endometriomas have no significant difference in AMH levels. There's also no significant difference of AMH levels before operation in both technique groups. Thus, it was found that the effect of partial excision laparoscopic cystectomy on AMH concentration was significantly lesser effect than in stripping laparoscopic cystectomy. Partial excision techniques may be considered for treatment of unilateral endometriomas of size 3 cm or greater.

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