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Ovarian Loss in Laparoscopic and Robotic Cystectomy Compared Using Artificial Intelligence Pathology

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ABSTRACT

A Comparison of Ovarian Loss Following Laparoscopic versus Robotic Cystectomy As Analyzed by Artificial Intelligence-Powered Pathology Software.

Background and Objective: To compare the area of ovarian tissue and follicular loss in the excised cystectomy specimen of endometrioma performed by laparoscopic or robotic technique.

Methods: Prospective observational study performed between April 2023 to August 2023. There were 14 patients each in Laparoscopic group (LC) and Robotic group (RC). Excised cyst wall sent was for to the pathologist who was blinded to the technique used for cystectomy. The pathological assessment was done by artificial intelligence-Whole Slide Imaging (WSI) software.

Results: The age was significantly lower in LC group; the rest of demographic results were comparable. The mean of the median ovarian area loss [Mean Rank, LC group (9.1 ± 15.1); RC (8.1 ± 12.4)] was higher in LC group. The mean of the median total follicular loss was higher in LC group (8.9 ± 9.2) when compared to RC group (6.3 ± 8.9) and was not significant. The area of ovarian loss in bilateral endometrioma was significantly higher in LC group (mean rank 7.5) as compared to RC group (mean rank 3) - ($P = .016$) despite more cases of bilateral disease in RC group. With increasing cyst size the LC group showed increased median loss of follicles when compared to RC group (strong correlation coefficient 0.347) but not statistically significant ($P = .225$). AAGL (American Association of Gynecologic Laparoscopists) score did not have any impact on the two techniques.

Conclusion: Robotic assistance reduces the area of ovarian and follicular loss during cystectomy of endometrioma especially in bilateral disease and increasing cyst size. It should be considered over the laparoscopic approach if available.

Key Words: Robotics, Endometrioma, Cystectomy, Artificial intelligence, Laparoscopy, Ovarian loss.

INTRODUCTION

Endometrioma is one of the three phenotypes that is seen in women suffering from endometriosis.[1] It can be easily diagnosed on an ultrasound scan as compared to superficial or deep infiltrating endometriosis. Pain or impaired fertility are the two common reasons for surgical intervention in cases presenting with endometrioma. Ovarian endometriomas are found in 17–44% of women with endometriosis.[2] Laparoscopic cystectomy is the gold standard in managing these cysts rather than drainage.[3] However, it is well established that there is ovarian loss during cystectomy.[4–7] Better surgical skills and techniques can reduce ovarian loss and prevent subsequent fertility compromise in young women.[8,9]

Although several studies report ovarian loss during laparoscopic cystectomy (LC), and it is documented that better surgical skills may reduce this loss, it is not known whether robot assistance in minimal access surgical technique can reduce ovarian loss.

We aim to analyze the inadvertent ovarian loss in the excised cyst wall obtained during endometrioma cystectomy done by laparoscopy and compare it with those done by robotic assistance. The loss was analyzed using

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the artificial intelligence-WSI (Whole Slide Imaging) both for the loss of area of ovarian tissue and for the loss of follicles by digital pathology. Whole slide scanners were introduced in 1990. USFDA approved the use of WSI in surgical pathology practice and its validation for introduction into the surgical pathology practice is now recommended by the College of American Pathologists. Subsequently, Philips received approval for a digital pathology whole-slide scanning solution in 2017.

AIMS AND OBJECTIVES

Our objective is to compare the amount of loss of ovarian area and follicles in the excised cystectomy specimen by an expert pathologist using artificial intelligence and WSI (Whole Slide Imaging) technique between the two techniques of ovarian cystectomy in endometrioma (laparoscopic cystectomy and robotic cystectomy).

MATERIAL AND METHODS

It was a prospective observational study performed at a tertiary care referral academic hospital. This clinical study was approved by the Institutional Ethical Committee.

Both groups had 14 cases each through convenient sampling. The study period was from April 2023 to August 2023.

The inclusion criteria were as follows:

(a) age 20–40 years

(b) regular menstrual cycles

(c) clinical and ultrasonographic finding of ovarian endometrioma.

The exclusion criteria were as follows:

(a) any suspicion of malignant ovarian diseases

(b) recurrent disease after previous surgery for endometriosis

(c) cases in which tissues were not well processed or not adequate for pathological examination.

The following data was collected prospectively: age, body mass index, parity, history of infertility, and severe dysmenorrhea which was graded based on visual analogue score. The visual analogue scale (VAS) is a validated, subjective measure for acute and chronic pain. Scores are based on self-reported measures of symptoms that are recorded with a single handwritten mark placed at one point along the length of a 10-cm line that represents a continuum between the two ends of the scale—"no pain" on the left end (0 cm) of the scale and the "worst pain" on the right end of the scale (10 cm).[10]

SURGICAL TECHNIQUE

All surgeries were performed by a single gynecological surgeon with the aim of performing ovarian cystectomy along with the removal of all visible endometriotic lesions. The surgery began with salpingo-ovariolysis. Endometrioma content was drained. In the laparoscopy technique (Karl Storz GmBH, Tuttlingen, Germany), a sharp incision was made with scissors and the cleavage plane was identified. The cyst wall was removed from the underlying ovarian parenchyma through traction and counter traction using one atraumatic and one traumatic grasping forceps without the use of any electrosurgery. If needed, after the removal of the cyst, minimal bipolar surface coagulation was done using 40 watts (Force Triad™-Medtronic, Minneapolis, USA) to control any significant bleeding. The robotic surgery was performed by da Vinci ξ system (Intuitive Surgical Inc., Sunnyvale, CA, USA). Three 8-mm ports were used. The optic port was at the umbilicus. Two 8 mm ports were placed laterally on either side of the abdomen. Fenestrated bipolar was introduced from the left side of the patient and hot shears (scissors) from the right side. An incision was made on the most prominent part of the cyst and the cleavage plane was identified. The endometrioma cyst wall was stripped from the ovarian parenchyma being held by the fenestrated bipolar forceps and dissection was done with the hot shears using short bursts of monopolar coagulation current (100 watts @level 3 da Vinci ξ). All patients were surgically staged according to the AAGL surgical staging system. AAGL staging allows to numerically scale the disease from a point of surgical complexity. This objective intraoperative staging system was used with a phone app at the end of each case. It is simple to do and avoids the limitations of noninvasive imaging.[11]

After the endometriomas were removed, all other remaining visible endometriotic lesions were excised and sent for histopathological analysis. Specimens were analyzed by a single pathologist who was blinded to the technique used to perform the procedure. The histopathological protocol was as follows. All specimens were grossed, processed, adequately sectioned, stained with hematoxylin and eosin staining, and scanned for digital viewing. The number of bits taken for analysis was based on cyst size. For ≤3 cm, we processed at least 3 bits. For cysts size

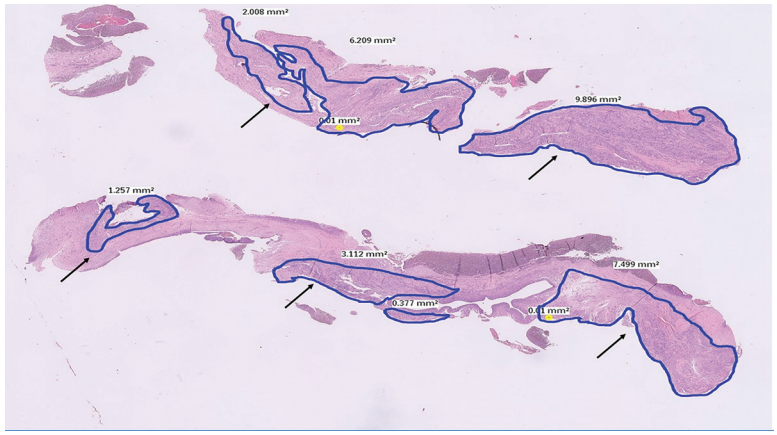

Figure 1. Arrow indicating, area of ovarian tissue in two dimensions (mm^2) in the digital slide of cyst wall tissue by Whole Slide Imaging (WSI) for calculation of ovarian follicles.

>3 cm and up to 7 cm, at least 6 bits were processed. For cysts >7 cm, additional 1 bit was processed for each extra 1 cm. The tissue sampling was done from the thickest portion of the cyst wall as seen in the gross examination. 4-µm sections from a paraffin block were prepared on glass slides. Then the slides were scanned using the AI-based Whole Slide Imaging [(WSI) with Philips Digital Pathology solution (Philips Ultra Scanner; software version 1.8.4)] to confirm the histological diagnosis of endometriosis.[12] Each case was analyzed for the area of ovarian tissue inadvertently removed and measured using a digital scanning technique in two dimensions. This area of ovarian tissue was calculated in two dimensions (mm^2) (**Figure 1**). The follicles in excised tissue were then categorized as primordial, primary, secondary, and cystic follicles by WSI criteria, however their number, was calculated manually (**Figures 2** and **3**). The endometriosis cyst showed 3 layers, the innermost lining epithelium followed by a fibrous wall then the adherent ovarian tissue; however, it is not always possible to exactly draw a line between these layers, and thus the demarcation was considered arbitrarily.

STATISTICAL ANALYSIS

Descriptive data was included, and cases were classified according to the clinical details and other lab parameters. For our sample population, ovarian tissue loss was recorded and compared in both the surgical techniques adopted (robotic versus laparoscopic). Data entry was done using M.S. Excel and was statistically analyzed using Statistical Package for Social Sciences (SPSS Version 26) for M.S. Windows 2010. Descriptive statistical analysis was carried out to explore the distribution of several categorical and quantitative variables. Categorical variables were summarized with n (%), while quantitative variables

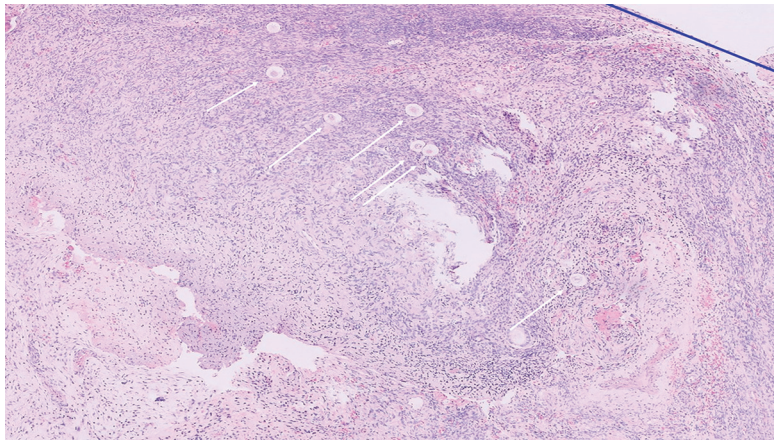

Figure 2. Follicles (*white arrow*) in area calculated in Whole Slide Imaging (WSI).

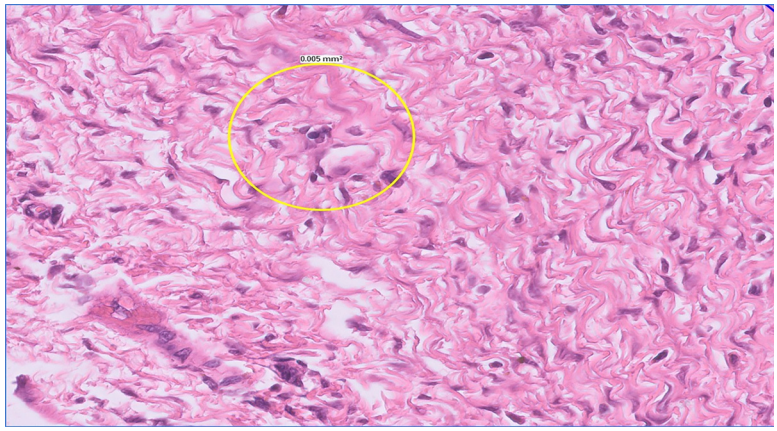

Figure 3. Primordial follicle in calculated lost area of ovarian tissue.

were summarized by mean ± SD. All results were presented in tabular form. Data were analyzed using parametric tests such as the *t* test and ANOVA test and nonparametric tests like Wilcoxon signed rank, Mann-Whitney *U*, and χ^2 tests. *P* values < .05 were considered statistically significant.

RESULTS

Baseline characteristics

Women in the laparoscopic cystectomy (LC) group were younger when compared to the robotic cystectomy (RC) group. The demographic data is tabulated in **Table 1**. In this study, the patients presented with the following symptoms: severe dysmenorrhea (78.57%), heavy menstrual bleeding (HMB, 35.71%), bloating (35.71%), dyschezia (28.57%), dyspareunia (7.14%), and Infertility (35.71%). The symptoms of HMB, bloating, dyschezia, and dyspareunia were similar in both groups (*P* > .05). The VAS score for dysmenorrhea did not differ between the two groups. A higher number of patients had infertility in the LC group (70%) when compared to patients in RC group (30%), however, this was not statistically significant (*P* = .11). The intraoperative factors are seen in **Table 2**. The mean AAGL score was lower in the LC group (27 ± 9.5) as compared to the RC group (32.6 ± 13.5). However, this difference was not statistically significant (*P* value = .21).

Bilateral ovarian endometrioma was seen in 44.4% in the LC group and 55.6% in the RC group. Average AAGL score was 27 ± 9.5 in LC group and 32 ± 13.5 in RC group. These differences were not statistically significant. The inadvertent excision of ovarian tissue and were determined by calculating the loss of ovarian area and the number of

Table 1.
Demographic Characteristics

Demographic Details	LC	RC	*P* value
Mean age (years)	30 ± 5.4	34.5 ± 3.5	*P* < .05
Mean BMI (kg/m^2)	23.5 ± 3.3	24.9 ± 3.8	*P* = .29
Laterality of cyst			*P* = .686
Unilateral cyst	52.6% (10)	47.4% (9)	
Bilateral cysts	44.4% (4)	55.6% (5)	
Duration of infertility (years)			*P* = .115
0 (18 cases)	38.9% (7)	61.1% (11)	
≤3 (6 cases)	66.7% (4)	33.3% (2)	
>3 (4 cases)	75% (3)	25% (1)	
AAGL score	27 ± 9.5	32.6 ± 13.5	*P* = .21

Table 2.
Intraoperative Details

Operative Parameters	LC Group	RC Group	*P* value
Mean operative time (minutes)	80.9 ± 28.7	100.3 ± 39.9	*P* = .15
Mean blood loss (ml)	83.5 ± 41.2	78.5 ± 46.8	*P* = .76
AAGL score (≥16)	27.0 ± 9.5	32.6 ± 13.5	*P* = .21

follicles lost in the excised specimen. Three intraoperative factors were recorded to assess the severity of the disease and its correlation with ovarian area and follicular loss. These were (I) history of bilateral ovarian endometrioma (II) advanced AAGL intra-operative score (score >16; stages 3 and 4), (III) size of cyst.

The mean rank was calculated for both groups and based for the area of the ovarian tissue that was inadvertently removed. In the LC group the value was more (mean rank 15.71) when compared to the RC group (mean rank 13.29). A nonparametric test (Mean rank) was used in this analysis as the sample size was small and ovarian loss values in our data were skewed. Some values were also at the extreme (outlier); hence we calculated the mean of the median area loss. The mean of the median ovarian area loss was high in LC group (9.1 ± 15.1) when compared to the mean of the median ovarian area loss in RC group (8.1 ± 12.4). Both the mean of the median and mean rank values showed higher loss of ovarian area in LC group thus indicating that inadvertent area of ovarian tissue loss is more in LC group when compared to excised specimens in RC group (**Figure 4**).

When we analyzed the follicles present in the excised specimen the mean rank follicles was higher in LC group (mean rank 15.21) than RC group (mean rank 13.79) although not statistically significant (*P* value = .667). When the mean of the median ovarian follicles were analyzed, we found it to be higher in LC group (8.9 ± 9.2) compared to the mean of the median ovarian follicle loss in RC group (6.3 ± 8.9). Both the mean of the median and mean rank values showed higher loss of follicles in LC group as compared to RC group.

Correlation with bilateral disease

Overall, when both groups were analyzed based on the mean rank of follicular loss and the bilaterality of disease, we found that the mean rank of loss was higher in bilateral disease (15.22) compared to unilateral disease (14.16).

We compared the area of ovarian loss in cases with bilateral endometrioma, the ovarian loss was higher in LC group (mean rank 7.5) as compared to RC group (mean rank 3). This difference was statistically significant (*P* = .016). However, bilateral endometrioma was found more in RC group (55.6%) than in LC group (44.4%) (*P* value = .686).

Correlation with the size of cyst

When cyst size was considered as a factor for follicular loss, the LC group showed increased median loss of follicles as the cyst size increased (strong correlation coefficient 0.347) but was not statistically significant (*P* = .225) (**Figure 5**). The RC group did not show increased follicular loss with increasing cyst size (correlation coefficient –0.006), statistically not significant (*P* value = .984).

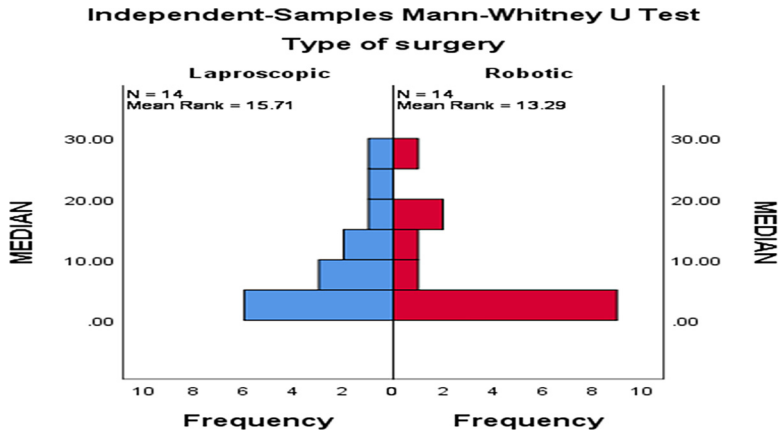

Figure 4. Loss of ovarian tissue (AREA) depending on type of surgery in our study population.

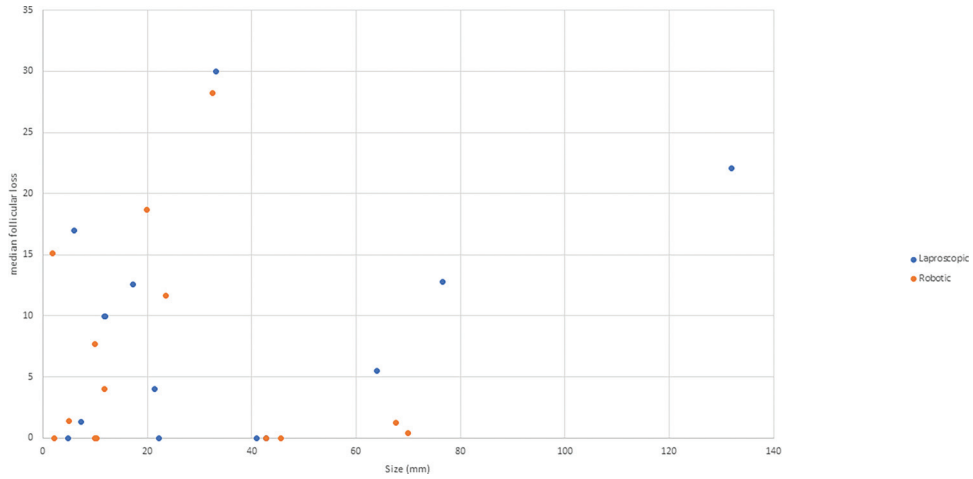

Figure 5. Correlation of median ovarian follicular loss with size of cyst.

DISCUSSION

Laparoscopic surgery for endometrioma is widely performed to reduce pain and increase spontaneous pregnancy.13,[14] Cystectomy is recommended over drainage and coagulation as it reduces recurrence and endometriosis-associated pain.15,[16] The absence of a clear cleavage plane between the endometrioma and normal ovarian tissue results in inadvertent removal of the ovarian cortex and loss of follicles,6,[7] which reduces the follicular reserve in young women. Muzii et al demonstrated excision of normal tissue along with endometrioma wall in >50% of cases of endometrioma cystectomy.[5] In fact, 13% severe ovarian damage (defined as the absence of follicular growth during ovarian hyperstimulation) is reported after endometrioma cystectomy.[17] The level of expertise in endometriosis surgery is inversely correlated with the inadvertent removal of healthy ovarian tissue along with the capsule.[18] We compared two different technologies (laparoscopic vs robotic) by a single surgeon to see the impact of robot assistance on the reduction of ovarian area loss and eventually follicular loss.

Ovary being a complex endocrine organ, shows significant changes in the lifespan of females. One is born with a certain number of follicles that slowly dwindle over several reproductive years. There are different types of follicles in the ovarian tissue. During histopathology analysis, the number of follicles in the ovary is usually counted manually by experts, which is a tedious, time-consuming and intense process and the counting can have subjective bias depending on the knowledge of the expert doing the counting.

Özkan İnika et al in their study, for the first time, proposed a method for automatically counting the follicles of ovarian tissue. This involves filter-based segmentation applied to whole slide Zoom histological images, based on a convolutional neural network (CNN).

The number of follicles obtained by this method was very close to the number of follicles manually counted by the experts and had an accuracy level of 86.67% for primordial type, 95.35% for primary follicles, 97.06% for preantral, 97.69% for secondary and 100% for tertiary follicles as compared to expert manual counting. The mean accuracy for all types of follicles together was 95.35%.[12] To our knowledge, this is the first study comparing the two techniques to assess the ovarian area and follicular loss in endometrioma cystectomy by using artificial intelligence (WSI) method.

No difference was noted between the laparoscopy versus laparotomy, when normal ovarian tissue loss was studied with endometrioma and other kinds of benign ovarian cyst by Saeed Alborzi.[19]

Ovarian follicular loss is seen more commonly among younger patients and patients with lower-stage endometriosis as reported by Hoon-Kyu Oh et al.[20] Similar to the finding of this group, in our study we noted more ovarian follicular loss in LC group and a lower mean age when compared to RC group. The AAGL score did not impact the ovarian loss.

Our results showed increased follicular loss with increasing cyst size in LC group correlating with the study by Roman H et al, where an additional loss of 200-µm ovarian parenchyma was seen with each 1-cm increase in cyst diameter.[21] However, the RC group did not show increase in ovarian area or follicular loss with increasing cyst size. Hence, results of our study point to the fact that there is

Table 3.
Correlation of Area of Ovarian Loss with Unilateral and Bilateral Disease

	Unilateral Disease (N/Mean Rank)	Bilateral Disease (N/Mean Rank)
Laparoscopic cystectomy (LC)	10 (9)	4 (7.5)
Robotic cystectomy (RC)	9 (11.1)	5 (3)
P value	.44	.016

less follicular loss in RC group as compared to LC group with increasing cyst size.

Higher ovarian loss in bilateral disease has been reported in earlier studies.22,[23] Similarly, our study showed higher follicular loss in cystectomy for bilateral disease compared to unilateral disease in both LC and RC groups. But when we compared the loss between the two technologies, in cases with bilateral disease, the follicular loss in LC group was significantly higher when compared to mean rank loss in RC group (mean rank 7.5 in LC and 3 in RC). This is a significant finding of our study. There were more cases of bilateral disease in RC group but statistically less ovarian loss in RC group (**Table 3**), suggests the fact that the use of robotic surgery can prevent excessive ovarian loss and preserve fertility in women with compromised ovarian reserve and bilateral disease.

The limitations of our study are a small sample size, single surgeon, and a single center. The results of this pilot study are over six months. These findings may not be representative and is challenging to extrapolate to a larger population. With our small sample size, there is a higher risk of sampling bias and the patients included may not be representative of the broader population. The outliers in our study can have a disproportionate impact on the results.

However, the strength of the study lies in the fact that this comparison has never been published before. It can fill gaps in existing knowledge of whether robotic technology can help surgeons to reduce ovarian area and follicular loss. Such loss is a pathological marker of ovarian functional loss seen in patients after ovarian cystectomy for endometrioma. This insight can lead to improved patient outcomes and more effective treatment strategies influencing clinical practice and surgical management of endometrioma. Addressing this unanswered question, creates opportunities for future research. Our study will follow with a larger sample base at our center and if possible a multicentric trial to see the impact of robotic surgery on the reduction of ovarian loss in endometrioma cystectomy.

CONCLUSION

Ovarian loss during endometrioma surgery is the main concern and in this study we have explored the benefits of a robotic platform to see if it could reduce ovarian loss. Intuitive and wristed movements with 3D magnified vision of a robotic platform gives an opportunity to do precise surgery. We have analyzed ovarian loss using an artificial intelligence-Whole Slide Imaging (WSI) software. Overall, the follicular loss and mean area of ovarian loss were higher in the LC group when compared to RC group. Statistically significantly lower ovarian loss in the RC group in cases with bilateral disease as well as less loss with increasing cyst size, supports the fact that robotic assistance can reduce the follicular and ovarian area loss during endometrioma cystectomy. If available, robot-assisted cystectomy for maybe offered for endometrioma surgery hoping to reduce the ovarian loss. However, a large-scale multicentric study is recommended in the future.

References:

1. Donnez J, Nisolle M, Casanas-Roux F, Bassil S, Anaf V. Rectovaginal septum, endometriosis or adenomyosis: laparoscopic management in a series of 231 patients. *Hum Reprod Oxf.* 1995;10(3):630–635.

2. Exacoustos C, De Felice G, Pizzo A, et al. Isolated ovarian endometrioma: a history between myth and reality. *J Minim Invasive Gynecol.* 2018;25(5):884–891.

3. Becker CM, Bokor A, Heikinheimo O, et al. ESHRE Endometriosis Guideline Group. ESHRE guideline: endometriosis. *Hum Reprod Open.* 2022;2022(2):hoac009.

4. Hachisuga T, Kawarabayashi T. Histopathological analysis of laparoscopically treated ovarian endometriotic cysts with special reference to loss of follicles. *Hum Reprod.* 2002;17(2):432–435.

5. Muzii L, Bianchi A, Crocè C, Manci N, Panici PB. Laparoscopic excision of ovarian cysts: is the stripping technique a tissue-sparing procedure? *Fertil Steril.* 2002;77(3):609–614.

6. Muzii L, Bianchi A, Bellati F, et al. Histologic analysis of endometriomas: what the surgeon needs to know. *Fertil Steril.* 2007;87(2):362–366.

7. Matsuzaki S, Houlle C, Darcha C, Pouly JL, Mage G, Canis M. Analysis of risk factors for the removal of normal ovarian tissue during laparoscopic cystectomy for ovarian endometriosis. *Hum Reprod.* 2009;24(6):1402–1406.

8. Bhat RG, Dhulked S, Ramachandran A, et al. Laparoscopic cystectomy of endometrioma: good surgical technique does not adversely affect ovarian reserve. *J Hum Reprod Sci.* 2014;7-(2):125–129.

9. Muzii L, Miller CE. The singer, not the song. *J Minim Invasive Gynecol.* 2011;18(5):666–667.

10. McCormack HM, Horne DJ, Sheather S. Clinical applications of visual analogue scales: a critical review. *Psychol Med [Internet].* 1988;18(4):1007–1019. Available from: https://pubmed.ncbi.nlm.nih.gov/3078045/.

11. Abrao MS, Andres MP, Miller CE, et al. AAGL 2021 endometriosis classification: an anatomy-based surgical complexity score. *J Minim Invasive Gynecol.* 2021;28(11):1941–1950.e1.

12. İnik Ö, Ceyhan A, Balcıoğlu E, Ülker E. A new method for automatic counting of ovarian follicles on whole slide histological images based on convolutional neural network. *Comput Biol Med.* 2019;112:103350.

13. Chapron C, Marcellin L, Borghese B, Santulli P. Rethinking mechanisms, diagnosis and management of endometriosis. *Nat Rev Endocrinol.* 2019;15(11):666–682.

14. Practice Committee of the American Society for Reproductive Medicine. Endometriosis and infertility: a committee opinion. *Fertil Steril.* 2012;98(3):591–598.

15. Hart RJ, Hickey M, Maouris P, Buckett W. Excisional surgery versus ablative surgery for ovarian endometriomata. *Cochrane Database Syst Rev.* 2008(2):CD004992.

16. Candiani M, Ottolina J, Schimberni M, Tandoi I, Bartiromo L, Ferrari S. Recurrence rate after "one-step" CO2 fiber laser vaporization versus cystectomy for ovarian endometrioma: a 3-year follow-up study. *J Minim Invasive Gynecol.* 2020;27(4):901–908.

17. Benaglia L, Somigliana E, Vighi V, Ragni G, Vercellini P, Fedele L. Rate of severe ovarian damage following surgery for endometriomas. *Hum Reprod.* 2010;25(3):678–682.

18. Muzii L, Marana R, Angioli R, et al. Histologic analysis of specimens from laparoscopic endometrioma excision performed by different surgeons: does the surgeon matter? *Fertil Steril.* 2011;95(6):2116–2119.

19. Alborzi S, Foroughinia L, Kumar PV, Asadi N, Alborzi S. A comparison of histopathologic findings of ovarian tissue inadvertently excised with endometrioma and other kinds of benign ovarian cyst in patients undergoing laparoscopy versus laparotomy. *Fertil Steril.* 2009;92(6):2004–2007.

20. Oh HK, Sin JI, Kim JH, Hong SY, Lee TS, Choi YS. Effect of age and stage of endometriosis on ovarian follicular loss during laparoscopic cystectomy for endometrioma. *Int J Gynaecol Obstet.* 2011;114(2):128–132.

21. Roman H, Tarta O, Pura I, et al. Direct proportional relationship between endometrioma size and ovarian parenchyma inadvertently removed during cystectomy, and its implication on the management of enlarged endometriomas. *Hum Reprod.* 2010;-25(6):1428–1432.

22. Coccia ME, Rizzello F, Mariani G, Bulletti C, Palagiano A, Scarselli G. Ovarian surgery for bilateral endometriomas influences age at menopause. *Hum Reprod.* 2011;26(11):3000–3007.

23. Busacca M, Riparini J, Somigliana E, et al. Postsurgical ovarian failure after laparoscopic excision of bilateral endometriomas. *Am J Obstet Gynecol.* 2006;195(2):421–425.