Laparoscopic cystectomy in treating women with endometrioma and pregnancy outcome – a case series

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ABSTRACT

Introduction: The aim of this study was to determine the spontaneous pregnancy rate and safety of our surgical technique of performing laparoscopy cystectomy for endometrioma.

Method: This is a 5-year retrospective study, carried out at Mahkota Medical Centre, Melaka, Malaysia. 143 patients with endometrioma associated with moderate to severe endometriosis underwent laparoscopic cystectomy from 2015 to 2019. The surgery commenced with dissection and excision of all the endometriotic lesions followed by injection of diluted vasopressin into the space between the cvst wall and the normal ovarian cortex. Stripping of the cvst wall was performed until the ovarian hilum was reached. The cyst wall was then excised, leaving some of the cyst wall on the hilum area. Minimal bipolar electrocoagulation was done on this remaining cyst wall. The ovary was then reconstructed with suturing. During the surgery, the severity of the disease was staged, endometrioma diameter and intraoperative findings were recorded. Fertility outcomes were determined among patients who were keen to conceive via telephone questionnaire and further analysed based on different factors.

Results: Among the 143 patients, 33.6% had Stage III endometriosis while 66.4% had Stage IV endometriosis. Of the 76 infertile patients, 42.1% conceived spontaneously in the mean duration of 6.9 months. 62.5% patients successfully conceived via assisted reproductive treatment and 10% conceived with ovulation induction. 47.4% patients had an uneventful delivery while 2.6% patients miscarried. 6.6% patients conceived twice post-surgery.

Conclusion: The aim of performing laparoscopic cystectomy for endometrioma in an infertile patient is to achieve a spontaneous pregnancy. Our technique of performing laparoscopic cystectomy resulted in a spontaneous pregnancy rate of 42.1% in patients with moderate and severe endometriosis.

KEYWORDS:

Bipolar coagulation; cystectomy; endometrioma; fertility; gynaecological ultrasound; laparoscopic; vasopressin

INTRODUCTION

Endometriosis is a chronic disease caused by the presence of endometrial-like glands and stroma outside the uterine

cavity. Endometriotic lesions can be present on the side wall of the pelvis or on the surface of pelvic organs such as uterus, ovaries, fallopian tubes, bladder, bowels, ureter and appendix¹ Endometriosis has been reported among 6-10% of women during their reproductive age.² Its prevalence among infertile patients was reported to be as high as 30-50[°].³ common The most manifestation of endometriosis is endometrioma which is the presence of the ectopic endometrial tissues in the ovary. A total of 17-44% of women with endometriosis were found to have endometrioma.⁴

Endometrioma is usually associated with moderate to severe endometriosis.⁵ It may cause dysmenorrhea, dyspareunia, pelvic pain and infertility. Medical management for endometrioma reduces its size and relieves the pain but does not improve fertility.⁶ The gold standard treatment for endometrioma is laparoscopic cystectomy. While decreasing dysmenorrhea, dyspareunia and pelvic pain, cystectomy also reduces recurrence rate while increasing spontaneous pregnancy rate. Pregnancy rate reported following excision of endometrioma was 30-67%, at the mean of 50%.⁷ However, studies have also shown that laparoscopic cystectomy will cause a significant negative impact on postoperative ovarian residual volume and reserve.^{8,9} During cyst excision, the absence of a clear cleavage plane between the cyst wall and ovarian stroma causes unintentional removal of the healthy ovarian tissues and cortex, resulting in reduction of follicles. To preserve the ovarian function, other surgical techniques have been proposed such as drainage, sclerotherapy or ablation. Cystectomy involves removing the cyst wall while ablative surgery involves opening the endometrioma and destroying the inner lining of the cyst wall with carbon dioxide laser vaporisation, plasma energy vaporisation or electrosurgical coagulation. Although these techniques could prevent the risk of excising healthy ovarian parenchyma, the risk of recurrence was generally higher compared to cystectomy.^{7,10,11}

Since different surgical techniques carry the risk of either impairment of the ovarian reserve or repeated surgery due to recurrence, some fertility specialist would prefer to proceed with *in-vitro* fertilisation (IVF) treatment first without surgery. However, the presence of endometrioma may theoretically interfere with ovarian responsiveness during ovarian stimulation as well as pose difficulties and risks during oocytes retrieval. Some difficulties that may be encountered are injury to the adjacent organs due to altered pelvic anatomy caused by adhesions, accidentally puncturing the

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endometrioma during oocyte retrieval causing infection and abscess formation as well as follicular fluid contamination with the endometrioma content. 12,13

To obtain the most favourable post-surgical outcome, a combined excisional and ablative technique has been proposed. In this technique, the endometrioma is excised using the stripping technique until the hilum is reached. Then the endometriosis at the hilum area is ablated. A study has shown that this combined technique, whereby excision of the endometrioma leading to a lower recurrence rates as well as non-excision at the hilum for preservation of normal ovarian tissues has led to a 32% cumulative pregnancy rate and a 2% recurrence rate.¹⁴

In this study, we would like to propose a surgical technique of endometrioma excision that involves the combined technique described above and at the same time injecting diluted vasopressin into the space between the cyst wall and the normal ovarian cortex. We would like to determine the spontaneous pregnancy rate as well as the safety of the first author's technique of performing laparoscopy cystectomy for endometrioma.

METHODS

A total of 143 women with endometrioma presenting with chronic pelvic pain and/or infertility who underwent laparoscopic cystectomy were recruited in this study. Also included were 78 patients from the previous study entitled 'Laparoscopic Transient Ovariopexy for Endometrioma and Fertility Outcome – a case series' based on the eligibility criteria. The surgeries were performed at Mahkota Medical Centre, Melaka, Malaysia from November 2015 to April 2019. Our institutional board approved this research and written informed consent were obtained pre-operatively from each woman for the surgery as well as to be involved in this retrospective study.

The pre-operative diagnosis of endometrioma was made by ultrasound scan (USS). In patients who were *virgo intacta* (VI), transabdominal ultrasound scan (TAUS) was performed and if the patient consented, transrectal ultrasound scan (TRUS) was done. For patients who were not VI, diagnosis was made by gynaecological examination and transvaginal ultrasound scan (TVUS). During the USS, the uterus and ovaries were carefully evaluated as well as the diameter of any ovarian cyst was measured and recorded. The severity of the disease was staged intra-operatively based on the revised American Society for Reproductive Medicine (rASRM) classification.

The duration of the surgery was calculated from the first incision for Verres needle insertion for pneumoperitoneum to completion of the last suture on the abdominal wall. All the surgeries were performed by the same surgeon.

Surgical technique

The surgery was performed using a 3D laparoscope (Aesculup – BBraun Einstein Vision). Adhesiolysis was performed to mobilise the endometriotic cyst. The contents of the endometriotic cyst was aspirated. This was then followed by temporarily hitching of both ovaries up to the abdominal

wall using Prolene 2.0 (Ethicon Inc, Somerville, NJ) sutures. This is to allow a better view of the pelvic side walls and Pouch of Douglas (POD). Ureters were dissected out if thought necessary. Dissection in the POD was carried out to release all adhesions between the rectum and the uterus, cervix and uterosacral ligaments. Any endometriotic lesions present on the rectum, in the uterosacral ligament, cervix and uterus were excised. If the vagina was involved, part of the vagina was removed and defect was sutured. If the rectal wall was involved, the endometriosis was shaved with caution to prevent the risk of rectal perforation. The rectal wall integrity was tested by inserting a urinary catheter in the rectum. Saline was placed in the POD. The rectum distal to the area of dissection was compressed with bowel grasper. Air was then injected into the rectum via the urinary catheter. If there are no bubbles seen, this will indicate an intact rectal wall.

After dissecting all the endometriotic lesions, the suspended ovary was released and laparoscopic cystectomy was performed. Diluted vasopressin (One ampoule containing 20 units of vasopressin was diluted in 200ml of saline) is injected into the space between the cyst wall and the normal ovarian cortex. If the cyst was large, this injection was made at several points. The aim of this injection is to separate the cyst wall from the ovarian cortex by hydrodissection. This will allow stripping of the cyst wall to be done easily and the vasopressin will provide haemostasis. Stripping of the cyst is performed by gentle traction and counter traction on the edges of the cyst wall until the fluid between the layers is spilled. At the hilum area, the cyst wall is cut using cold scissors. The remaining part of the cyst wall at the hilar region was left in place. Light coagulation with bipolar forceps was performed on this remaining cyst wall. When there was bleeding on the ovarian parenchyma, light coagulation was performed. The exposed area of the ovary was sutured using absorbable polyglactin 2.0 sutures (Ethicon Inc, Somerville, NJ). This was to prevent adhesion formation between the raw areas of the ovary and other structures in the pelvis.

Before the end of the surgery, the surgeon performed extra surgical steps on certain patients. In some patients, (when the ovary is mobile enough and the patient has given consent) the repaired ovary was pulled towards the anterior abdominal wall and suspended temporary to the peritoneum of the lower anterolateral abdominal wall next to the ipsilateral round ligament of the uterus by using 2.0 absorbable suture (Vicryl, Ethicon Inc, Somerville, NJ). A 2-3cm gap was left between the abdominal peritoneum and the ovary. This temporary ovariopexy was done to avoid the repaired ovary from becoming adherent to the raw peritoneal surface that had resulted from the extensive dissection and excision of endometriosis that had been done in the pelvis. In some patients whom the surgeon felt that the uterus was retroverted and there is a risk of readhesion of the uterus to the rectum, the round ligament was plicated using polyglactin 1 suture (Vicryl, Ethicon Inc, Somerville, NJ).

Outcomes

The primary outcome of this study is the fertility outcome in terms of clinical pregnancy rate. At the beginning of this study, all patients involved were contacted to complete a telephone questionnaire. The questions included desire to conceive, success in conceiving, methods of conceiving, time taken to conceive and outcomes of the pregnancy. For patients who did not conceive spontaneously, a detailed information regarding the types of treatment they underwent either via ovulation, induction, insemination or assisted reproductive treatment (ART) was recorded. The last patient included in this study was at least 6 months post-operation.

The secondary outcomes of this study are the safety of this surgical technique. This was determined by the absence of any intra- and/or post-operative complications.

RESULTS

A total of 143 patients with at least 1 endometrioma underwent laparoscopic cystectomy. The characteristics of the patients recruited in this study is shown in Table I. The mean age of patients in this study was 31.9. At the time of the surgery, 104 patients were married while 39 patients were single. Between the time of surgery and the beginning of the study, 7 single women got married. 99 (69.2%) of the patients were nulliparous while 44 (30.8%) had parity \geq 1. Thirteen patients had miscarriages and 76 (53.1%) patients were keen to conceive after the surgery.

During the clinical examination, 51.7% of the endometrioma was bilateral, 26.6% was on the left and 21.7% was on the right. The distribution of size of the cysts was as follows: 1-3cm (13.4%), 3-6cm (38.4%) and >6cm (48.1%). 20 (14%) patients had a previous history of cystectomy before visiting us.

Based on the intra-operative rASRM staging, 48 (33.6%) had Stage III endometriosis while 95 (66.4%) patients had Stage IV endometriosis. The mean rASRM score was 59.3. Most of the patients were found to have deep infiltrating endometriotic nodules and 65 (45.5%) of the patients had the POD completely obliterated. Concomitant adenomyosis was seen in 42 (29.4%) patients. During the surgery, the surgeon carried out additional procedures for some of the patients when necessary and this was believed to improve their chances of pregnancy. The mean duration of the surgery was 94.1 minutes.

Pregnancy outcomes

Among these 143 patients, 76 of them wished to become pregnant. The post-operative pregnancy outcomes are shown in Table II. Out of the 76 patients, 53 were trying actively to conceive immediately after the surgery, 15 patients deferred attempt to conceive after a period of rest post-surgery and 8 patients were not married at the time of the surgery. Based on the conditions of the patients, infertility factor and preference, different mode of conception was practiced such natural conception, in-vitro fertilization as intracytoplasmic semen injection (IVF-ICSI), intrauterine insemination (IUI) and ovulation induction via clomiphene citrate or letrozole.

A total of 32 (42.1%) of them conceived spontaneously at a mean duration of 6.9 months of actively trying to conceive, 30 (93.8%) patients had an uneventful delivery while 2

(6.3%) patients miscarried. Five (6.6%) patents conceived twice after the surgery.

Among the 76 patients, 8 patients underwent IVF-ICSI, 2 IUI and 10 patients underwent ovulation induction. As a result, 5 (62.5%) patients successfully conceived via IVF-ICSI and only 1 (10%) patient conceived with ovulation induction.

Factors affecting the spontaneous pregnancy outcomes

We have analysed several factors which may affect the fertility outcomes such as the site of the endometrioma, severity of the disease, presence of adenomyosis, history of cystectomy and maternal age. Table III show the overall relationship between each factor and pregnancy outcomes. Among the 76 patients who were keen to conceive, 35 of them underwent unilateral cystectomy and 41 patients underwent bilateral cystectomy. After trying actively to conceive, 17 (48.6%) patients who underwent unilateral cystectomy and 16 (39%) patients who underwent bilateral cystectomy conceived spontaneously. In other words, patients who underwent bilateral cystectomy had lower pregnancy rate compared to unilateral cystectomy. The spontaneous pregnancy rate was also lower in patients with severe endometriosis as compared to moderate endometriosis, 34.6% vs 62.5% respectively.

Adenomyosis is also an important uterine factor that may affect embryo implantation. A total of 18 patients were found to have either focal or diffuse adenomyosis. Only 4 (22.2%) of them conceived spontaneously after the surgery. Besides, repeated cystectomy may also influence the chances of pregnancy. This was demonstrated in this study where 2 out of 13 (15.4%) patients with previous history of cystectomy conceived spontaneously. Lastly, the fertility outcome is also influenced by the reproductive age of the patients. The rate of spontaneous pregnancy decreases as the age increases (Table IV).

Safety of the procedure

Among the 143 patients recruited in this study, 217 ovaries were excised. There were no intra-operative or post-operative complications such as excessive bleeding, infection, haematoma or bradycardia reported. The mean duration of hospital stay was 2.7 days. No changes in the ovarian function post-operatively as determined by any changes in the menstrual cycle were reported by any of the patients during the follow-up period.

DISCUSSION

The effect of endometrioma on fertility has been given much attention. Endometrioma causes focal inflammation in the surrounding ovarian cortex, and subsequently reduces vascularization and increases oxidative stress, resulting in antral follicle count reduction, interstitial fibrosis and microvascular injury in the ovary. Superficial and deep infiltrative endometriosis are also commonly associated with pelvic adhesions. Pelvic adhesions may distort the anatomy of pelvic organs causing mechanical interference to oocyte pickup by the fallopian tubes and transportation of the oocytes in the tubes. All these factors may reduce fecundity rate.

Total number of patients recruited in this study = 143					
Mean age (years)	31.9				
Marital status	At the time of surgery	Married	104		
		Single	39		
	At the beginning of the study	Married	111		
		Single	32		
Obstetric history	Nulliparous	99 (69.2%)			
	Parous	44 (30.8%)			
	Miscarriage	13 (9.1%)			
Total number of patients who keen to conceive	_	76 (53.1%)			
Previous cystectomy surgery		20 (14%)			
TVUS / TRUS findings	Laterality of endometrioma	Left	38 (26.6%)		
-		Right	31 (21.7%)		
		Bilateral	74 (51.7%)		
	Mean diameter (cm)	Left	6.0		
		Right	6.3		

Table I: The demographic of the study population

Table II: Post-operative pregnancy outcome. (in-vitro fertilization – intracytoplasmic semen injection = IVF-ICSI)

Total number of patients who were keen to conceive, n = 76					
Time planned to trying to conceive	Immediately after surgery	53			
	Sometime after surgery	15			
	After getting married	8			
Mode of conception of all patients	Natural	56			
	IVF-ICSI	8			
	Intrauterine insemination	2			
	Ovulation induction	10			
Total number of patients who conceived successfully		38 (50%)			
Mode of successful conception	Spontaneous pregnancy	32 (42.1%)			
·	IVF-ICSI	5 (62.5%)			
	Ovulation induction	1 (10%)			
Number of patients who conceived more than once		5 (6.6%)			
Miscarriage		2			
Mean duration of trying to conceive (months)		6.9			

Table III: shows the spontaneous pregnancy rate influenced by the infertility factors

Factors which affect pregnancy outcomes	Number of patients who keen to conceive, n	Spontaneous pregnancy rate, n (%)	
Unilateral cystectomy	35	17 (48.6)	
Bilateral cystectomy	41	16 (39.0)	
Moderate endometriosis	24	15 (62.5)	
Severe endometriosis	52	18 (34.6)	
Adenomyosis	18	4 (22.2)	
History of cystectomy	13	2 (15.4)	

Table IV: The number of patients with successful spontaneous pregnancy according to the maternal age

Age (years)	23 – 25	26 – 28	29 – 31	32 – 34	35 – 37	38 – 40	41 – 43	44 – 46
Number of patients	10	16	15	22	7	4	1	1
who keen to conceive								
Number of patients	7	7	10	6	0	1	0	0
conceived spontaneously, n (%)	(70)	(43.8)	(66.7)	(27.3)		(25)		

There is an ongoing debate regarding the most appropriate surgical technique to treat endometrioma at the same time enhancing fertility. Laparoscopic cystectomy is the gold standard in managing patients with endometrioma. However, the main worry is its potential deleterious effect on ovarian reserve. The absence of a clear cleavage plane between ovarian stroma and cyst wall may cause inadvertent removal of the healthy ovarian parenchyma along with the cyst wall which may lead to loss of follicular reserve. Besides, the excessive use of coagulation during the surgery will also cause thermal destruction on the ovarian follicles, subsequently impair fertility.

In this retrospective study, we would like to propose the feasibility and safety of our surgical technique in which the ovarian pathology is removed with optimal preservation of ovarian function to give the best spontaneous pregnancy rates. During the surgery, we injected vasopressin into the space between the cyst wall and the normal ovarian cortex to provide a hydrodissection effect. When a certain amount of

		Diagnosis	Mean age of the	Surgical technique	Spontaneous pregnancy
			participants		rate
1	Donnez et al (2010)	Endometrioma >3cm	29.2 + 3.7 years	Combined technique (stripping + CO2 laser vaporization)	12/52 (32%) at 6-month post- operatively 15/52 (41%) at 8.3-month post-operatively
2	Maggiore ULC et al (2017)	Rectovaginal endometriosis with endometrioma	33.3 + 3.8 years	Stripping technique	Crude pregnancy of 38/125 (30.4%) Cumulative pregnancy of 34.5%
3	Taniguchi et al (2016)	Endometrioma	31.7 + 5.4 years	Stripping technique	10/40 (25%)
4	Mircea et al (2016)	Endometrioma >3cm	28 + 3.8 years	Combined technique (excision + bipolar coaqulation)	6/40 (15%)
5	Shervin et al (2016)	Deep infiltrative endometriosis with endometrioma	31.4 + 4.9 years	Global laparoscopic resection of endometriotic lesions and excisional cystectomy	26%
6	Current study (2020)	Endometrioma with endometriosis stage III and IV	31.9 years	Combined technique (stripping + excision and bipolar coagulation)	32/76 (42.1%)

Table V: Review of other studies on surgical treatment of endometrioma and fertility outcomes

saline diluted with vasopressin is injected into the correct space, the space between the cyst wall and the ovary will swell up, providing a clear boundary for excision, thus preventing the risk of accidental removal of normal ovarian tissue. Besides, vasopressin acts as vasoconstrictor. It helps to reduce the oozing from the ovarian cortex, thus reduce the frequency of electrocoagulation which may cause thermal damage to the ovarian follicles. Studies which have compared diluted vasopressin injection with control group showed that the frequency of electrocoagulation for haemostasis as well as the operation time is lesser in the vasopressin group.^{15,16} In another similar study, Ren Qiongzhen et al., reported that there was no significant difference in the thickness of the healthy ovarian tissue excised in both these groups.¹⁷ Bradycardia is a known side effect of the usage of vasopressin. This was not seen in any of our patients in our study.

At the ovarian hilus region, the ovarian tissue is more functional and the plane of cleavage is less visible. One needs to be cautious when approaching this region. In 69% of cases of cystectomy where ovarian tissue at the hilar region was excised, primordial, primary and secondary follicles were seen in the excised specimen.¹⁸ To reduce this loss of follicles at the hilum, carbon dioxide vaporisation or bipolar coagulation was used at the hilum instead of stripping of the cyst wall in this area. $^{\scriptscriptstyle 14,19,20}$ In this study, we resected the cyst wall up to the hilum area and the cyst wall at the hilum was lightly coagulated using bipolar electrocoagulation. Reconstructing the ovary after endometrioma cystectomy is also not a commonly practiced procedure perhaps because it requires laparoscopic suturing skills and will increase the duration of the surgery. We believe that reconstruction of the ovary is necessary to ensure that the raw surface of the ovary after cystectomy will not become adherent to the peritoneal area in the pelvis caused by the extensive excision of endometriosis and endometriotic nodule. Coric et al., demonstrated that suturing the ovarian tissue and reconstructing the ovary at the end of cystectomy resulted in lesser adverse effect on ovarian reserve as compared to bipolar coagulation.²¹

In this retrospective study, 32 out of 76 (42.1%) patients who were keen to conceive, conceived spontaneously by the 7th month post-operatively. This is comparably higher compared to other studies.^{14,22} Donnez et al., used a combined technique of excisional and ablative surgery and reported the cumulative pregnancy rate of 32% at 6month and 41% at 8.2-month post-surgery.¹⁴ Roberti et al., also reported the crude spontaneous pregnancy rate of 30.4% and cumulative spontaneous pregnancy rate of 34.5% post-surgery.²² Our spontaneous pregnancy rate was much higher compared with results reported by Taniguchi et al., and Mircea et al., (42.1% vs 25% and 18.8% respectively).^{23,24} Shervin et al., reported a total pregnancy rate of 35.6% and spontaneous pregnancy rate around 26% after a global laparoscopic resection of nodules laparoscopic excisional endometriotic and for cystectomy patients with deep infiltrative endometriosis and endometrioma.25 Table V shows the comparison of the spontaneous pregnancy rate between the studies. The results of spontaneous pregnancy differ due to the different surgical techniques applied during the excision of endometrioma and no diluted vasopressin was injected during the surgery as compared to our study.

In the subgroup analysis, several factors affected the chances of spontaneous pregnancy. The presence of adenomyosis negatively affects pregnancy rates. Only 22.2% of patients with adenomyosis conceived. There are many factors that cause a decrease in fertility rate in patients with adenomyosis. This includes poorer implantation rate, which may be caused by dysfunction of the uterine junctional zone. Another poor prognostic factor for pregnancy is a history of previous ovarian cystectomy for endometrioma. Only 2 out of 13 patients (15.4%) of patients with a previous history of cystectomy conceived spontaneously. The impact of maternal age on fertility outcomes after cystectomy is clearly demonstrated in our study. Spontaneous pregnancy rate was only 7.7% in the age group after 34 years. This result is consistent with the other studies which reported that the fecundity rate significantly decreased after the age of 32 and more rapidly after 37.26,27

As in all other studies,^{14,22-25} no complications were encountered during the surgery. Our surgical technique can be considered as a safe procedure to perform for patients with endometrioma.

The main limitation of this study is that it is a retrospective study. We performed the same technique for all patients. The sample size of patients who were keen to conceive was also small. There are several factors which may affect patient's ability to conceive such as male infertility factor and the tubal patency of the patients. We did not perform semen analysis for all the partners of our patients. Since some of the patients were VI at the time of the surgery, we did not check for tubal patency. Despite this, the spontaneous pregnancy rate in our study was fairly high.

CONCLUSION

The primary outcome of this study is the fertility outcome in terms of clinical pregnancy rate after undergoing laparoscopic cystectomy for endometrioma. In this case series, we looked at a particular method of performing surgery on patients with endometrioma to see whether spontaneous pregnancy rates are within acceptable range. We found that the spontaneous pregnancy rate after surgery using our technique was 42.1% in women with moderate to severe endometriosis. This result appears superior to most other published reports on this subject. The secondary outcome of this study is the safety outcome. No postoperative complications were encountered in all the patients indicating that this is a safe technique.

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ETHICAL APPROVAL

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The ethical approval has been exempted by our local institutional board.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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