Original Article

Prognostic Factors for Pain and Fertility Outcomes Following Laparoscopic Endometriosis Surgery: A Single-Center Experience

Mania Kaveh [1], Fatemeh Khodayari [1], Shahla Chaichian [2], Abolfazl Mehdizadeh Kashi [3], Mehdi Afshari [4], Zahra Shahraki [1], Kambiz Sadegi [5*]

1- Department of Obstetrics and Gynecology, School of Medicine, Amiralmomenin Hospital, Zabol University of Medical Sciences, Zabol, Iran
2- Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran
3- Department of Obstetrics and Gynecology, School of Medicine, Endometriosis Research Center, Rasoul Akram Hospital, Iran University of Medical Sciences, Tehran, Iran
4- Department of Community Medicine, School of Medicine, Pediatric Gastroenterology and Hepatology Research Center, Zabol University of Medical Sciences, Zabol, Iran
5- Department of Anesthesiology, School of Medicine, Amiralmomenin Hospital, Zabol University of Medical Sciences, Zabol, Iran

* *Corresponding Author:*
Kambiz Sadegi, Department of Anesthesiology, School of Medicine, Amiralmomenin Hospital, Zabol University of Medical Sciences, Zabol, Iran
E-mail:
Kamsadegi@yahoo.co.uk

Abstract

Background: Endometriosis is a prevalent condition among women, often leading to infertility. Laparoscopic surgery is widely employed as a therapeutic intervention for endometriosis. This study investigated the prognostic factors influencing the outcome of laparoscopic surgery for endometriosis.

Methods: This cross-sectional study included 60 women with endometriosis referred for laparoscopic surgery at Amiralmomenin Hospital, Zabol, Iran, between 2022 and 2024. Pain intensity was measured using a visual analog scale (VAS). Statistical analyses were performed using SPSS version 26. Descriptive statistics summarized the data, while univariate analyses (t-tests and chi-square tests) assessed relationships between variables. Multivariate logistic regression identified independent predictors of pain reduction and pregnancy outcomes.

Results: Patients with moderate endometriosis showed statistically significant pain reduction from 8.8 preoperatively to 1.8 at 9 months (p<0.001) and 2.2 at 12 months post-surgery (p=0.003). Those with severe endometriosis had non-significant pain reduction (8 to 6 at 12 months, p=0.12). Both intrauterine (9 to 1.1 at 12 months, p<0.001) and extrauterine involvement groups (8.6 to 3.3, p=0.004) demonstrated significant pain improvement, with no significant difference between the groups (p=0.779). Regarding fertility outcomes, treatment before the age of 30 significantly increased pregnancy likelihood (AOR=20.57, 95%CI 1.4-295.3), while other factors including BMI, CA125 levels, and parity showed no significant associations (all p>0.05).

Conclusion: These preliminary findings suggest that laparoscopic surgery may reduce pain in moderate endometriosis, while the age under 30 may be associated with improved pregnancy outcomes. However, given the study's limited sample size and wide confidence intervals, these results require validation in larger, multicenter cohorts.

Keywords: Endometriosis, Laparoscopic surgery, Postoperative pain, Surgical pain management.

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Introduction

According to the American College of Obstetricians and Gynecologists (ACOG), endometriosis is a condition where tissue similar to the uterine lining (the endometrium) grows outside the uterus (1). This abnormal tissue growth can cause inflammation, scarring, and adhesions,

often leading to chronic pain, particularly during menstruation, and is a major cause of infertility. It can be found on the ovaries, fallopian tubes, outer surface of the uterus, and other organs in the pelvic area. Although endometriosis is commonly associated with pelvic pain and infertility, some women may experience no symptoms at all. The gastrointestinal tract represents the most frequent site of extrapelvic endometriosis, particularly when involving the rectum, sigmoid colon, or bladder (2, 3). Gastrointestinal involvement is reported in up to 3.8–37% of women diagnosed with endometriosis (4). Endometriosis affects approximately 6–10% of women in the general population, with peak incidence occurring between the ages of 25 and 35 years. The annual incidence is about 0.1% among women aged 15–49 years. Endometriosis is diagnosed in 30–80% of patients with chronic pelvic pain and dysmenorrhea. Among women struggling with infertility, the prevalence of endometriosis ranges from 20 to 50%, and approximately 35 to 50% of those with endometriosis are infertile (5-7). Accurate diagnosis of superficial endometriosis currently requires laparoscopy. However, preoperative transvaginal ultrasound (TVUS) has shown high accuracy for detecting ovarian (93% sensitivity and 96% specificity) and deep endometriosis (79% sensitivity and 94% specificity). Transvaginal ultrasound with bowel preparation (TVUS-BP) demonstrates high sensitivity and specificity for detecting bowel (98.0% and 100.0%) and retrocervical endometriosis (95% and 98%), respectively. Several studies have also shown that MRI has good accuracy for diagnosing endometriosis (8-12).

Laparoscopy is indicated in patients with painful symptoms and subfertility to remove endometriotic lesions and adhesions and restore pelvic anatomy (13-15). Surgery is also required in patients with contraindications or poor response to medical treatments, in cases of acute pelvic pain episodes, and to establish a differential diagnosis with a malignant adnexal mass (16).

Despite the well-established relationship between endometriosis and infertility, the prognostic factors that influence the outcomes of laparoscopic surgery for endometriosis remain inadequately addressed in the literature. Many studies have primarily focused on factors like disease severity, CA125 levels, and the age of the patient at treatment, with limited research on how these factors influence long-term surgical outcomes such as pain relief and fertility improvement (11, 17-19).

This study differs from previous research by considering a broader set of factors, including BMI, parity, and the timing of surgery in relation to age, to provide a more comprehensive understanding of their impact on post-operative outcomes.

Given the importance of timely and effective treatment, an effort was made to identify the prognostic factors that influence the success of laparoscopic surgery for endometriosis, focusing on both short-term pain relief and long-term fertility outcomes. By examining the interactions of various factors over an extended follow-up period, new insights into the predictors of successful treatment were provided, thus contributing valuable information to the existing body of literature.

Methods

This cross-sectional study included women with endometriosis referred for laparoscopic surgery at the gynecology clinic of Amiralmomenin Hospital, Zabol, Iran, between 2022 and 2024. After applying the inclusion and exclusion criteria, 60 eligible patients were enrolled in the study.

The inclusion criteria comprised women aged 18–40 years diagnosed with endometriosis, who were candidates for laparoscopic surgery and provided informed consent to participate in the study. Notably, surgical indications for patients aged 18 or older included severe pelvic pain (VAS score >6) unresponsive to medical treatments, extensive endometriosis causing bowel obstruction, ureteral involvement, or a large cyst size. Additionally, patients were required to have a complete medical record and follow-up data for at least 12 months after surgery.

Exclusion criteria included women with a history of hysterectomy, congenital uterine abnormalities, abdominal adhesions from previous surgeries, prior laparoscopic surgery for endometriosis, or underlying medical conditions such as diabetes, hypertension, thyroid disorders, or cardiovascular diseases.

The primary categorization of patients in our study was not based on pain severity, but rather on clinical indications for surgery, as outlined in our inclusion criteria. Patients were selected based on one or more of the following criteria: an anti-Müllerian hormone (AMH) level below 2.52.5, where ART was not either feasible or had failed; severe pelvic pain with VAS score greater than 6 that was unresponsive to medical therapy; progressive cyst growth or atypical findings on imaging; and involvement of vital structures such as

bowel or ureter. The analysis based on pain severity (moderate vs. severe) was conducted as a secondary exploratory analysis to assess whether baseline pain intensity influenced postoperative outcomes.

The study was approved by the Ethics Committee of Zabol University of Medical Sciences (IR.ZBMU.REC.1401.109). Written informed consent was obtained from all participants before enrollment.

Data collection: Data collection included demographic information (age, BMI, parity), clinical parameters (CA125 levels, stage of endometriosis based on rASRM criteria), and outcomes (pain intensity and pregnancy rates). Pain severity was measured preoperatively and postoperatively at 3, 9, and 12 months using the 10-point VAS. Pregnancy outcomes were assessed through patient follow-ups during the study period.

Pain severity was recorded using VAS, where 0 represents no pain and 10 represents the worst imaginable pain. For classification purposes, moderate pain was defined as VAS scores between 4 and 7, while severe pain was defined as VAS scores of 8 or higher. Blood samples were collected to measure CA125 levels, with values above 35 *U/ml* considered abnormal.

Surgical method: This approach was considered part of our surgical decision-making algorithm, particularly in cases of progressive cyst enlargement during follow-up. Patients were monitored using TVUS, and those with progressively increasing cyst size, even if asymptomatic, were considered candidates for surgery due to the potential risk of complications and diminished ovarian reserve.

Cysts with atypical sonographic features were also considered for surgical intervention. In some patients, TVUS findings showed atypical morphologic characteristics, such as irregular walls or echogenic content, raising concerns for borderline or malignant pathology. These cases were referred to the oncology team and discussed in a multidisciplinary setting before making surgical decisions. Cyst size >5–6 *cm* with associated symptoms or infertility was also considered in surgical planning. While size alone was not an inclusion criterion, large cysts exceeding 5–6 *cm* that caused pain or impaired ovarian function were prioritized for surgical intervention.

Medical treatments were indeed prescribed prior to surgery in accordance with standard clinical protocols. All patients included in this study had either failed to respond to at least 6 months of medical therapy such as GnRH analogs, combined oral contraceptives, or progestins, or they presented with clinical indications necessitating surgical intervention. Non-responsiveness to medical therapy was defined by persistent high pain scores (VAS >6) and/or progressive enlargement of endometriomas on serial transvaginal ultrasounds. These patients were considered refractory to medical treatment and were therefore recommended for surgical management.

Additionally, when endometriosis involved vital organs (*e.g.*, bowel or ureters) or when deeply infiltrating disease with suspected organ dysfunction was present, patients were referred directly for surgery without prior medical management, consistent with international guidelines. These cases were typically identified through imaging (TVUS or MRI) and clinical examination, and surgical planning was made accordingly.

All patients underwent preoperative assessment of AMH levels. Following infertility service consultation, patients with an AMH level above 2.5, who suffered from severe pain unresponsive to medical treatments, or those with very large or progressively increasing cysts were classified as surgical emergencies for endometriosis, regardless of their age. For patients experiencing infertility, the infertility service assessed the need for oocyte or embryo preservation, which was performed before the surgical procedure.

Laparoscopic surgery is a corrective procedure for endometriosis, performed based on the areas involved. The initial approach involved retroperitoneal dissection, followed by ureteral mobilization, and, if necessary, dissection of the pararectal and paravesical spaces, along with excision of the posterior cul-de-sac. In cases where endometriotic implants were identified, they were excised; similarly, all identified endometriomas were surgically excised. During the excision process, special attention was given to maintaining AMH levels through meticulous and targeted hemostasis. Electrosurgery was minimized to reduce damage, and suturing was used for hemostasis. Special attention was given to preserving ovarian reserve (as indicated by AMH levels), ensuring minimal damage to ovarian tissue, which was sutured at the end of the procedure.

Treatment after the surgery: In patients not planning to conceive, Verogest tablets were adminis-

tered for up to 18 months. For patients who desired pregnancy, Duphaston 10 *mg* was prescribed during the second half of the menstrual cycle for 14 nights. After three months, patients who were candidates for IVF were referred to an IVF center, and finally, patients who were not IVF candidates attempted to conceive naturally.

For patients who did not wish to conceive, progestin-based therapy (*e.g.*, Verogest) was typically initiated within 1–2 weeks after surgery, once postoperative recovery was confirmed and no signs of infection or complications were present. In cases where patients had intolerance or contraindications to progestins, combined oral contraceptive pills (OCPs) were used as an alternative. For patients desiring pregnancy, after the first spontaneous ovulatory cycle, typically occurring within 4–6 weeks post-surgery, Dydrogesterone (Duphaston) or an equivalent progestin was administered during the luteal phase (second half of the cycle) for 14 days. Patients were then advised to attempt natural conception. For patients with cryopreserved embryos or oocytes, following recovery and the first spontaneous cycle, referrals were made to the infertility center for planned embryo transfer or assisted reproductive treatment.

Statistical analysis: Statistical analyses were performed using SPSS version 26 (IBM, USA). Descriptive statistics were used to summarize the data, while univariate analyses including t-tests and chi-square tests, were performed to evaluate relationships between individual variables. Multivariate logistic regression was conducted to identify independent predictors of postoperative pain reduction and pregnancy outcomes. Variables included in the regression model were selected based on clinical relevance and prior evidence, including age at surgery, BMI, parity, CA125 levels, and disease severity. Statistical significance was set at $p < 0.05$.

Results

In this study, 60 women with endometriosis who underwent laparoscopic surgery were examined.

Table 1 shows that the ovarian involvement was most frequent, observed in 31 cases (51.7%), moderate pain was reported by 55 patients (91.7%), and a positive CA125 marker was present in 31 cases (51.7%).

Results from the multivariate repeated measures models, adjusted for factors such as severity and location of involvement, BMI, age at surgery, par-

Table 1. Frequency Distribution of Involved Sites, Pain Level, and CA125 Marker

	Frequency	**%**
Site of involvement		
Uterus	8	13.3
Ovaries	31	51.7
Uterus and ovaries	16	26.7
Rectum	5	8.3
Pain intensity		
Moderate	55	91.7
Severe	5	8.3
CA125		
Negative	29	48.3
Positive	31	51.7

ity, and CA125 levels are described below. Figure 1 shows that the mean pain score for patients with moderate endometriosis decreased from 8.8 before surgery to 1.8 at 9 months and 2.2 at 12 months, which was statistically significant. For patients with severe endometriosis, the pain intensity at these times was 8, 4, and 6, respectively, but this reduction was not statistically significant. The change in pain between the moderate and mild endometriosis groups was not statistically significant ($p = 0.476$), indicating that both groups experienced a similar reduction in pain after surgery. This suggests that the severity of endometriosis did not affect pain reduction.

Figure 2 shows that the mean pain score for patients with intrauterine involvement decreased from 9 before surgery to 2.2 at 9 months and 1.1 at 12 months, which was statistically significant.

Table 2. Adjusted odds ratios for the factors studied in relation to pregnancy occurrence after endometriosis treatment

Examined factors	Adjusted odds ratio (AOR)	p-value
Pain intensity	0.39 [1]	0.448
CA125	0.38 [2]	0.331
Multiparity	3.4 [3]	0.227
Intrauterine involvement	0.39 [4]	>0.99
Overweight	0.24 [5]	0.256
Treatment before the age of 30	20.57 [6]	0.027

1: Adjusted for CA125 and parity
2: Adjusted for severity, parity, location, overweight/obesity, and age at treatment
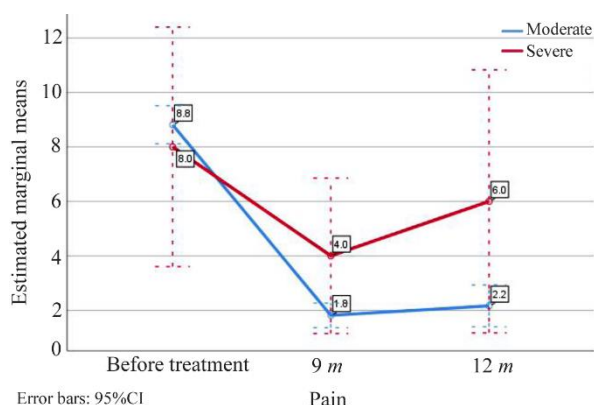3. Adjusted for severity, location, overweight/obesity, CA125, and age at treatment
4. Adjusted for severity, parity, overweight/obesity, CA125, and age at treatment
5. Adjusted for severity, parity, location, and CA125
6. Adjusted for parity, location, CA125, and overweight/obesity

Figure 1. Changes in pain intensity before surgery, at 9 months, and 12 months after surgery in patients with moderate and severe endometriosis
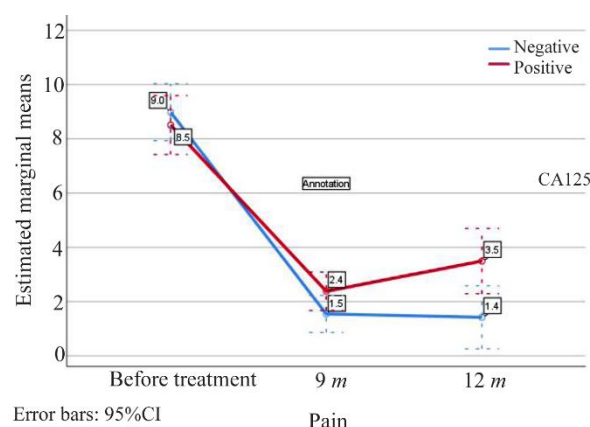
For patients with extrauterine involvement, the pain intensity was 8.6, 2, and 3.3, respectively, and this reduction was also statistically significant. The change in pain between the intrauterine and extrauterine groups was not statistically significant (p=0.779), indicating that the location of endometriosis did not affect pain reduction.

Figure 3 shows that the mean pain score for patients with normal CA125 decreased from 9 before surgery to 1.5 at 9 months and 1.4 at 12 months, but this reduction was not statistically significant. For patients with abnormal CA125, the pain intensity was 8.5, 2.4, and 3.5, respectively, and this reduction was also not statistically significant. The change in pain between the normal and abnormal CA125 groups was not statistically significant (p=0.107), indicating that CA125 levels did not affect pain reduction.
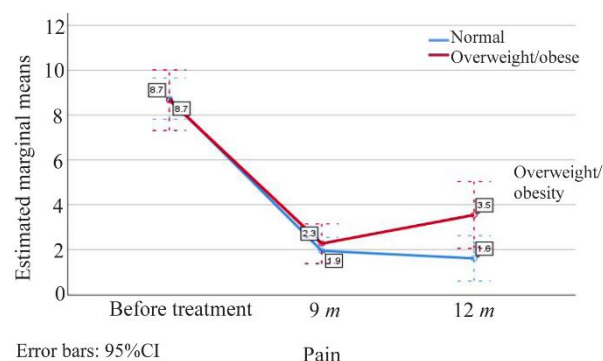
Figure 4 shows that the mean pain score for patients with normal BMI decreased from 8.7 before surgery to 1.9 at 9 months and 3.5 at 12 months,
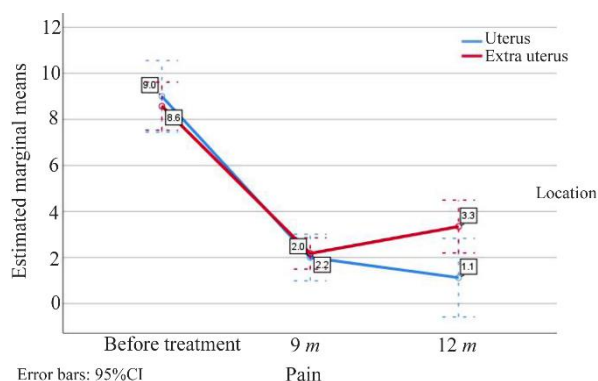
Figure 2. Changes in pain intensity at different times in patients with intrauterine and extrauterine involvement

Figure 3. Changes in pain intensity at different times in patients with normal and abnormal CA125 levels

Figure 4. Changes in pain intensity at different times in patients with normal and high BMI

but this reduction was not statistically significant. For patients with high BMI, the pain intensity was 8.7, 2.3, and 3.5, respectively, and this reduction was also not statistically significant. The change in pain between the high and normal BMI groups was not statistically significant (p=0.546), indicating that BMI did not affect pain reduction.

Among the 60 patients studied, 39 desired pregnancies after surgery, and 15 (38%) successfully achieved pregnancy within one year after surgery. As shown in table 2, the odds ratio for the age at treatment was 20.57, which was statistically significant, meaning that treating endometriosis before the age of 30 increased the odds of a successful pregnancy by 20.6 times. However, the odds ratios for other factors such as severity and location of involvement, parity, BMI, and CA125 were not statistically significant. This means that none of these factors had an effect on pregnancy occurrence after endometriosis treatment.

Discussion

Endometriosis is a complex and multifactorial condition with an unclear pathogenesis. Despite significant advancements in understanding the disease, many aspects remain poorly defined (20). In this study, a significant reduction in pain intensity was observed in all patients, 9 months after treatment for endometriosis. However, by the twelfth month, a slight increase in pain intensity was observed across all groups, although this increase was not statistically significant when compared to the ninth month.

An important finding in this study was that none of the variables examined, including disease severity, location, age at treatment, BMI, parity, or CA125 levels, had a significant impact on pain reduction following surgery. This contrasts with some previous studies that have linked disease severity with pain intensity reduction. It is important to consider that the small sample size and methodological limitations may have contributed to these findings, and larger studies are needed to validate these results.

Regarding pregnancy outcomes, 38% of women who desired pregnancy were able to conceive within 9 to 12 months after treatment. Notably, women who underwent laparoscopic surgery before the age of 30 had a significantly higher chance of becoming pregnant within a year post-surgery. In contrast, other factors, such as disease severity, location, age at treatment, BMI, parity, and CA125 levels did not show significant effects on pregnancy outcomes.

Our findings align partially with those of Signorile et al., who conducted a large retrospective study over ten years with 4401 endometriosis patients at the Endometriosis Center of Italy. They found that 81.6% of patients had one or more children, with no significant association between disease location, severity, or age of treatment with pregnancy occurrence. Similar to our study, they also found that most patients had normal CA125 levels. The reliability of CA125 as a serum marker for endometriosis has been questioned due to its weak sensitivity and specificity, and our results support this view, as CA125 did not significantly correlate with pain reduction or pregnancy outcomes (21).

In contrast, studies by Porpora et al., which included 425 women (143 with endometriosis), reported that 56% of women became pregnant after treatment, a higher rate than observed in our study. Their findings suggest that treatment for endometriosis can significantly improve fertility, which is consistent with the growing body of literature on the positive impact of surgical and medical treatments on fertility (22).

Jacobson et al. conducted a study on 164 suspected endometriosis patients, confirming the disease in 138 (84.1%). They found that patients with minimal and mild endometriosis experienced greater pain reduction post-treatment. Contrary to our findings, a significant association was observed between the severity of endometriosis and pain, while other factors like age and location showed no significant relationships (23). Similarly, Marcoux et al. studied 341 women with endometriosis and found no significant association between age, severity, and post-laparoscopy fertility, which contrasts with our finding that treatment before the age of 30 significantly improved pregnancy chances (24). Moini et al., in a study of 314 suspected endometriosis patients, confirmed the disease in 213 (67.8%) cases. They reported a significant reduction in pain post-treatment, but most patients experienced severe pain a year later, similar to our findings. This underscores the transient nature of pain reduction following treatment for endometriosis (25).

Inoue examined 2080 infertile patients who underwent laparoscopy, finding that 60.7% had endometriosis. The results showed that only 23% of these patients became pregnant after laparoscopy, with no significant difference between treatment and fertility outcomes (26). This highlights the variability in fertility outcomes post-treatment and emphasizes the need for further investigation into factors that might influence pregnancy success in endometriosis patients.

In a study by Nademi and Rasekhi, 403 patients with endometriosis were categorized into mild, moderate, and severe disease stages. They found a significant relationship between pelvic pain and disease severity. Lower BMI was also associated with higher pain intensity. These findings align with our observations, particularly regarding the relationship between BMI and pain (27). Similarly, Hemmings et al. reported a positive association between lower BMI and severity of endometriosis, while Shum et al. found no significant relationship between age, type of pain, and BMI with endometriosis severity (28, 29).

In another study, a fourfold higher rate of infertility was found in the endometriosis group compared to controls. Moreover, significant associations were identified among age, irregular men-

struation, and other variables in relation to pain severity, underscoring the multifactorial nature of endometriosis and its impact on fertility (30).

Conclusion

This study offers preliminary evidence regarding pain and fertility outcomes following laparoscopic treatment of endometriosis. While apparent reductions in pain scores and pregnancy rates were observed within 9-12 months post-surgery, the subgroup analyses were limited by sample size constraints, particularly for severe endometriosis cases and rare outcomes like pregnancy.

The association between age <30 years and pregnancy success (AOR=20.57, p=0.027) should be interpreted cautiously, as the wide confidence interval (95%CI: 1.4-295.3) reflects substantial uncertainty. No other clinical factors demonstrated statistically significant associations, though this may reflect limited statistical power rather than the absence of true effects.

These results highlight the need for larger, multicenter studies to validate the potential age-dependent treatment responses, better characterize pain recurrence patterns across endometriosis subtypes, and identify predictive biomarkers beyond CA125.

Clinical implications should be considered preliminary until replicated and validated in adequately powered cohorts before definitive conclusions can be drawn.

Conflict of Interest

Authors declare no conflict of interest.

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