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ORIGINAL ARTICLE

Intrauterine Perfusion Combined with Ovarian Injection of PRP for Improving Pregnancy Outcomes in Infertile Women with EMT

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ABSTRACT

Background: **Endometriosis (EMT) is a major cause of infertility. Laparoscopic surgery is the standard treatment but carries a risk of recurrence and has limited effectiveness in improving pregnancy outcomes. Platelet-rich plasma (PRP) has been shown to promote endometrial repair and improve ovarian function, yet few studies have explored its combined application with surgery.**
Methods: **A total of 60 infertile patients with EMT were allocated into three groups according to their treatment plan: Group A (n = 20) received laparoscopic surgery only; Group B (n = 20) received surgery combined with intrauterine PRP perfusion; Group C (n = 20) received surgery along with both intrauterine PRP perfusion and PRP injection into the affected ovary. Clinical efficacy, endometrial thickness and morphology, serum markers of ovarian function (luteinizing hormone [LH], follicle-stimulating hormone [FSH], estradiol [E2], anti-Müllerian hormone [AMH]), and pregnancy outcomes were compared among the three groups.**
Results: **The total clinical effective rate in Group C (95%) was significantly higher than that in Group A (60%). Postoperative endometrial thickness and the proportion of linear endometrium were higher in Groups B and C than in Group A, with the most significant improvement observed in Group C. Regarding ovarian function, postoperative FSH and LH levels in Group C were significantly lower than those in Groups A and B, while E2 and AMH levels were significantly higher. The clinical pregnancy rate, natural pregnancy success rate, and live birth rate in Group C were significantly higher than those in Group A. There were no significant differences in the incidence of pregnancy complications among the three groups.**
Conclusions: **Laparoscopic surgery combined with intrauterine PRP perfusion and ovarian injection can effectively improve endometrial receptivity and ovarian reserve function in infertile patients with EMT, significantly increasing clinical pregnancy and live birth rates without increasing the risk of pregnancy complications. This combination represents a safe and effective adjuvant treatment strategy.**
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KEYWORDS

Endometriosis, infertility, platelet-rich plasma (PRP), laparoscopic surgery, ovarian function, pregnancy outcomes

INTRODUCTION

Endometriosis (EMT) is a condition characterized by the growth of endometrial tissue outside the uterine cavity [1]. Early symptoms of EMT are often nonspecific and may include irregular vaginal bleeding, lower

abdominal pain, and dysmenorrhea [2]. The exact etiology of EMT remains unclear, but one widely accepted theory suggests that microstructural alterations in the endometrium allow endometrial cells to enter the pelvic cavity or migrate via the bloodstream to ectopic sites [3]. Infertility affects 40 - 50% of women with EMT, likely resulting from extensive adhesions involving pelvic organs and tissues that impair ovum release, as well as disrupted tubal motility due to adhesions, ultimately leading to infertility [4].

The internationally recognized gold standard for the diagnosis and treatment of EMT-associated infertility is laparoscopic surgery [5]. However, this approach has limitations. EMT exhibits features such as implantation, infiltration, and distant metastasis. During surgery, cysts may rupture, and complete removal of concealed or deeply infiltrating lesions remains challenging [6]. Additionally, since estrogen promotes endometrial proliferation, there is a risk of disease recurrence after surgery, which may adversely affect natural conception [7]. Platelet-rich plasma (PRP) is an autologous blood product obtained through centrifugation, containing a high concentration of platelets - approximately 4 to 8 times that of normal plasma. It is rich in growth factors and cytokines that promote cell proliferation and tissue repair. PRP is widely used in hematology, plastic surgery, orthopedics, and pain management. Recent studies have indicated its potential value in reproductive medicine, particularly in enhancing endometrial regeneration. Evidence suggests that intrauterine perfusion of autologous PRP can improve endometrial thickness. A retrospective study reported significantly increased endometrial thickness and improved clinical pregnancy rates following PRP treatment [8,9]. Melo et al. demonstrated that intraovarian injection of autologous PRP led to significant improvements in follicle-stimulating hormone (FSH), anti-Müllerian hormone (AMH), and antral follicle count levels [10]. Similarly, Sfakianoudis et al. observed enhanced hormonal profiles, ovarian reserve markers, and outcomes in intracytoplasmic sperm injection cycles after PRP injection into both ovaries, resulting in both natural and IVF-conceived pregnancies [11]. However, current research on EMT predominantly focuses on surgical treatment alone or prognostic evaluation [12], with limited studies investigating the combined effect of laparoscopy with intrauterine PRP perfusion and ovarian injection in patients with EMT-related infertility.

This study aimed to evaluate the effects of combining laparoscopic surgery with intrauterine PRP perfusion and ovarian injection on endometrial receptivity, ovarian function, and pregnancy outcomes in infertile patients with EMT, thereby providing new therapeutic strategies and theoretical evidence for clinical practice.

MATERIALS AND METHODS

Study subjects

A total of 60 patients with EMT complicated by infertility who were admitted to our hospital from June 2023 through March 2024 were selected as study subjects. Based on the treatment option chosen by the patients, they were divided into three groups: Group A (no PRP application), Group B (intrauterine perfusion of PRP only), and Group C (intrauterine perfusion of PRP combined with injection into the affected ovary).

Inclusion criteria: 1) Patients were women of reproductive age between 20 and 40 years; 2) patients met the diagnostic criteria for EMT and infertility as outlined in the Diagnosis and Treatment Guidelines for Endometriosis and the Diagnostic Guidelines for Infertility; 3) patients were clinically and pathologically diagnosed with EMT accompanied by infertility; 4) patients had infertility duration of more than one year but not exceeding three years; 5) patients had fertility desires; 6) patients demonstrated good treatment compliance; 7) patients had partners with normal semen analysis without functional or organic abnormalities; and 8) patients agreed to attempt conception for two years post-surgery. All patients underwent laparoscopic surgical treatment.

Exclusion criteria: 1) Patients with a previous history of EMT surgery; 2) patients complicated with malignant tumors; 3) patients complicated with adenomyosis or pelvic inflammatory disease; 4) patients with a history of pelvic or abdominal surgery; 5) patients with allergies to the drugs used in this study; 6) patients with other causes of infertility (e.g. abnormal factors related to the partner, uterine, cervical, or vaginal abnormalities); 7) patients with cervical factors such as cervicitis, abnormal cervical mucus secretion, or cervical fibroids; 8) patients with ovulatory disorders; 9) patients with severe dysfunction or failure of vital organs such as the heart, lungs, liver, or kidneys; 10) patients with other autoimmune or connective tissue diseases; and 11) patients with endocrine diseases including hyperthyroidism, hypothyroidism, polycystic ovary syndrome, hyperprolactinemia, amenorrhea, or premature ovarian failure.

All patients and their families were fully informed of the study and voluntarily signed informed consent forms. The study was approved by the Institutional Ethics Committee of Putian 95th Hospital.

Methods

Laparoscopic surgery (Group A)

Patients underwent laparoscopic surgery only and were advised to attempt conception as soon as possible after the procedure.

Laparoscopic surgery combined with intrauterine PRP perfusion (Group B)

PRP was prepared via centrifugation. Venous blood was collected from the patients preoperatively, after the first postoperative menstrual cycle, and after the second postoperative menstrual cycle to obtain PRP. The Roya-

gen kit (cat. no.: 312569, Arya Mabna Tashkis Co., Iran) was used for PRP preparation according to the manufacturer's instructions. A 16 G needle connected to a 5 mL syringe was inserted into the tube and advanced to the leukocyte layer. By rotating the needle tip, the entire PRP fraction was collected. For intrauterine PRP perfusion, a disposable hysterography catheter was gently inserted into the uterine cavity until the tip was located 0.5 cm from the uterine fundus. The PRP was then slowly injected into the uterine cavity. After the procedure, patients were instructed to remain supine for 5 minutes. Intrauterine PRP perfusion was performed once after the first postoperative menstrual cycle and once after the second postoperative menstrual cycle.

Laparoscopic surgery combined with intrauterine perfusion and ovarian injection of PRP (Group C)

Venous blood was drawn from the patients to prepare PRP. Intrauterine PRP perfusion was performed once after the first postoperative menstrual cycle and once after the second postoperative menstrual cycle. PRP ovarian injection was administered during the laparoscopic procedure after the removal of endometrial lesions. Approximately 2 mL of autologous PRP was injected into the cortex of both ovaries using a 35 cm 17G single-lumen needle. Color Doppler ultrasound [DW-F3 (DW-C80), China] was employed during the injection to avoid injury to major blood vessels. Laboratory tests and transvaginal ultrasound were performed during the second menstrual cycle after PRP injection. Patients subsequently received another injection using the same method and dosage. If ovarian cysts were detected during this process and confirmed again in the following menstrual cycle, low-dose estrogen (LD, OVOCEPT-LD, Abouraihan Pharma. Co., Iran) tablets were administered for one month.

Observation indicators and relevant criteria

Baseline data including age at surgery, body mass index (BMI), revised American Fertility Society classification (r-AFS) stage, type, and duration of infertility were collected from all patients.

Efficacy evaluation criteria

Markedly effective: Significant improvement in clinical symptoms and signs, absence of pelvic masses, and no positive physical signs. Effective: Moderate improvement in clinical symptoms and signs, with no significant pelvic masses or positive physical signs. Ineffective: No improvement or worsening of clinical symptoms, with persistent significant masses and positive physical signs. The clinical effective rate was calculated as: (number of markedly effective cases + number of effective cases)/total number of cases × 100%.

Evaluation of ovarian function

Endometrial receptivity

Endometrial thickness was measured via ultrasound during the ovulation period before and after surgery by an experienced sonographer. Measurements were taken three times at the thickest point along the uterine longitudinal axis, and the average value was recorded. Endometrial ultrasound patterns were classified into types A, B, or C according to the criteria established by Gonen et al. [13]. Type A: Triple-line pattern, with hyperechoic outer lines and central midline, and a hypoechoic area between them. Type B: Uniform intermediate echogenicity with a partially visible midline. Type C: Homogeneous hyperechogenicity without a visible midline. Types A and B were classified as linear endometrium, while type C was considered non-linear. Examinations were performed using a Philips IE33 color Doppler ultrasound system (Philips, Netherlands).

Measurement of serum biomarkers

Venous blood samples (5 mL) were collected from all patients after an overnight fast during the follicular phase, both preoperatively and 3 months postoperatively. Samples were left at room temperature for 2 hours, followed by centrifugation at 3,000 r/minute for 15 minutes to separate the serum. The supernatant was collected and stored at -80 °C until analysis. Serum levels of luteinizing hormone (LH), FSH, and estradiol (E2) were measured using electrochemiluminescence immunoassays performed on an automated biochemical analyzer (AU5800, Health Biomed Co., Ltd., China). Serum AMH levels were quantified using an enzyme-linked immunosorbent assay kit (Diagnostic Systems Laboratories, USA), strictly following the manufacturer's instructions.

Pregnancy outcomes

During the 1-year follow-up period, the clinical pregnancy rate within the planned postoperative period, pregnancy status, live birth rate, and adverse pregnancy outcomes were recorded.

The clinical pregnancy rate within the planned period was defined as the proportion of patients who achieved pregnancy during the 1-year follow-up among the total number of patients. Natural pregnancy success was recorded based on the following criteria: conception without assisted reproductive technology, confirmed by transvaginal ultrasound showing an intrauterine gestational sac, elevated serum β-hCG levels, and detection of fetal cardiac activity. Biochemical pregnancies and embryonic arrest were excluded. Patients were followed for 1 year after treatment to document pregnancy status, and the natural pregnancy success rate was calculated. The number of deliveries resulting in live births was recorded, and the live birth rate was calculated as the number of deliveries with live births divided by the number of clinically pregnant patients.

Adverse pregnancy outcomes were analyzed, including preterm birth, miscarriage, postpartum hemorrhage, and fetal asphyxia. Preterm birth was defined as delivery between 28 and 37 weeks of gestation. Miscarriage was defined as loss of a clinical intrauterine pregnancy before 12 weeks. Postpartum hemorrhage was defined as blood loss ≥ 500 mL within 24 hours after vaginal delivery, or ≥ 1,000 mL after cesarean section. The Apgar

Table 1. Comparison of baseline characteristics among the three groups of patients.

Variables	Group A (n = 20)	Group B (n = 20)	Group C (n = 20)	p-value
Age	27.51 ± 1.19	27.50 ± 1.11	27.38 ± 0.92	0.92
BMI (kg/m^2)	23.15 ± 2.18	22.83 ± 2.00	22.79 ± 2.38	0.85
r-AFS stage				0.82
I - II	9 (45%)	8 (40%)	10 (50%)	
III - IV	11 (55%)	12 (60%)	10 (50%)	
Infertility type				0.79
Primary	14 (70%)	13 (65%)	15 (75%)	
Secondary	6 (30%)	7 (35%)	5 (25%)	
Infertility duration (years)	2.14 ± 0.59	1.99 ± 0.57	2.27 ± 0.61	0.32

Normally distributed continuous data are presented as mean ± standard deviation and were compared using the one-way ANOVA test. Categorical data are expressed as number (n) and percentages (%) and were compared using the chi-squared test. $p < 0.05$ was considered statistically significant. Group A: Treated with laparoscopic surgery only, Group B: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine PRP infusion, Group C: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine infusion and ovarian injection of PRP, BMI: body mass index, r-AFS: Revised American Fertility Society classification.

Table 2. Comparison of treatment efficacy among the three groups.

Group	Markedly effective	Effective	Ineffective	Total effectiveness
Group A	7 (35%)	5 (25%)	8 (40%)	12 (60%)
Group B	13 (65%)	4 (20%)	3 (15%)	17 (85%)
Group C	16 (80%)	3 (15%)	1 (5%)	19 (95%)
adj. $p_{\text{Group A/Group B}}$				0.12
adj. $p_{\text{Group A/Group C}}$				0.01
adj. $p_{\text{Group B/Group C}}$				0.61
p-value				0.04

Categorical data are presented as n (%). Pearson´s chi-squared test was used for overall difference analysis. When the minimum theoretical frequency was less than 5, Fisher's exact test was employed for difference analysis. If the test results showed statistically significant differences, post hoc comparisons were further conducted using the Bonferroni method. A corrected p-value < 0.05 was considered statistically significant. Group A: Treated with hysteroscopic and laparoscopic surgery, Group B: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine PRP infusion, Group C: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine infusion and ovarian injection of PRP.

score at 5 minutes after birth was recorded to assess neonatal asphyxia. The Apgar score evaluates muscle tone, pulse, respiration, response to stimulation, and skin color, with a maximum score of 10. A score of 7 - 10 was considered normal, 4 - 6 indicating mild asphyxia, and < 4 indicating severe asphyxia. Neonatal asphyxia was defined as a 5-minute Apgar score < 7 with failure to establish effective spontaneous breathing. The neonatal asphyxia rate was calculated accordingly.

Pregnancy complications

Postoperative pregnancy complications primarily included gestational diabetes mellitus, gestational hypertension, preeclampsia, intrahepatic cholestasis of pregnancy, and placenta previa. The occurrence of these complications was recorded. The incidence rate of postoperative pregnancy complications was calculated as the number of patients who developed pregnancy-related complications divided by the total number of pregnant patients.

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences 22.0. The normality of data was assessed using the Shapiro-Wilk test. Continuous data were expressed as mean ± standard deviation

Table 3. Comparison of pregnancy complications among the three groups.

Complication	Group A (n = 20)	Group B (n = 20)	Group C (n = 20)	p-value
Gestational diabetes	4 (20%)	2 (10%)	1 (5%)	0.48
Gestational hypertension	4 (20%)	3 (15%)	2 (10%)	0.90
Preeclampsia	3 (15%)	1 (5%)	1 (5%)	0.60
Intrahepatic cholestasis of pregnancy	3 (15%)	2 (10%)	1 (5%)	0.86
Placenta previa	2 (10%)	0 (0%)	0 (0%)	0.32

Categorical data are presented as n (%). Pearson´s chi-squared test was used for overall difference analysis. When the minimum theoretical frequency was less than 5, Fisher's exact test was employed for difference analysis. If the test results showed statistically significant differences, post hoc comparisons were further conducted using the Bonferroni method. A corrected p-value < 0.05 was considered statistically significant. Group A: Treated with hysteroscopic and laparoscopic surgery, Group B: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine PRP infusion, Group C: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine infusion and ovarian injection of PRP.

Table 4. Comparison of pregnancy outcome indicators among the three groups.

Outcome measure	Group A	Group B	Group C	p-value	p'-value
Clinical pregnancy rate	7 (35%)	10 (50%)	15 (75%)	0.04	adj. $p_{\text{Group A/Group B}}$ = 0.52
					adj. $p_{\text{Group A/Group C}}$ = 0.03
					adj. $p_{\text{Group B/Group C}}$ = 0.19
Natural pregnancy success rate	3 (15%)	5 (25%)	12 (60%)	0.01	adj. $p_{\text{Group A/Group B}}$ = 0.69
					adj. $p_{\text{Group A/Group C}}$ = 0.01
					adj. $p_{\text{Group B/Group C}}$ = 0.05
Preterm birth	3 (15%)	1 (5%)	3 (15%)	0.68	-
Miscarriage	2 (10%)	3 (15%)	2 (10%)	1	
Postpartum hemorrhage	1 (5%)	2 (10%)	1 (5%)	1	
Fetal distress	0 (0%)	1 (5%)	0 (0%)	1	
Take-home baby rate	5 (25%)	7 (35%)	13 (65%)	0.01	adj. $p_{\text{Group A/Group B}}$ = 0.73
					adj. $p_{\text{Group A/Group C}}$ = 0.01
					adj. $p_{\text{Group B/Group C}}$ = 0.06

Categorical data are presented as n (%). Pearson´s chi-squared test was used for overall difference analysis. When the minimum theoretical frequency was less than 5, Fisher's exact test was employed for difference analysis. If the test results showed statistically significant differences, post hoc comparisons were further conducted using the Bonferroni method. A corrected p-value < 0.05 was considered statistically significant. Group A: Treated with hysteroscopic and laparoscopic surgery, Group B: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine PRP infusion, Group C: Treated with hysteroscopic and laparoscopic surgery combined with intrauterine infusion and ovarian injection of PRP.

or median and interquartile range, depending on parametric or nonparametric distribution. For comparisons of baseline characteristics among groups, one-way analysis of variance was used for normally distributed continuous variables with homogeneity of variances. Pearson´s chi-squared test was applied for overall group differences in categorical data. If the minimum expected frequency was less than 5, Fisher's exact test was used instead. When overall tests indicated statistically significant differences ($p < 0.05$), multiple comparisons for continuous variables were conducted using Tukey's HSD test, while categorical variables were compared pairwise with Bonferroni correction. A significance level of 0.05 was used for all statistical tests.

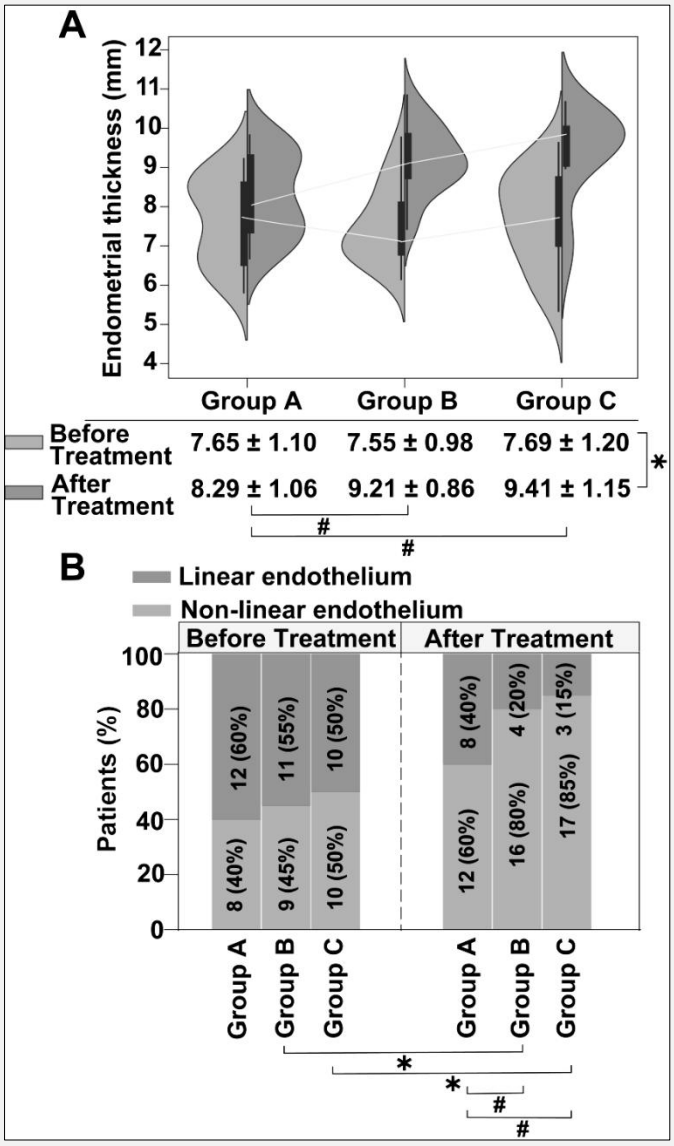

Figure 1. Comparison of endometrial thickness and ultrasonographic morphology before and after surgery in the three groups.

*** $p < 0.05$ indicates a statistically significant difference in intra-group comparisons before and after treatment, $^{\#}p < 0.05$ indicates a statistically significant difference in inter-group comparisons.**
A: Half-violin plots showing changes in endometrial thickness during the ovulation period before and after surgery in the three groups.
B: Stacked bar charts illustrating the composition of endometrial ultrasonographic patterns (Type A, B, and C) before and after surgery in the three groups.

RESULTS

Baseline patient characteristics

A total of 60 patients with EMT and infertility were included in this study and divided into Group A, Group B, and Group C according to the surgical approach. No statistically significant differences were observed among the three groups in terms of age, BMI, r-AFS stage, type of infertility, or duration of infertility (all $p > 0.05$), indicating comparability (Table 1).

Comparison of clinical efficacy among the three groups

Regarding therapeutic efficacy, Group C showed the highest total effective rate (95%), which was significantly higher than that of Group A (60%) (adjusted p =

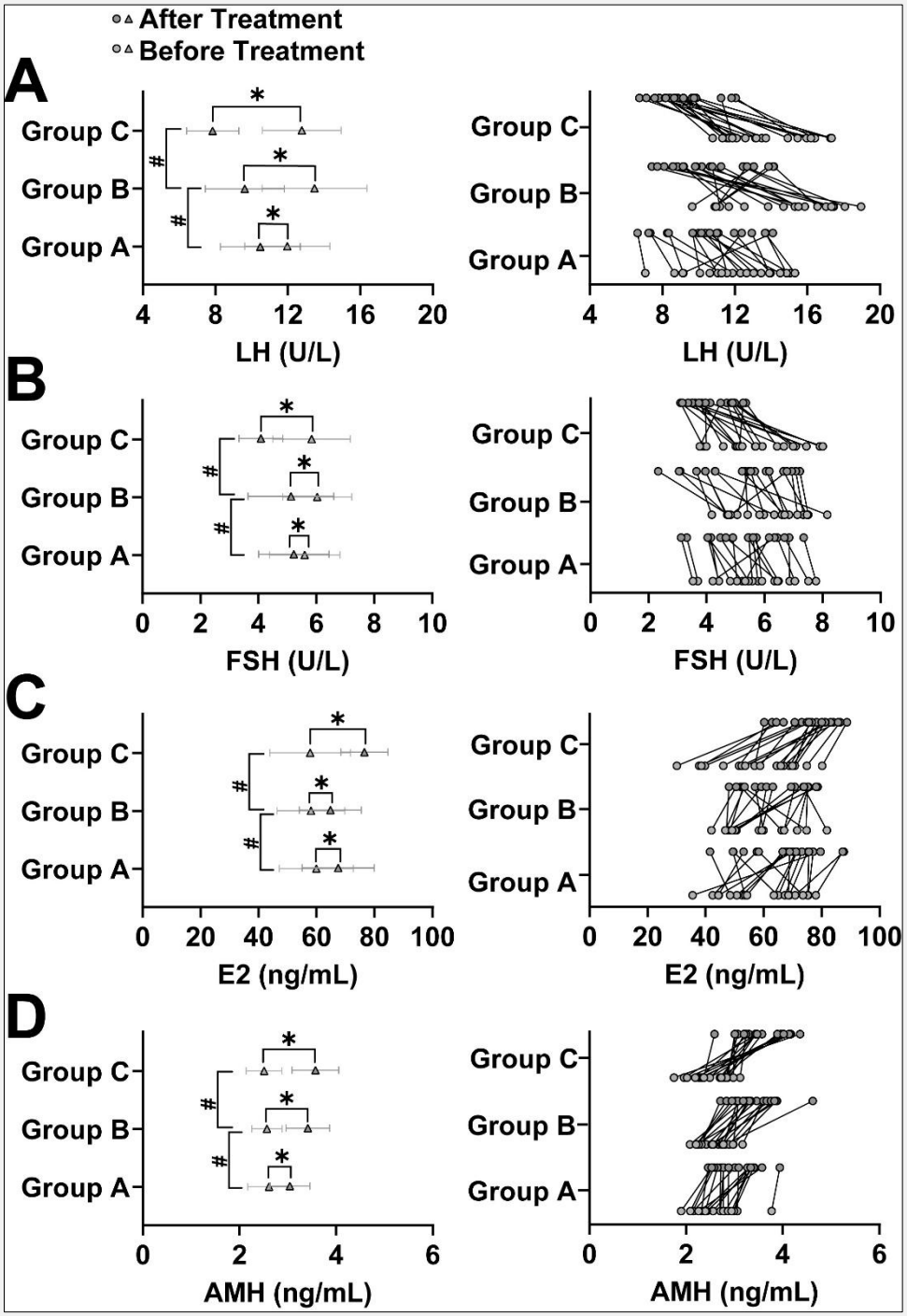

Figure 2. Comparison of serum markers of ovarian function before and after surgery in the three groups.

*** $p < 0.05$ indicates a statistically significant difference in intra-group comparisons before and after treatment, $^{\#}p < 0.05$ indicates a statistically significant difference in inter-group comparisons.**
A - D: Trends in serum levels of LH, FSH, E2, and AMH before and after surgery, respectively.

0.01). The total effective rate in Group B was 85%, which was higher than that in Group A but did not reach statistical significance (adjusted p = 0.12). No significant difference in efficacy was found between Group B and Group C (adjusted p = 0.61). The overall comparison among the three groups showed a significant difference (p = 0.04) (Table 2).

Comparison of ovarian function among the three groups

As shown in Figure 1A, endometrial thickness significantly increased postoperatively in all three groups compared to preoperative values ($p < 0.05$). Postoperative endometrial thickness was significantly greater in Group B (9.21 ± 0.86 mm) and Group C (9.41 ± 1.15 mm) than in Group A (8.29 ± 1.06 mm), with the most pronounced improvement observed in Group C. Endometrial morphology classification revealed that the proportion of linear endometrium in Group C increased significantly from 40% preoperatively to 85% postoperatively, which was higher than that in Group A (60%) and Group B (80%) (Figure 1B). Regarding serum markers, LH and FSH levels decreased postoperatively in all three groups, while E2 and AMH levels increased compared to preoperative values. Notably, postoperative LH and FSH levels in Group C were significantly lower than those in Groups A and B ($p < 0.05$), while E2 and AMH levels were significantly higher ($p < 0.05$). See Figure 2A - D.

Incidence of pregnancy complications among the three groups

No significant differences were observed among the three groups in the incidence of pregnancy complications, including gestational diabetes mellitus, gestational hypertension, preeclampsia, intrahepatic cholestasis of pregnancy, and placenta previa ($p > 0.05$). See Table 3.

Comparison of pregnancy outcomes among the three groups

Analysis of pregnancy outcomes revealed statistically significant differences among the groups in clinical pregnancy rate, natural pregnancy success rate, and live birth rate ($p < 0.05$), while no significant differences were found in the incidence of preterm birth, miscarriage, postpartum hemorrhage, or fetal asphyxia ($p > 0.05$). Post hoc analysis using Bonferroni correction showed that Group C had significantly higher clinical pregnancy rate, natural pregnancy success rate, and live birth rate compared to Group A. See Table 4.

DISCUSSION

EMT is a common condition affecting women of reproductive age, characterized by the presence of endometrial tissue outside the uterine cavity. These ectopic lesions can occur throughout the body, often with insidious onset and invasive behavior, leading to infertility, pelvic adhesions, and chronic pain [14]. Severe tubal obstruction, adhesions, or extensive pelvic involvement in EMT patients often result in comorbid infertility [15]. With continuous advances in laparoscopic techniques, clinical management of EMT has shifted from open surgery and medication toward minimally invasive conservative surgery, with significantly improved outcomes. Studies have shown that laparoscopic excision can markedly increase postoperative pregnancy rates in patients with stage I-II EMT and infertility [16]. However, due to the invasive, metastatic, and recurrent nature of EMT, complete removal of deeply infiltrating lesions remains challenging in stage III or higher patients, often leaving microscopic residues that increase recurrence risk. This study compared three treatment strategies - laparoscopic surgery alone, laparoscopy combined with intrauterine PRP perfusion, and laparoscopy combined with both intrauterine PRP perfusion and ovarian PRP injection - and demonstrated the significant advantages of combined PRP therapy in improving endometrial receptivity, enhancing ovarian function, and increasing pregnancy rates, providing important insights for clinical management of infertility associated with EMT.

Infertile patients with EMT often present with severe disease and dense adhesions, making complete resection of deep, atypical, or microscopic lesions difficult via laparoscopy alone. Moreover, as ectopic endometrial tissue is hormone-dependent, postoperative recurrence is common. Adjunctive medical therapy has thus become a standard approach. LH stimulates estrogen secretion, promotes follicular maturation and rupture, and facilitates corpus luteum formation and progesterone production [17]. FSH reflects ovarian reserve and, in synergy with estrogen during the late follicular phase, induces LH receptor expression in granulosa cells to prepare for ovulation [18]. E2, a steroid sex hormone, promotes endometrial proliferation and the development of secondary sexual characteristics [18]. In this study, Group C exhibited significantly lower FSH and LH levels and higher E2 and AMH levels compared to Groups A and B, indicating improved ovarian reserve. AMH serves as a reliable biomarker for ovarian reserve and female fertility potential [19]. EMT-related ovarian lesions can disrupt normal folliculogenesis and reduce AMH production, thereby diminishing ovarian reserve. Autologous PRP injection into the ovaries has been shown to significantly improve ovarian reserve parameters, oocyte yield, and embryo quality in patients with poor ovarian response. A single injection was as effective as double injections, although the increase in AMH reached statistical significance only after two injections [20]. Two mechanisms may explain PRP-induced follicular development: first, PRP may reactivate dormant follicles (approximately 1,000 remain in menopausal ovaries), improving hormonal profiles and estrogen-deficiency symptoms in perimenopausal women [21]; second, growth factors in PRP may interact with ovarian stem cells to promote primordial follicle activation and

subsequent antral follicle development, though this mechanism remains controversial [22]. Additionally, endometrial thickness and the proportion of linear endometrium were higher in Group C than in Groups A and B, indicating improved endometrial receptivity - a critical factor for successful embryo implantation. Optimal receptivity requires adequate thickness, morphological integrity, and sufficient blood supply, all of which enhance implantation potential and pregnancy rates.

No significant differences were observed among the three groups in the incidence of gestational complications, including diabetes, hypertension, preeclampsia, intrahepatic cholestasis, or placenta previa ($p > 0.05$), suggesting that the surgical approach did not substantially affect complication risk. However, significant differences were observed in pregnancy outcomes ($p < 0.05$). After Bonferroni correction, Group C showed significantly higher rates of clinical pregnancy, natural pregnancy, and live birth compared to Group A, underscoring the value of the combined PRP approach in improving outcomes without increasing complications. These findings are consistent with studies by Melo et al. [10] and Nazari et al. [23], who reported significant improvements in pregnancy rates following intraovarian PRP injection in patients with diminished ovarian reserve.

Several challenges remain in optimizing PRP therapy for EMT-related infertility. Variability in PRP preparation, activation methods, injection techniques, dosage, and postoperative protocols complicates standardization. Some studies suggest that chemical activation maximizes growth factor release [24], while others argue that mechanical activation during centrifugation or natural activation by tissue collagen is sufficient [25]. The duration of PRP effects, optimal injection frequency, and timing also require further investigation. As most growth factors are short-acting, repeated injections may be necessary to sustain follicular activation. Since recruitment of preantral to antral follicles takes approximately three months, the maximal effect of PRP is likely observed around three months post-injection [26]. However, the ideal interval between injections remains unclear. Additionally, patients with higher baseline platelet counts may respond better to PRP, suggesting that platelet concentration should be evaluated before treatment, and concentration adjusted if counts are below 250,000/μL [27]. Thus, PRP administration should be individualized based on patient-specific factors.

This study has several limitations. The relatively small sample size of 60 patients divided into three groups may limit statistical power to detect subtle differences. The underlying molecular mechanisms - such as changes in inflammatory factors, oxidative stress, or the cellular microenvironment - were not explored. PRP dosage was not standardized due to the need for individualized adjustment based on lesion size, ovarian volume, endometrial thickness, and body weight, which may affect reproducibility. Reasons for treatment failure in non-pregnant patients, such as re-adhesion or ovulation disorders, were not investigated. Future large-scale, prospective, randomized controlled trials are needed to validate these findings, evaluate long-term impacts on live birth rates, elucidate molecular mechanisms, and refine protocols regarding injection timing, frequency, and dosage.

In conclusion, the combination of intrauterine PRP perfusion and ovarian PRP injection significantly enhances clinical efficacy in infertile patients with EMT by improving endometrial receptivity, ovarian reserve, and clinical pregnancy rates. As a safe and effective biological treatment, combined PRP therapy offers a promising alternative for patients with EMT-related infertility.

Declaration of Generative AI in Scientific Writing:
The authors declare that no generative AI was used in the writing of this manuscript.

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Availability of Data and Materials:
The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Ethical Approval Statement:
The present study was approved by the Ethics Committee of Putian 95th Hospital, and written informed consent was provided by all patients prior to the study start. All procedures were performed in accordance with the ethical standards of the Institutional Review Board and the Declaration of Helsinki and its later amendments or comparable ethical standards.

Declaration of Interest:
The authors have no conflicts of interest to declare.

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