

Impact of Short-Term Estrogen Therapy on Endometrial Polyps Recurrence in Women with Intrauterine Adhesion and Endometrial Polyps: A Retrospective Cohort Study

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Objective: To investigate whether short-term postoperative estrogen-related therapy is associated with recurrence of intrauterine adhesions (IUA), endometrial polyps (EPs), and pregnancy outcomes in women with concomitant IUA and EPs.

Methods: This single-center retrospective cohort study included women (18–45 years) diagnosed with both IUA and EPs who underwent concurrent hysteroscopic transcervical resection of adhesions (TCRA) and polypectomy from January 2019 to June 2024. Patients were grouped by postoperative regimen: (1) estradiol–dydrogesterone sequential therapy (Femoston; estradiol 2 mg/dydrogesterone 10 mg; 2–3 months), (2) combined oral contraceptive (Yaz; ethinylestradiol 0.02 mg/drospirenone 3 mg; 3 months), or (3) no hormonal therapy. Recurrence was confirmed by transvaginal ultrasound and/or hysteroscopy.

Results: A total of 166 women were included (sequential therapy, n=47; COC, n=32; no hormone, n=87). Baseline polyp multiplicity differed among groups (P=0.003), with a higher proportion of multiple EPs in the COC group. Postoperative IUD/balloon placement also differed among groups (P=0.012). Overall recurrence rates were 6.6% for IUA and 4.8% for EPs. No statistically significant differences were observed among groups in postoperative menstrual changes, recurrence rates, time to recurrence, or pregnancy outcomes (all P>0.05). Follow-up duration did not differ significantly among groups.

Conclusion: In this retrospective cohort, no statistically significant differences were observed among short-term sequential estrogen–progestin therapy, COC use, and no hormonal therapy with respect to IUA recurrence, EP recurrence, or pregnancy outcomes. Short-term estradiol–dydrogesterone therapy was not associated with increased EP recurrence in women with IUA and a single EP. These findings are observational and should be confirmed in prospective studies.

Keywords: intrauterine adhesions, endometrial polyps, estrogen, recurrence, pregnancy outcomes

Introduction

Intrauterine adhesions (IUA) and endometrial polyps (EPs) are common intrauterine disorders that can adversely affect reproductive outcomes, including reduced pregnancy rates and increased miscarriage rates.^{1,2} IUA (Asherman's syndrome) often results from injury to the basal endometrium following intrauterine procedures, leading to fibrous tissue formation and partial or complete obliteration of the uterine cavity.^{3,4} Hysteroscopy is considered the gold standard for diagnosis and for evaluating postoperative uterine cavity restoration.

EPs are a common cause of abnormal uterine bleeding and are frequently detected on transvaginal ultrasound, whereas hysteroscopic resection is the definitive treatment.^{5,6} Recurrence rates after polypectomy vary widely,⁷ and recurrence is associated with factors such as polyp multiplicity and polyp size.⁸

Postoperative management after hysteroscopic adhesiolysis aims to prevent re-adhesion and to promote endometrial regeneration. The American Association of Gynecologic Laparoscopists (AAGL) and the European Society of Gynecological Endoscopy (ESGE) recommend cyclic estrogen–progestin therapy after transcervical resection of adhesions (TCRA) to facilitate endometrial repair.⁹ However, estrogen exposure is also implicated in the pathogenesis of EPs, creating a clinical dilemma for women with concomitant IUA and EPs: estrogen may support endometrial healing after adhesiolysis, yet it may theoretically increase the risk of polyp recurrence.

Evidence guiding postoperative hormonal strategies specifically for women with coexisting IUA and EPs remains limited, and postoperative regimens are often individualized in real-world practice. Therefore, we conducted a retrospective cohort study to evaluate whether short-term postoperative estrogen-related therapy is associated with recurrence of IUA and EPs and with pregnancy outcomes in women undergoing concurrent hysteroscopic adhesiolysis and polypectomy.

Materials and Methods

Study Design and Population

This was a single-center retrospective cohort study approved by the Institutional Review Board of Sun Yat-sen Memorial Hospital, Sun Yat-sen University (SYSKY-2025-070-01). Women aged 18–45 years diagnosed with both IUA and EPs who underwent concurrent hysteroscopic TCRA and polypectomy between January 2019 and June 2024 were eligible. Patients with incomplete clinical data or loss to follow-up were excluded. Informed consent was obtained from patients. All procedures involving human participants were performed in accordance with the Declaration of Helsinki.

Treatment Groups and Postoperative Hormonal Regimens

Participants were categorized according to the postoperative hormonal regimen received (non-randomized, real-world practice):

- Group 1 (Sequential therapy): cyclic estradiol–dydrogesterone sequential therapy (Femoston; estradiol 2 mg/dydrogesterone 10 mg) for 2–3 months postoperatively.
- Group 2 (COC group): combined oral contraceptive (Yaz; ethinylestradiol 0.02 mg/drospirenone 3 mg) for 3 months postoperatively.
- Group 3 (No-hormone group): no postoperative hormonal medication.

Regimen selection was based on clinical judgement considering adhesion severity and polyp characteristics; therefore, selection bias and confounding by indication are possible.

Surgical Procedure and Postoperative Management

All surgeries were performed by experienced hysteroscopic surgeons under general anesthesia using a STORZ hysteroscopic system. IUA severity was assessed intraoperatively according to the American Fertility Society (AFS) classification (1988).¹⁰ Adhesiolysis was performed using hysteroscopic scissors or a needle electrode. Polypectomy was performed using a loop electrode until the uterine cavity anatomy was restored.

Immediately after surgery, depending on intraoperative findings, an intrauterine device (IUD) or balloon was placed, sodium hyaluronate gel was applied, or no adjuvant barrier was used. If placed, the IUD/balloon was typically removed at second-look hysteroscopy approximately 2–3 months postoperatively.

Outcome Measures and Follow-Up

Primary outcomes were recurrence of IUA and EPs, confirmed by transvaginal ultrasound and/or hysteroscopy, and time to recurrence. Time to recurrence was defined as the interval from the index surgery date to the first confirmatory

examination date at which recurrence was identified. If recurrence was detected during routine second-look hysteroscopy (typically ~2–3 months postoperatively), that date was used.

Secondary outcomes included patient-reported postoperative menstrual volume change (less/same/more than before) and pregnancy outcomes among women attempting conception during follow-up. Follow-up was conducted through outpatient visits, telephone contact, and ultrasound review. Chronic endometritis was diagnosed histopathologically by the presence of plasma cells in the endometrial stroma.¹¹

Follow-up duration did not differ significantly among groups; detailed follow-up time will be summarized in the final dataset table.

Statistical Analysis

Normality was assessed using the Kolmogorov–Smirnov test. Normally distributed continuous variables are presented as mean ± standard deviation and compared using one-way ANOVA. Non-normally distributed variables are presented as median (interquartile range) and compared using the Kruskal–Wallis *H*-test. Categorical variables are presented as n (%) and compared using the chi-square test or Fisher’s exact test, as appropriate. Statistical analysis was performed using SPSS 25.0 (IBM), with two-sided $P < 0.05$ considered statistically significant.

Results

Participant Selection and Baseline Characteristics

After eligibility assessment, 166 women were included: 47 in the sequential therapy group, 32 in the COC group, and 87 in the no-hormone group (Figure 1). Baseline characteristics and outcomes are presented in Table 1.

The proportion of multiple EPs differed significantly among groups ($P = 0.003$), with a higher proportion in the COC group. Postoperative IUD/balloon placement also differed among groups ($P = 0.012$). Age distribution and IUA severity were comparable among groups (Table 1).

Recurrence and Pregnancy Outcomes

Overall recurrence rates were 6.6% (11/166) for IUA and 4.8% (8/166) for EPs. No statistically significant differences were observed among the three groups in postoperative menstrual volume change, IUA recurrence, EP recurrence, time to recurrence, or pregnancy outcomes (all $P > 0.05$; Table 1).

Among women attempting conception during follow-up ($n = 145$; Group 1 $n = 42$, Group 2 $n = 30$, Group 3 $n = 73$), postoperative pregnancy occurred in 111 women (76.6%). Pregnancy outcomes did not differ significantly among groups (Table 1). Comparisons between women with and without IUA recurrence (Table 2) and between women with and without EP recurrence (Table 3) showed no statistically significant differences in baseline characteristics or pregnancy outcomes; however, recurrence subgroup sizes were small.

Discussion

In this retrospective cohort of women with concomitant IUA and EPs undergoing concurrent hysteroscopic adhesiolysis and polypectomy, we observed no statistically significant differences among short-term postoperative sequential estrogen–progestin therapy (Femoston), COC use (Yaz), and no hormonal therapy with respect to IUA recurrence, EP recurrence, time to recurrence, menstrual changes, or pregnancy outcomes. Notably, short-term estradiol–dydrogesterone therapy was not associated with an increased EP recurrence rate in women with IUA and a single EP.

The pathogenesis of endometrial polyps is often attributed to a local imbalance between estrogen and progesterone, characterized by relative estrogen excess and progesterone deficiency.¹² Given the critical role of steroid hormones and their receptors in polyp development and growth,^{12,13} a theoretical concern exists that postoperative estrogen therapy for IUA could increase the risk of EPs recurrence in patients with both conditions. To date, no prior studies have confirmed that short-term estrogen use elevates this risk. Literature indicates that polyp multiplicity¹⁴ and chronic endometritis^{15,16} are significant risk factors for recurrence. Established strategies to reduce postoperative recurrence in premenopausal patients include levonorgestrel-releasing intrauterine systems (LNG-IUS), COCs, and dydrogesterone.^{17,18}

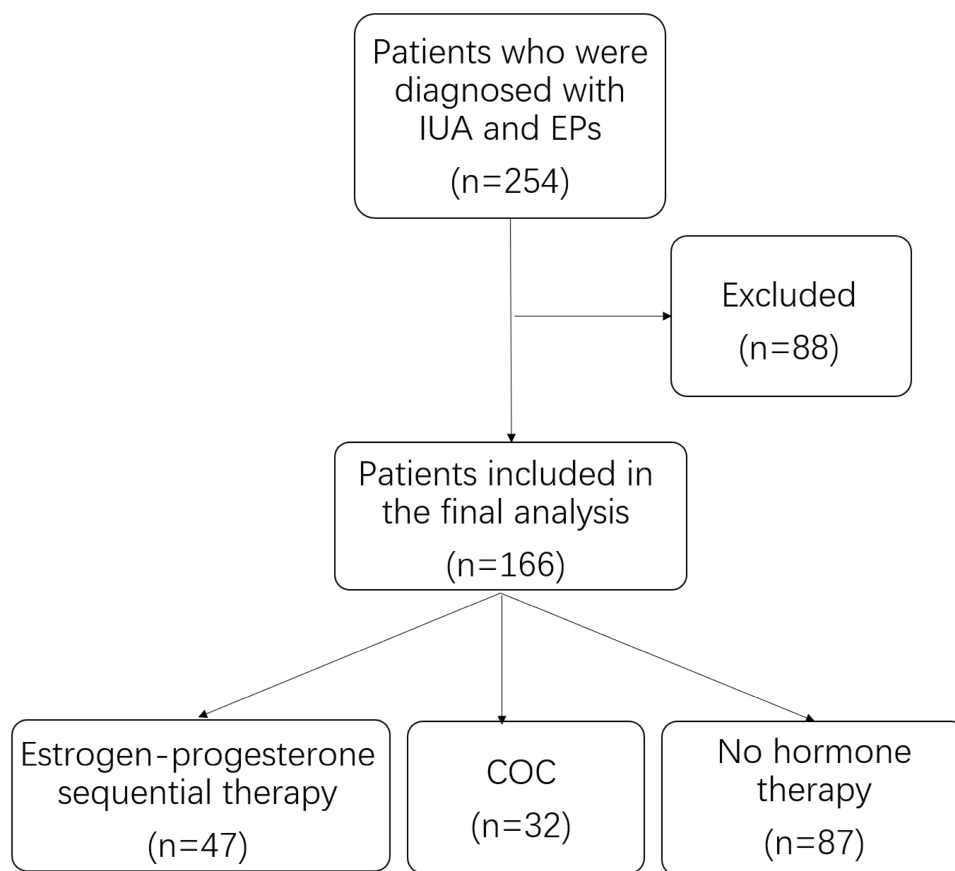


Figure 1 Flow chart of participant selection and group allocation.

Clinically, estrogen therapy is widely used to promote endometrial regeneration after adhesiolysis and is supported by AAGL/ESGE guidance.^{9,19} At the same time, EP development has been linked to estrogen exposure and endometrial proliferation, raising concern regarding potential recurrence in women with EPs.^{20,21} When IUA and EPs coexist, clinicians face a real-world dilemma in balancing endometrial healing needs against a theoretical risk of promoting

Table 1 Comparison of Clinical Characteristics and Pregnancy Outcomes Among the Three Groups

Characteristics	Estrogen-Progestin (N=47)	COC (N=32)	No Hormone Therapy (N=87)	P value
Age (years), mean ± SD	31.94 ± 4.29	33.41 ± 4.39	33.17 ± 5.41	0.125
Severity of intrauterine adhesion, n (%)				0.958
Mild	38 (80.9)	24 (75.0)	68 (78.2)	
Moderate	8 (17.0)	7 (21.9)	17 (19.5)	
Severe	1 (2.1)	1 (3.1)	2 (2.3)	
Number of endometrial polyps, n (%)				0.003**a,c
Single	28 (59.6)	8 (25.0)	50 (57.5)	
Multiple	19 (40.4)	24 (75.0)	37 (42.5)	

(Continued)

Table 1 (Continued).

Characteristics	Estrogen-Progestin (N=47)	COC (N=32)	No Hormone Therapy (N=87)	P value
IUD or balloon placed after surgery, n (%)				0.012 ^{*a,b}
Yes	43 (91.5)	25 (78.1)	60 (69.0)	
No	4 (8.5)	7 (21.9)	27 (31.0)	
Pathological diagnosis of endometritis, n (%)				0.209
Yes	3 (6.4)	7 (21.9)	17 (19.5)	
No	19 (40.4)	8 (25.0)	25 (28.7)	
Unexamined	25 (53.2)	17 (53.1)	45 (51.7)	
Postoperative menstrual volume, n (%)				0.479
Less than before	3 (6.4)	5 (15.6)	9 (10.3)	
Same as before	37 (78.7)	23 (71.9)	71 (81.6)	
More than before	7 (14.9)	4 (12.5)	7 (8.0)	
Recurrence of intrauterine adhesion, n (%)				0.092
Yes	2 (4.3)	5 (15.6)	4 (4.6)	
No	45 (95.7)	27 (84.4)	83 (95.4)	
Time to IUA recurrence (months), median (IQR)	24 (22–25)	13 (6–28)	20 (6–24)	0.333
Recurrence of endometrial polyps, n (%)				0.198
Yes	3 (6.4)	3 (9.4)	2 (2.3)	
No	44 (93.6)	29 (90.6)	85 (97.7)	
Time to EP recurrence (months), median (IQR)	20 (2–37)	14 (2–19)	13 (4–21)	0.665
Attempting conception during follow-up, n (%)	42 (89.4)	30 (93.8)	73 (83.9)	0.247
Postoperative pregnancy[†], n (%)	33/42 (78.6)	27/30 (90.0)	51/73 (69.9)	0.085
Method of pregnancy[†], n (%)				0.228
Natural pregnancy	22/33 (66.7)	13/27 (48.1)	26/51 (51.0)	
IVF-ET	11/33 (33.3)	14/27 (51.9)	25/51 (49.0)	
Pregnancy outcome[‡], n (%)				0.291
Live birth	23/31 (74.2)	15/27 (55.6)	32/46 (69.6)	
Non-live birth	8/31 (25.8)	12/27 (44.4)	14/46 (30.4)	

Notes: [†]Calculated among women who became pregnant. [‡]Calculated among pregnancies with available outcome data (total outcomes available n=104). *P < 0.05; **P < 0.01. ^aP < 0.05 between Group 1 and Group 2; ^bP < 0.05 between Group 1 and Group 3; ^cP < 0.05 between Group 2 and Group 3.

Abbreviations: COC, combined oral contraceptives; EP, endometrial polyp; IQR, interquartile range; IUA, intrauterine adhesions; IUD, intrauterine device; IVF-ET, in vitro fertilization–embryo transfer.

polyp recurrence.¹⁹ Our findings provide observational data suggesting that short-term postoperative estrogen–progestin sequential therapy, as administered in our cohort, was not associated with higher EP recurrence in the subgroup of women with single EPs.

Table 2 Comparison of Clinical Characteristics and Pregnancy Outcomes Between Recurrent and Non-Recurrent IUA

Characteristics	Overall (N=166)	IUA Recurrence (N=11)	No IUA Recurrence (N=155)	P value
Severity of intrauterine adhesion, n (%)				0.335
Mild	130 (78.3)	8 (72.7)	122 (78.7)	
Moderate	32 (19.3)	2 (18.2)	30 (19.4)	
Severe	4 (2.4)	1 (9.1)	3 (1.9)	
IUD or balloon placed after surgery, n (%)				0.700
Yes	128 (77.1)	9 (81.8)	119 (76.8)	
No	38 (22.9)	2 (18.2)	36 (23.2)	
Pathological diagnosis of endometritis, n (%)				1.000
Yes	27 (16.3)	2 (18.2)	25 (16.1)	
No	52 (31.3)	3 (27.3)	49 (31.6)	
Unexamined	87 (52.4)	6 (54.5)	81 (52.3)	
Postoperative menstrual volume, n (%)				0.736
Less than before	17 (10.2)	1 (9.1)	16 (10.3)	
Same as before	131 (78.9)	10 (90.9)	121 (78.1)	
More than before	18 (10.8)	0 (0.0)	18 (11.6)	
Attempting conception during follow-up, n/N (%)	145/166 (87.3)	11/11 (100.0)	134/155 (86.5)	0.369
Postoperative pregnancy[†], n/N (%)	111/145 (76.6)	11/11 (100.0)	100/134 (74.6)	0.060
Pregnancy outcome[‡], n (%)				0.088
Live birth	70/104 (67.3)	2/6 (33.3)	68/98 (69.4)	
Non-live birth	34/104 (32.7)	4/6 (66.7)	30/98 (30.6)	

Notes: [†]Calculated among women attempting conception.[‡]Calculated among pregnancies with available outcome data: 104/111 (93.7%) overall, 6/11 (54.5%) in the recurrence group, and 98/100 (98.0%) in the non-recurrence group.

Abbreviations: IUA, intrauterine adhesions; IUD, intrauterine device.

Table 3 Comparison of Clinical Characteristics and Pregnancy Outcomes Between Recurrent and Non-Recurrent EPs

Characteristics	Overall (N=166)	EP Recurrence (N=8)	No EP Recurrence (N=158)	P value
Severity of intrauterine adhesion, n (%)				1.000
Mild	130 (78.3)	7 (87.5)	123 (77.8)	
Moderate	32 (19.3)	1 (12.5)	31 (19.6)	
Severe	4 (2.4)	0 (0.0)	4 (2.5)	
Number of endometrial polyps, n (%)				0.536
Single	86 (51.8)	5 (62.5)	81 (51.3)	
Multiple	80 (48.2)	3 (37.5)	77 (48.7)	

(Continued)

Table 3 (Continued).

Characteristics	Overall (N=166)	EP Recurrence (N=8)	No EP Recurrence (N=158)	P value
IUD or balloon placed after surgery, n (%)				0.884
Yes	128 (77.1)	6 (75.0)	122 (77.2)	
No	38 (22.9)	2 (25.0)	36 (22.8)	
Pathological diagnosis of endometritis, n (%)				0.435
Yes	27 (16.3)	2 (25.0)	25 (15.8)	
No	52 (31.3)	1 (12.5)	51 (32.3)	
Unexamined	87 (52.4)	5 (62.5)	82 (51.9)	
Attempting conception during follow-up, n/N (%)	145/166 (87.3)	7/8 (87.5)	138/158 (87.3)	1.000
Postoperative pregnancy†, n/N (%)	111/145 (76.6)	6/7 (85.7)	105/138 (76.1)	0.678
Pregnancy outcome‡, n (%)				0.722
Live birth	70/104 (67.3)	3/5 (60.0)	67/99 (67.7)	
Non-live birth	34/104 (32.7)	2/5 (40.0)	32/99 (32.3)	

Notes: †Calculated among women attempting conception. ‡Calculated among pregnancies with available outcome data: 104/111 (93.7%) overall, 5/6 (83.3%) in the recurrence group, and 99/105 (94.3%) in the non-recurrence group.

Abbreviations: EP, endometrial polyp; IUD, intrauterine device.

We also acknowledge that adjuvant barrier measures (IUD/balloon placement and hyaluronate gel) were used in a clinically individualized manner and differed between groups. Because these measures may affect endometrial healing and adhesion reformation, they may confound recurrence comparisons in observational data.

Strengths

This study focuses on an understudied but clinically relevant population—women with concomitant IUA and EPs treated in the same operative setting—and compares commonly used real-world postoperative hormonal strategies. Surgeries were performed by experienced hysteroscopists, and clinically meaningful outcomes included both recurrence and pregnancy-related endpoints.

Limitations

Several limitations should be considered. First, the retrospective single-center design limits generalizability. Second, treatment allocation was non-random and based on clinical judgement, introducing selection bias and confounding by indication (eg, baseline polyp multiplicity and IUD/balloon use differed between groups) Third, the number of recurrence events was small, which may limit statistical power and increase the risk of type II error; therefore, a lack of statistical significance should not be interpreted as evidence of equivalence. Fourth, recurrence assessment was based on real-world practice (ultrasound and/or hysteroscopy), which may introduce heterogeneity in detection. Finally, some follow-up information relied on patient report, which may be subject to recall bias. Prospective studies with larger samples and adjusted analyses are needed to confirm these findings.

Conclusion

In this retrospective cohort, no statistically significant differences were observed among short-term sequential estrogen–progestin therapy (Femoston), COC use (Yaz), and no hormonal therapy in terms of IUA recurrence, EP recurrence, time to recurrence, or pregnancy outcomes. Short-term estradiol–dydrogesterone sequential therapy was not associated with

increased EP recurrence in women with IUA and a single EP. These findings are observational and hypothesis-generating and require confirmation in prospective studies.

Data Sharing Statement

The data supporting the findings of this study are available from the corresponding authors Xiaozhu Zhong and Dongmei Chen upon reasonable request, subject to institutional and ethics approval.

Ethics Approval and Consent to Participate

The study was approved by the Institutional Review Board of Sun Yat-sen Memorial Hospital, Sun Yat-sen University (SYSKY-2025-070-01). Informed consent was obtained from all patients. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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