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Original research

IMPACT OF HYSTEROSCOPY ON REPRODUCTIVE OUTCOMES IN PATIENTS WITH RECURRENT IMPLANTATION FAILURE

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ABSTRACT

Background: *Hysteroscopy is considered the gold standard for diagnosing intrauterine abnormalities and allows simultaneous management. However, its role in improving outcomes in patients with recurrent implantation failure (RIF) remains controversial. This study aimed to describe hysteroscopic findings and to evaluate reproductive outcomes following surgical intervention in these patients.*

Methods: *This prospective study included 41 women with RIF at the Center for Assisted Reproduction, Hue Central Hospital, from March 2025 to March 2026. Diagnostic and operative hysteroscopy was performed during the follicular phase of the menstrual cycle (day 6 - 10). Patients subsequently underwent embryo transfer cycle.*

Results: *The mean age of the study population was 33.6 ± 4.6 years, with an average of 2.2 ± 0.5 previous failed embryo transfers, with most patients having two failed transfers (78.1%). Intrauterine abnormalities were detected in 78.1% of cases. The most common lesions included endometrial polyps (58.5%), chronic endometritis (29.3%), and micropolyps (17.1%), followed by submucosal fibroids, cesarean scar defects, and uterine anomalies. The biochemical, clinical and ongoing pregnancy rate was 61.3%, 51.6%, and 45.2%, respectively. Although pregnancy outcomes were higher after hysteroscopic intervention, the differences were not statistically significant ($p > 0.05$).*

Conclusion: *Hysteroscopy may be a valuable tool for both diagnosis and treatment of intrauterine abnormalities in patients with RIF, with a trend toward improved reproductive outcomes. Larger controlled studies are needed to confirm these findings*

Keywords: *Hysteroscopy; Recurrent Implantation Failure; In Vitro Fertilization.*

I. INTRODUCTION

Recurrent implantation failure is defined as the inability of embryos to implant after multiple embryo transfer cycles, which represents a major challenge in assisted reproductive technology nowadays. In clinical practice, RIF not only leads to treatment failure but also causes significant psychological stress, time burden, and financial costs for infertile couples. Despite substantial advances in IVF/ICSI techniques for improving embryo quality, implantation failure still occurs in approximately 10 - 15% of cases [1].

The definition of RIF remains inconsistent. According to the European Society of Human Reproduction and Embryology (ESHRE), RIF is defined as the failure to achieve clinical pregnancy after repeated transfers of viable embryos, warranting further diagnostic evaluation and targeted interventions [1]. Other authors define RIF based on the number of failed embryo transfer cycles (≥2 cycles) with at least one good-quality embryo and no pregnancy, defined as serum β-hCG < 5 mIU/mL) [2, 3].

Uterine factors, particularly abnormalities in the uterine cavity, are considered important causes of

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RIF. Common abnormalities include endometrial polyps, submucosal fibroids, intrauterine adhesions, uterine malformations, and chronic endometritis. The prevalence of previously undiagnosed uterine abnormalities among patients with RIF ranges from 14% to 51%. Most patients remain asymptomatic until hysteroscopic evaluation is performed [4, 5].

Hysteroscopy is regarded as the gold standard for diagnosing uterine cavity abnormalities because it allows direct visualization of the entire uterine cavity and enables the detection of subtle lesions or non-structural abnormalities that may be missed by other diagnostic methods. In addition, hysteroscopy allows treatment during the same procedure, including polypectomy, submucosal myomectomy, adhesiolysis and endometrial biopsy. Several studies have reported that hysteroscopy detects uterine abnormalities in 30 - 60% of women with RIF, the most common findings including endometrial polyps, chronic endometritis (CE), and mild intrauterine adhesions [3, 6]. Identification and management of these abnormalities are expected to improve endometrial receptivity and enhance the success rate of subsequent assisted reproductive cycles.

Evidence from previous studies suggests that hysteroscopy may provide certain benefits in improving reproductive outcomes among patients with RIF. A meta-analysis demonstrated a higher live birth rate in patients undergoing hysteroscopy compared with those who did not (RR = 1.29; 95% CI: 1.03 - 1.62) [1]. However, another randomized controlled trial reported no statistically significant difference in reproductive outcomes between the two groups when no obvious uterine abnormality was detected beforehand [2]. Moreover, evidence regarding the impact of specific interventions such as polypectomy, submucosal myomectomy, or adhesiolysis on pregnancy or live birth rates in RIF patients remains limited [2].

In Vietnam, studies evaluating the role of hysteroscopy in patients with RIF are still limited. Most available studies mainly describe hysteroscopic findings without evaluating reproductive outcomes following surgical intervention. Therefore, we conducted the study entitled "Impact of Hysteroscopy on Reproductive Outcomes in Patients with Recurrent Implantation Failure" to describe intrauterine abnormalities detected by hysteroscopy in women with RIF and evaluating reproductive outcomes of embryo transfer cycles following surgical intervention.

II. MATERIALS AND METHODS

2.1. Study population

All women undergoing IVF treatment who were diagnosed with RIF and indicated for hysteroscopy at the Center for Assisted Reproduction, Hue Central Hospital during the study period were eligible if they met the inclusion and exclusion criteria.

Inclusion criteria: Female age < 40 years; Diagnosis of RIF (two or more consecutive embryo transfer cycles with at least one good-quality embryo and no pregnancy, defined as serum β-hCG < 5 mIU/mL) [2, 3]; Indication for hysteroscopy; Willingness to participate in the study; Availability of good-quality embryos for transfer after surgical intervention.

Exclusion criteria: Previously diagnosed uterine abnormalities (e.g., complex congenital uterine anomalies, large fibroids distorting the uterine cavity); Contraindications to hysteroscopy (Acute genital tract infection; Current or suspected pregnancy; Uncontrolled severe systemic disease); Incomplete medical records for study purposes; Loss to follow-up after hysteroscopy.

2.2 Study design

Study design: Prospective study.

Study location and duration: Center for Assisted Reproduction - Department of Obstetrics and Gynecology - Hue Central Hospital, from March 2025 to March 2026.

Sample size: Convenience sampling including all patients meeting the inclusion criteria during the study period.

Study Procedures: Patients who met the inclusion and exclusion criteria and provided informed consent were included. Data collected included demographic information, infertility and obstetric history, prior uterine surgery and intrauterine procedures, number of failed embryo transfer cycles, and characteristics of previous embryo transfer cycles.

Diagnostic and operative hysteroscopy was performed during the follicular phase of the menstrual cycle (day 6 - 10). Patients received spinal anesthesia and were placed in the lithotomy position. Cervical dilation was performed using

Hegar dilators. Hysteroscopy was performed using the Karl Storz IMAGE 1 HD H3 Z Camera Head system with a rigid 0° hysteroscope. The uterine cavity was distended with Sorbitol solution at a pressure of 80 mmHg.

The uterine cavity was systematically evaluated including:

- Tubal ostia
- Uterine cornua
- Anterior and posterior uterine walls
- Endometrial morphology

If treatable lesions were detected (e.g., polyps or submucosal fibroids), monopolar electrosurgery was used for resection, and specimens were sent for histopathological examination. Endometrial biopsy was also performed to assess CE and endometrial hyperplasia. Cesarean scar defect was detected during hysteroscopy and defect correction was performed when appropriate.

CE was suspected hysteroscopically based on the hysteroscopic scoring system proposed by Liu et al. (2020) [7]. Histopathological diagnosis of CE was established when ≥ 5 plasma cells per 10 high-power fields were observed [8]. Patients with histologically confirmed CE subsequently received antibiotic therapy according to the institutional protocol before proceeding with the next embryo transfer cycle.

Recording operative details during procedure: volume of sorbitol used, intraoperative complications.

After hysteroscopy, patients proceeded with embryo transfer cycles. Endometrial thickness, number of embryos transferred, embryo quality, and reproductive outcomes, including pregnancy rate, implantation rate, clinical pregnancy rate, and ongoing pregnancy rate were recorded.

2.3. Statistical analysis

Data were analyzed using SPSS version 20.0 and Microsoft Excel. The normality of continuous variables was assessed using the Kolmogorov - Smirnov test. Normally distributed variables were presented as mean ± standard deviation (SD), whereas non-normally distributed variables were expressed as median and interquartile range (IQR). Categorical variables were presented as frequency and percentage. The Chi-square test or Fisher's exact test, was used to compare categorical variables between groups when appropriate. A p value < 0.05 was considered statistically significant.

2.4. Ethics statement

The study was approved by the Ethics Committee in Biomedical Research at Hue Central Hospital. All participants who agreed to take part in the study provided written informed consent prior to enrollment.

III. RESULTS

The mean age of the study participants was 33.6 ± 4.6 years, with a nearly equal distribution between women aged < 35 years and those aged ≥ 35 years. Most patients had a normal BMI, accounting for 58.5%. Primary infertility was more common, representing 63.4% of cases, whereas 36.6% had secondary infertility. The mean duration of infertility was 3.6 ± 3.1 years, the mean number of failed embryo transfer cycles was 2.2 ± 0.5. Most patients had experienced two failed embryo transfers (78.1%), while 21.9% had three or more failed cycles. Concerning prior uterine surgery, 14.6% had a history of cesarean section, and 4.9% had previously undergone myomectomy (Table 1).

Table 1: Baseline characteristics of the study population

Characteristics		**n**	**%**
Age (years)	< 35	20	48.8
	≥ 35	21	51.2
	Mean ± SD	33.6 ± 4.6	
BMI (kg/m^2)	Underweight	6	14.6
	Normal weight	24	58.5
	Overweight	8	19.5

Characteristics		n	%
	Obesity	3	7.3
	Mean ± SD	21.4 ± 2.4	
Type of infertility	Primary infertility	26	63.4
	Secondary infertility	15	36.6
Duration of infertility	< 3 years	20	48.8
	≥ 3 years	21	51.2
	Mean ± SD	3.6 ± 3.1	
Number of failed embryo transfer cycles	2	32	78.1
	> = 3	9	21.9
	Mean ± SD	2.2 ± 0.5	
History of uterine surgery	None	33	80.5
	Cesarean section	6	14.6
	Myomectomy	2	4.9

Among the 41 patients included in the study, 78.1% were found to have intrauterine abnormalities detected by hysteroscopy. Various types of uterine lesions were identified, with endometrial polyps being the most common finding (58.5%), followed by chronic endometritis (29.3%). Combined lesions were observed in 14.6% of cases. Histopathological examination showed that the majority of lesions were endometrial polyps (68.3%), followed by endometritis (26.8%). During the surgical procedures, one case of uterine perforation was recorded, which was managed conservatively. No other complications were observed such as significant bleeding or fluid overload (Table 2).

Table 2: Hysteroscopic findings and intrauterine interventions

Characteristics		n	%
Hysteroscopic findings	Normal	9	21.9
	Abnormal	31	78.1
	Endometrial polyps	24	58.5
	Micropolyps	7	17.01
	Submucosal fibroid	1	2.4
	Cesarean scar defect	2	4.9
	Endometritis	12	29.3
	Uterine malformation	2	4.9
	Multiple combined lesions	6	14.6
Hysteroscopic interventions	Hysteroscopic interventions	30	73.2
	Myomectomy	1	2.4
	Endometrial biopsy	14	34.2

Characteristics		n	%
	Septum resection	2	4.9
	Cesarean scar repair	2	4.9
Histopathological findings	Normal	12	29.3
	Endometrial polyps	28	68.3
	Endometritis	11	26.8
	Uterine fibroid	1	2.4
	Endometrial hyperplasia	0	0.00
Complications after hysteroscopy	None	0	0.00
	Bleeding	1	2.4
	Uterine perforation	0	0.00
	Fluid overload	0	0.00

A total of 31 patients underwent embryo transfer after hysteroscopic intervention. Day-3 embryos were most commonly used (61.3%), followed by day-5 embryos (29.0%). Good- and fair-quality embryos accounted for 54.8% and 45.2%, respectively. The mean endometrial thickness was 9.4 ± 1.1 mm. The βhcg positive, clinical, and ongoing pregnancy rates were 61.3%, 51.6%, and 45.2%, respectively (Table 3).

Table 3: Characteristics of embryo transfer cycles and reproductive outcomes after hysteroscopy (n = 31)

Characteristics		n	%
Characteristics of embryo transfer after hysteroscopy			
Number of embryos transferred	1	3	9.7
	2	28	90.3
Embryo stage	Day 2	1	3.2
	Day 3	19	61.3
	Day 5	9	29.0
	Day 6	2	6.5
Embryo quality	Good-quality	17	54.8
	Fair-quality	14	45.2
Endometrial thickness ($\underline{X}$ ± SD) mm		9.4 ± 1.1	
Reproductive outcomes after hysteroscopy			
Bhcg positive		19	61.3
Clinical pregnancy		16	51.6
Ongoing pregnancy		14	45.2

In patients undergoing hysteroscopic polypectomy, pregnancy, clinical pregnancy, and ongoing pregnancy rates were higher than in those without polyps (66.7% vs. 44.4%, 50.0% vs. 33.3%, and 50.0%

vs. 33.3%, respectively), although differences were not statistically significant (p > 0.05). Similarly, among patients treated for endometritis, pregnancy rates were higher than in those without detected or treated endometritis (44.4% vs. 36.4%), with comparable trends in clinical and ongoing pregnancy rates, but without statistical significance. In cases with combined intrauterine abnormalities, pregnancy outcomes were also higher in patients with detected lesions (50.0% vs. 37.0%), including clinical and ongoing pregnancy rates (both 50.0% vs. 48.2% and 44.4%, respectively), though all differences were not statistically significant (p > 0.05) (Table 4).

Table 4: Association between embryo transfer outcomes and hysteroscopic treatment of intrauterine lesions

Characteristics		Bhcg positive		Clinical pregnancy		Ongoing pregnancy	
Intervention		**n (%)**	**p**	**n (%)**	**p**	**n (%)**	**p**
After endometrial polypectomy	Yes	15 (68.2)	0.253	13 (59.1)	0.252	11 (50.0)	0.456
	No	4 (44.4)		3 (33.3)		3 (33.3)	
After treatment for endometritis	Yes	4 (44.4)	0.704	5 (55.6)	0.704	6 (66.7)	0.456
	No	8 (36.4)		10 (45.5)		11 (50.0)	
Combined lesions	Yes	2 (50.0)	0.63	2 (50.0)	1.00	2 (50.0)	1.00
	No	10 (37.0)		13 (48.2)		12 (44.4)	

IV. DISCUSSION:

The mean age of the study participants was 33.6 ± 4.6 years. The mean duration of infertility was 3.6 ± 3.1 years, and the patients had experienced an average of 2.2 ± 0.5 failed embryo transfer cycles. These characteristics are similar to those reported in studies conducted both domestically and internationally, such as Vũ Thị Ngọc et al. (2023) [9], Walid El Toukhy et al. (2016) [3], and Minzhi Gao et al. (2015) [10]. Advanced maternal age, prolonged infertility duration, and multiple failed embryo transfers indicate that patients with RIF often present with unfavorable prognostic factors, highlighting the need for more in-depth evaluation and appropriate interventions to improve pregnancy and live birth rates.

Hysteroscopic findings revealed a low proportion of normal endometrium, while multiple small polyps represented the predominant pattern, followed by CE and micropolyps. These findings suggest that mild or microscopic endometrial alterations may be common among patients with RIF, although their functional significance remains unclear.

When compared with the existing literature, the distribution of hysteroscopic abnormalities in our study shows both similarities and differences. A meta-analysis by Cao Hanyu et al. (2018) reported that hysteroscopy detected intrauterine abnormalities in approximately 40 - 50% of patients with RIF, with endometrial polyps being the most common finding (about 20 - 30%), followed by intrauterine adhesions and submucosal lesions [11]. Compared with these results, our study observed a relatively higher proportion of multiple small polyps, suggesting that subtle or microscopic lesions may not have been fully recognized in earlier studies that primarily focused on more apparent macroscopic abnormalities.

Similarly, the randomized controlled TROPHY Trial conducted by Walid El Toukhy et al. (2016) [3], which evaluated routine hysteroscopy prior to IVF in patients with previous IVF failure, reported uterine cavity abnormalities in approximately 30% of patients and endometrial polyps is the most common lesion [12]. However, this study did not provide a detailed classification distinguishing solitary polyps from multiple small polyps, which may partly explain the differences in lesion distribution compared with our findings.

Chronic endometritis is a highly heterogeneous condition. The reported prevalence of CE ranges

from 14.1% in the study by Yang Jing et al. and from 3.7% to 67.5% in the systematic review by Andrea Vitagliano et al., depending on diagnostic criteria and sampling methods [13]. Meanwhile, Antonio Cicinelli et al. demonstrated that micropolyps were present in 93% of histologically confirmed CE cases, although these findings are considered suggestive rather than diagnostic, and therefore cannot replace endometrial biopsy [14]. Magdalena Szafarowska et al. emphasized that hysteroscopic findings such as micropolyps and the presence of plasma cells may support the diagnosis of CE and may be associated with reproductive outcomes; however, histopathological confirmation remains necessary before giving treatment decisions [15]. In our study, the discrepancy between hysteroscopic suspicion of CE and histopathological confirmation may be related to the focal distribution of lesions and the limitations of random biopsy sampling.

A notable finding in our study is the predominance of multiple small polyps, a morphological pattern that has not yet been standardized in the context of RIF. Endometrial polyps have been shown to be associated with reduced implantation potential and poorer IVF outcomes [16], whereas chronic endometritis may contribute to the formation or recurrence of polyps [17]. These observations suggest the possible existence of a spectrum of endometrial changes related to localized inflammation and proliferative alterations, although their direct relationship with RIF has not yet been clearly established.

Overall, hysteroscopy and histopathological examination provide complementary but not completely concordant information in the evaluation of the endometrium in patients with RIF. The differences observed among studies such as the meta-analysis by Cao Hanyu (2018), the TROPHY Trial, and our study may reflect heterogeneity in lesion classification, especially the limitation in recognition of subtle abnormalities such as multiple small polyps [11]. Therefore, standardization of hysteroscopic definitions and further prospective studies correlating hysteroscopic findings with reproductive outcomes are necessary to clarify the clinical significance of these observations.

During surgery, most procedures were performed safely, with only one case of uterine perforation occurring at the site of a previous cesarean scar, this complication occurred in a patient with high-risk factors, specifically a history of surgical repair of a cesarean scar defect, with thin myometrium at the scar site identified on preoperative ultrasound. The patient required only postoperative observation, and no additional intervention was necessary. The safety profile of diagnostic and operative hysteroscopy in our study is consistent with the findings reported by Vu Thi Ngoc et al. (2023) [9] and Nguyen Quang Bac et al. (2023) [18], which reported no complications or only one uterine perforation among 262 patients included in their studies.

The pregnancy rate after embryo transfer in our study was 61.3%, with a clinical pregnancy rate of 51.6% and an ongoing pregnancy rate of 45.2%. In studies involving patients with RIF, embryo transfer on day 3 or day 5 after correction of intrauterine abnormalities through hysteroscopy has been associated with clinical pregnancy rates of approximately 35 - 45%, depending on the characteristics of the study population [19].

Our findings suggest that the application of hysteroscopy, including both diagnostic evaluation and therapeutic intervention, is associated with improved reproductive outcomes in patients with RIF during subsequent embryo transfer cycles. The observed benefit appears to arise mainly from the detection and treatment of intrauterine abnormalities, rather than from the diagnostic procedure alone. In subgroup analysis, the β-hCG positivity rate, clinical pregnancy rate, and ongoing pregnancy rate were significantly higher in patients in whom endometrial polyps, chronic endometritis, or combined intrauterine lesions were detected and treated, compared with those in whom no abnormalities were identified.

Table 5: Summary of evidence on hysteroscopy in RIF patients

Study	Year	Design	Population	Sample Size (Intervention vs Control)	Risk of Bias	GRADE	Key Findings (Effect size)
TROPHY Trial [3]	2016	Multicenter RCT	RIF	350 vs 352	Low	High	Live birth: RR = 1.00 (95% CI 0.85-1.18); Clinical pregnancy: RR = 1.02 (95% CI 0.90-1.16), NS
Cao et al [11]	2018	Meta-analysis	RIF (ART)	1,691 (8 studies)	Moderate	Moderate	Clinical pregnancy: RR = 1.46 (95% CI 1.20-1.78); Live birth: not consistently reported
Mao et al. [20]	2019	Meta-analysis	RIF	3,134 (13 studies)	Moderate	Moderate-High	Clinical pregnancy: RR = 1.37 (95% CI 1.18-1.59); Implantation: RR = 1.22 (95% CI 1.05-1.41); Live birth: RR = 1.08 (95% CI 0.92-1.27), NS
Vitale et al. [21]	2023	Meta-analysis (RCTs)	ART (incl. RIF subset)	2,541 (RCTs included)	Moderate	Moderate	Clinical pregnancy: RR = 1.15 (95% CI 1.03-1.28); Live birth: RR = 1.05 (95% CI 0.94-1.17), NS
Pradnyana et al.[22]	2023	Systematic review & Meta-analysis	RIF (ART)	4679 (3 RCTs included)	Moderate	Moderate-High	Clinical pregnancy rate: OR = 1.64 (95% CI 1.32-2.03, $p < 0.001$). Live birth rate: OR = 1.50 (95% CI 1.17-1.92, $p = 0.001$).

When reviewing the literature, studies with stronger levels of evidence evaluating the role of operative hysteroscopy in women with RIF are summarized in Table 5. The multicenter randomized TROPHY Trial demonstrated no statistically significant improvement in the live birth rate when routine hysteroscopy was performed prior to IVF [3]. However, this study mainly assessed hysteroscopy as a diagnostic procedure in an unselected RIF population, with limited therapeutic intervention; therefore, it may not fully reflect the potential benefit of operative hysteroscopy.

In contrast, several recent pooled analyses suggest a favorable trend. Meta-analyses by Cao Hanyu et al. (2018) [11] and Mao Xue et al. (2019) [23] reported improvements in clinical pregnancy rates and implantation rates among patients with RIF. Similarly, Antonio Vitale et al. (2023) and Pradnyana et al (2023) reported an increase in live birth rates, particularly in women with a history of RIF [21, 22]. The discrepancy between these findings and the results of the TROPHY Trial may be explained by heterogeneity in study populations, variations in the definition of RIF, and especially the difference between purely diagnostic hysteroscopy and hysteroscopy combined with therapeutic intervention.

In terms of mechanistic perspective, hysteroscopy may improve reproductive outcomes by enhancing endometrial receptivity. Intrauterine abnormalities such as endometrial polyps, submucosal fibroids, or intrauterine adhesions may impair implantation through mechanical effects, alterations in the endometrial microenvironment, and localized inflammatory responses [1]. Removal of these lesions may restore the structural and functional integrity of the endometrium, thereby improving conditions for embryo implantation during the window of implantation, which is a key determinant of IVF success [24]. In addition, biological evidence suggests that endometrial intervention may trigger a physiological inflammatory response and modulate cytokine expression, thereby enhancing embryo receptivity [25].

The main limitation of this study is the absence of a control group, which reduces the ability to establish a causal relationship between hysteroscopic intervention and reproductive outcomes. The follow - up period was relatively short, and some patients were still continuing their pregnancies at the end of data collection; therefore, live birth outcomes could not be fully assessed. In addition, the single-center design may limit the generalizability of the findings to other populations and assisted reproductive centers. Further well-designed randomized controlled trials are needed to clarify the role of hysteroscopy in improving reproductive outcomes in patients with RIF.

V. CONCLUSION

Hysteroscopy combining diagnostic evaluation and therapeutic intervention has the potential to improve reproductive outcomes in patients with RIF undergoing IVF, mainly through the detection and treatment of intrauterine abnormalities. However, due to the lack of a control group, causal inference should be interpreted with caution. Future randomized controlled trials, clearly distinguishing diagnostic hysteroscopy from operative hysteroscopy, are necessary to determine the true role of this procedure in the management of RIF.

Conflict of interest statement

All authors declare that no conflicts of interest exist regarding the research, authorship, or publication of this article.

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