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ORIGINAL RESEARCH

Platelet Count and Platelet Hematocrit Correlate to the Occurrence and Postoperative Recurrence in Intrauterine Adhesion Patients

Yuhui Wei[1], Suli Kao[2], Mei Chen[3], Xuexue Yin[4]

[1]Department of Obstetrics and Gynecology, The First Hospital of Anhui University of Science & Technology, Huainan, Anhui, 232000, People's Republic of China; [2]Clinical Laboratory, The First Hospital of Anhui University of Science & Technology, Huainan, Anhui, 232000, People's Republic of China; [3]Center for Reproductive Medicine, Jinhua People's Hospital, Jinhua, Zhejiang, 321000, People's Republic of China; [4]Department of Gynecology, Zibo Central Hospital, Zibo, Shandong, 255000, People's Republic of China

Correspondence: Xuexue Yin, Department of Gynecology, Zibo Central Hospital, Zibo, Shandong, 255000, People's Republic of China, Tel +86-18678186013, Email y20182021@126.com

Background: Platelet count (PLT) has been identified as a predictor for the development of pelvic adhesions. However, it remains unclear whether platelet-related parameters can also serve as indicators for the occurrence of intrauterine adhesions (IUA).

Methods: Patients diagnosed with IUA were included for further analysis, with platelet-related parameters assessed through routine blood tests. The predictive value of PLT and platelet hematocrit (PCT) was evaluated using receiver operating characteristic (ROC) curve analysis. Recurrence of IUA was determined based on a one-year follow-up.

Results: Our study included 69 IUA patients and 60 matched healthy women. We found that PLT and PCT levels were significantly elevated in IUA patients compared to the healthy controls. ROC analysis demonstrated that both PLT and PCT effectively predicted the occurrence of IUA. Additionally, higher PLT and PCT levels were noted in patients with recurrent IUA, suggesting their potential for predicting recurrence.

Conclusion: Elevated PLT and PCT levels were observed in patients with IUA and were further increased in those with recurrent cases. These findings suggest that high PLT and PCT levels may serve as valuable predictors for both the occurrence and recurrence of IUA. Specifically, the study is limited by the small sample size of recurrent IUA cases and potential confounders. These limitations should be considered when interpreting the findings.

Keywords: platelet, platelet crit, intrauterine adhesions, occurrence, recurrence

Introduction

Intrauterine adhesions (IUA) arise from endometrial damage caused by factors such as uterine procedures, infections, and hormonal influences, all of which can impede the endometrial repair process.[1,2] During this repair process, fibrous or muscular adhesions may form between the cervical canal and the uterine muscle wall, potentially altering the shape of the uterine cavity and leading to a reduction in uterine size.[1–4] Clinically, IUA can manifest as abnormal menstrual flow, amenorrhea, and lower abdominal pain, with more severe complications including infertility, miscarriage, and preterm birth. Detecting IUA can be challenging due to its subtle symptoms, limited awareness, and uncertain contributing factors.[5–8]

The current gold standard for diagnosing IUA is hysteroscopy, with hysteroscopic adhesiolysis as the primary treatment method. For non-surgical cases, IUA is typically diagnosed using transvaginal B-mode ultrasound, hysterosalpingography, and magnetic resonance imaging; however, their detection rates are considerably lower than that of hysteroscopy.[9] Studies indicate that the recurrence rate of IUA after surgery exceeds 60%.[10] To better guide clinical diagnosis and treatment, it is crucial to identify a reliable indicator for predicting both the occurrence and prognosis of IUA.

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Recent research has highlighted the critical role of platelet quantity and function in the onset and progression of various diseases.[11] Platelets have been shown to play essential roles not only in coagulation but also in malignant tumors, microthrombus formation, inflammatory responses, scar formation, and tissue stability.[12–14] Platelets have a potential role in the pathogenesis of endometriosis, as patients with this condition exhibited a higher proportion of platelet biomarker-positive particles.[15] Additionally, the combined marker of platelet-to-lymphocyte ratio (PLR) and CA125 has been identified as a potential inflammatory biomarker in diagnosing and assessing pelvic adhesion in endometriosis,[16] further linking platelets to pelvic adhesion. Platelets are known to be involved in inflammatory processes,[17] and dulaglutide has been shown to reduce inflammation and fibrosis in IUA.[18] These findings suggest a potential correlation between platelets and the pathogenesis of IUA, likely mediated through inflammatory pathways. Jiang et al demonstrated that platelet count (PLT) reliably predicts the presence of pelvic adhesions.[19] Furthermore, several studies suggest that IUA formation closely mirrors the generation and repair of scar tissue.[20] Following trauma, a series of physiological processes occur that contribute to scar tissue and IUA development. These processes are regulated by platelets, monocytes, macrophages, fibroblasts, vascular endothelial growth factor, platelet-derived growth factor, and basic fibroblast growth factor,[21] and they may persist from several days to over a year post-trauma. Current research primarily focuses on the roles of inflammatory cells, angiogenesis, and cytokines in IUA formation, while the involvement of platelets remains relatively underexplored.

This study aims to compare platelet-related parameters-including PLT, mean platelet volume (MPV), platelet hematocrit (PCT), and platelet distribution width (PDW)—between healthy women and IUA patients. The primary objective is to evaluate the diagnostic value of these parameters for detecting IUA. Additionally, the study seeks to compare preoperative platelet-related parameters between recurrent and non-recurrent IUA patients to assess the predictive value of these indicators for postoperative recurrence.

Materials and Methods

Participants

This study included 69 IUA patients from our department and 60 age-matched healthy women as controls during the same period. Exclusion criteria were applied to all participants. Healthy women did not have the clinical symptoms of IUA. Platelet-related parameters, including PLT, MPV, PCT, and PDW, were collected for each participant. This study was approved by the First Hospital of Anhui University of Science & Technology (#2024.271.k4).

Sample Size Estimation

The formula of "$n = (Z\alpha/2 \times \sigma/E)2$" was used to calculate the sample size, where n = sample size, $Z\alpha/2$ = degree of confidence, σ = standard deviation, E = margin of error. Estimates of effect size and standard deviation were based on the existing literature. To calculate the power of analysis we assumed $\alpha = 0.05$ and $\beta = 0.2$.

Receiver Operating Characteristic (ROC) Analysis

In ROC analysis, the Youden index was defined as the sum of sensitivity and specificity. The sensitivity, specificity, and cutoff corresponding to the maximal Youden index were typically selected to optimize diagnostic performance.

The Inclusion Criteria

Patients were included in the study if they met the following criteria: diagnosis of IUA based on the 2015 Chinese Expert Consensus on Clinical Diagnosis and Treatment of Uterine Adhesions; first-time diagnosis; moderate to severe disease severity; tolerance for hysteroscopic surgery and compliance with postoperative oral medication; age over 18 with fertility needs; availability of complete clinical data; and provision of informed consent along with willingness to participate in follow-up.

The Exclusion Criteria

Patients were excluded from the study if they met any of the following criteria: severe liver or kidney dysfunction; coagulation disorders; perimenopausal status; concurrent female reproductive system diseases (eg, endometrial polyps,

endometritis, submucosal fibroids, endometrial hyperplasia, or endometrial malignancies); concurrent non-reproductive diseases (eg, blood disorders, autoimmune diseases, or malignancies in other areas); long-term use of medications affecting blood parameters, such as antiplatelet agents, leukocyte-boosting drugs, immune modulators, glucocorticoids, or other similar drugs requiring regular blood monitoring; and history of blood product transfusion within the last six months.

The Treatment Procedure

All IUA patients underwent hysteroscopic adhesiolysis and uterine cavity separation. Menstruating patients administered 400 μg of misoprostol vaginally the evening before and the morning of surgery to facilitate cervical softening. This protocol was applied between the 7th and 14th day of menstruation, while non-menstruating patients were exempt. After receiving general anesthesia, the patient was positioned in the lithotomy position, and a uterine probe was inserted into the uterine cavity. Under ultrasound guidance, the adhesions were carefully separated from one end to the other or from bottom to top within the uterus until reaching the uterine fundus. Cervical dilation was achieved with a dilation rod, followed by hysteroscope insertion to thoroughly examine the uterine cavity for any adhesions. For more challenging adhesion tissue, a ring or needle electrode was used to assist with separation, ensuring the formation of a complete uterine cavity with clear visualization of both fallopian tube openings. After surgery, routine postoperative care was provided, and outpatient follow-up was conducted for 12 months, with recurrence assessment at the 12-month mark. Patients were then classified into two cohorts based on postoperative recurrence status: a recurrence cohort and a non-recurrence cohort.

The Detection of Platelet-Related Parameters

Fasting venous blood was collected from the enrolled patients, and a complete blood count was performed using a fully automated hematology analyzer (Mindray BC-5390, Shenzhen, China). Subsequently, PLT, MPV, PCT, and PDW were calculated.

Statistical Analysis

The data are presented as mean ± standard deviation (SD) or n (percentage). Comparisons between the two groups were conducted using the Mann–Whitney test, Chi-square test, or Fisher's exact test, as appropriate. A box plot was used to visually represent the data, and p-values were calculated using the unpaired *t*-test with Welch's correction.

Results

Demographic and Clinical Characteristics of Women with IUA and Health Control

Initially, the clinical characteristics of the women were compared, revealing no significant differences in age and body mass index (BMI) (Table 1). Notably, the percentage of patients with IUA who had a history of multiple abortions was significantly higher than that of healthy women (Table 1). Additionally, a greater percentage of IUA patients experienced oligomenorrhea or amenorrhea compared to healthy women (Table 1). These findings suggest that IUA is associated with a history of abortion and abnormal menstrual patterns.

The Comparison of Platelet-Related Parameters

To determine whether IUA was associated with platelet-related parameters, these parameters were compared between the two groups. Both PLT and PCT were significantly elevated in IUA patients compared to healthy women, with p-values less than 0.001 (Figure 1A and B). In contrast, MPV and PDW did not show any significant differences between the two groups (Figure 1C and D). Therefore, it was hypothesized that PLT and PCT are associated with the occurrence of IUA.

ROC Analysis for the Diagnostic Values of PLT and PCT

To evaluate the diagnostic value of PLT and PCT for identifying IUA, a ROC analysis was performed. The cutoff values for the ROC curve were determined to be 232.2×10^9/L for PLT and 0.245% for PCT (Figure 2 and Table 2). The area

Table 1 Demographic and Clinical Characteristics of Women with Intrauterine Adhesions (IUA) and Health Control

Characteristics	Control (n=60)	IUA (n=69)	p value
Age (years)	28.12 ± 3.15	28.61 ± 2.75	0.773
BMI (kg/m^2)	23.07 ± 1.89	23.44 ± 2.06	0.691
Abortion history, %			
0	45 (75%)	10 (14.49%)	< 0.001
1	11 (18.33%)	37 (53.63%)	
≥ 2	4 (6.67%)	22 (31.88%)	
Menstruation before the surgery			
Normal	52 (86.67%)	15 (21.74%)	< 0.001
Oligomenorrhea	8 (13.33%)	32 (46.38%)	
Amenorrhea	0 (0%)	22 (31.88%)	

Notes: The data are presented as mean ± SD or n (percentage). The comparisons of data between the two group were done by Mann–Whitney test, Chi-square test or Fisher's exact test.
Abbreviation: BMI, body mass index.

under the curve (AUC) for the ROC analysis was found to be 0.73 for PLT and 0.71 for PCT, indicating high sensitivity and specificity (Figure 2 and Table 2). Notably, the combination of PLT and PCT demonstrated a greater predictive capacity for IUA diagnosis, as reflected by the higher AUC, sensitivity, and specificity of the ROC curve (Figure 2 and Table 2). Thus, it can be concluded that PLT and PCT are useful predictors for diagnosing IUA.

Baseline Demographic and Clinical Characteristics

After surgery, 69 IUA patients received routine postoperative care as outpatients. They were classified into a recurrence group, consisting of 21 cases, and a non-recurrence group, comprising 48 cases, based on postoperative outcomes. The preoperative clinical data of both groups were subsequently compared, including age, BMI, duration of disease, IUA severity, operation time, use of intrauterine devices, pelvic inflammation, abortion history, and menstrual patterns prior to surgery. No significant differences were found in age, BMI, operation time, use of intrauterine devices, pelvic inflammation, or menstrual patterns before surgery (Table 3). However, significant differences were observed in the

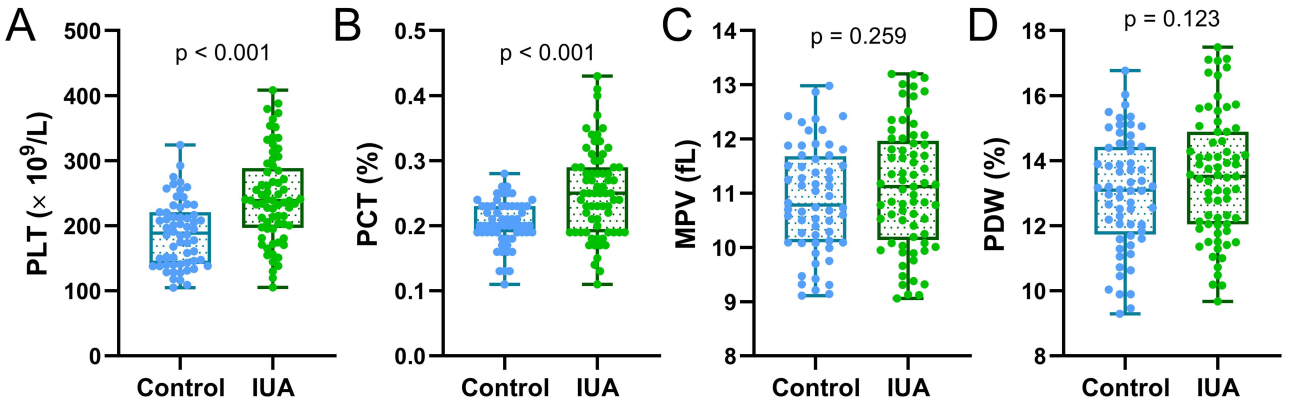

Figure 1 Comparisons of platelet count (PLT, (**A**)), platelet crit (PCT, (**B**)), mean platelet volume (MPV, (**C**)), and platelet distribution width (PDW, (**D**)) between women with intrauterine adhesions (IUA) and health control. Box plot was used to show the data, and p values were calculated by Unpaired *t*-test with Welch's correction.

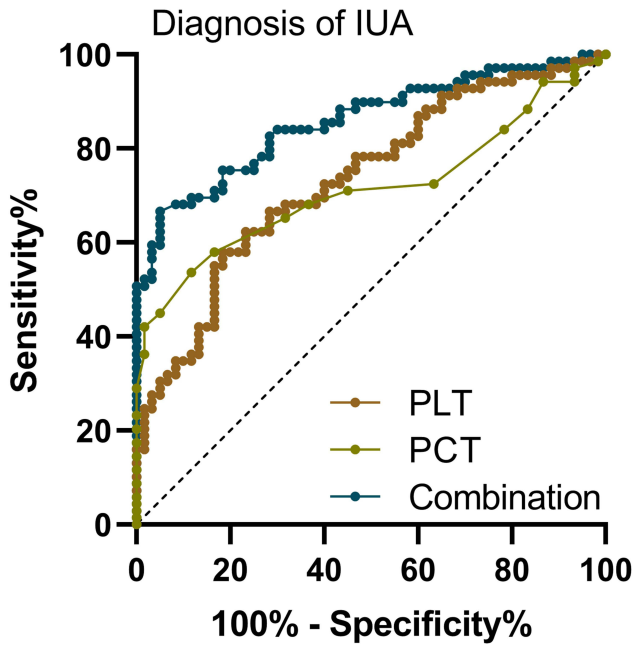

Figure 2 ROC analysis for the diagnostic values of PLT and PCT and their combined test for intrauterine adhesions (IUA).

duration of the disease, IUA severity, and history of abortion between the two groups (Table 3). Thus, it was concluded that IUA patients with recurrence had a longer duration of disease, more severe IUA, and a higher number of abortions.

Comparisons of Platelet-Related Parameters

To determine whether platelet-related parameters were associated with recurrence, these parameters were compared between patients with and without recurrence. It was observed that both PLT and PCT were significantly elevated in IUA patients with recurrence after surgery (Figure 3A and B). In contrast, MPV and PDW did not show any significant differences between the two groups (Figure 3C and D). Therefore, it can be concluded that PLT and PCT are positively associated with IUA recurrence after surgery.

ROC Analysis for the Predictive Values of PLT and PCT for the Recurrence of IUA

ROC analysis was conducted to validate the predictive value of PLT and PCT for IUA recurrence. The cutoff values for the ROC curve were determined to be 227.8 × 10^9/L for PLT and 0.235% for PCT (Figure 4 and Table 4). The area under the curve (AUC) for the ROC analysis was found to be 0.71 for PLT and 0.69 for PCT, indicating high sensitivity and specificity (Figure 4 and Table 4). Notably, combined test could improve the specificity for prediction of IUA recurrence after surgery (from 50% and 56.25% to 70.83%), but has limited improvement of sensitivity (from 80.95% and 76.19% to 76.19%). Thus, it can be concluded that PLT and PCT can effectively predict IUA recurrence following surgery.

Table 2 Diagnostic Values of PLT, PCT and Their Combined Test for Intrauterine Adhesions (IUA)

	Cut-off Value	AUC (95% CI)	p	Sensitivity (%)	Specificity (%)	Youden Index
PLT	232.2 × 10^9/L	0.73 (0.65–0.82)	< 0.001	57.97	81.67	0.40
PCT	0.245%	0.71 (0.62–0.81)	< 0.001	53.62	88.33	0.42
Combination	–	0.86 (0.79–0.92)	< 0.001	66.67	95.00	0.62

Note: Logit (Combination) = 0.016 × PLT + 18.69 × PCT.
Abbreviation: CI, confidence interval.

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Table 3 Baseline Demographic and Clinical Characteristics of Women with Intrauterine Adhesions (IUA) Who Had Postoperative Recurrence or Non-Recurrence During the One year of Follow-up After the Surgery

Characteristics	Non-Recurrence (n=48)	Recurrence (n=21)	p value
Age (years)	28.27 ± 2.63	28.89 ± 2.95	0.573
BMI (kg/m^2)	23.19 ± 2.11	23.66 ± 1.92	0.682
Course of disease (months)			
< 12	33 (68.75%)	7 (33.33%)	0.008
≥ 12	15 (31.25%)	14 (66.67%)	
IUA severity			
Moderate	34 (70.83%)	4 (19.05%)	< 0.001
Severe	14 (29.17%)	17 (80.95%)	
Operation time (min)			
< 20	23 (47.92%)	12 (57.14%)	0.603
≥ 20	25 (52.08%)	9 (42.86%)	
Intrauterine device			
Yes	31 (64.58%)	8 (38.09%)	0.064
No	17 (35.42%)	13 (61.91%)	
Pelvic inflammation			
Yes	22 (45.83%)	11 (52.38%)	0.794
No	26 (54.17%)	10 (47.62%)	
Abortion history, %			
0	9 (18.75%)	1 (4.76%)	0.009
1	29 (60.42%)	8 (38.09%)	
≥ 2	10 (20.83%)	12 (57.15%)	
Menstruation before the surgery			
Normal	11 (22.92%)	4 (19.05%)	0.169
Oligomenorrhea	25 (52.08%)	7 (33.33%)	
Amenorrhea	12 (25%)	10 (47.62%)	

Notes: The data are presented as mean ± SD or n (percentage). The comparisons of data between the two group were done by Mann–Whitney test, Chi-square test or Fisher's exact test.
Abbreviation: BMI, body mass index.

Comparison of Preoperative and Postoperative PLT and PCT

Previous findings have demonstrated that PLT and PCT can diagnose IUA and predict recurrence after surgery. However, it is important to determine whether PLT and PCT differ in IUA patients before and after the operation. Therefore, platelet-related parameters were compared in IUA patients upon admission and at the time of recurrence. It was found that both PLT and PCT significantly increased in IUA patients at the time of recurrence (Figure 5A and B). In contrast,

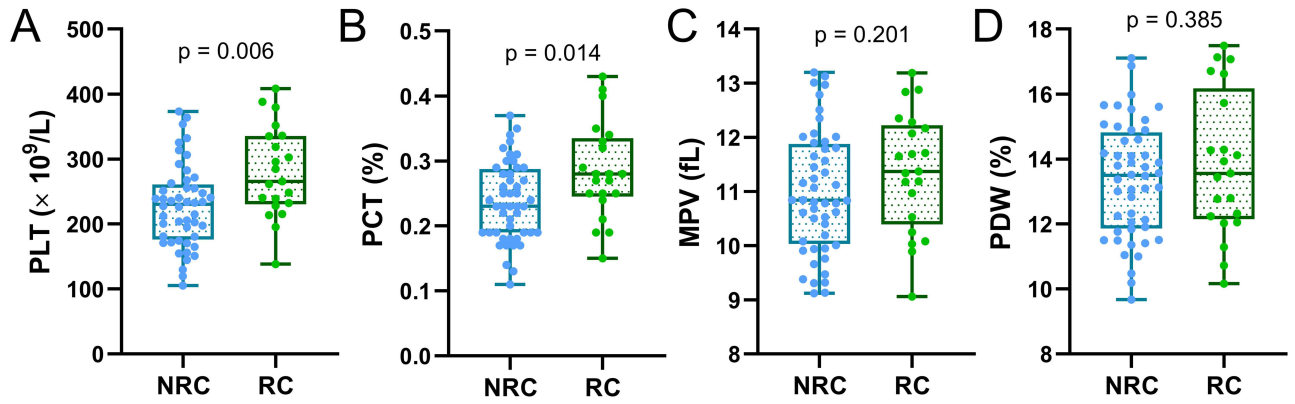

Figure 3 Comparisons of platelet count (PLT, (**A**)), platelet crit (PCT, (**B**)), mean platelet volume (MPV, (**C**)), and platelet distribution width (PDW, (**D**)) of women with intrauterine adhesions (IUA) who had postoperative recurrence (RC, n = 21) or non-recurrence (NRC, n = 48) during the one year of follow-up after the surgery. Box plot was used to show the data, and p values were calculated by Unpaired *t*-test with Welch's correction.

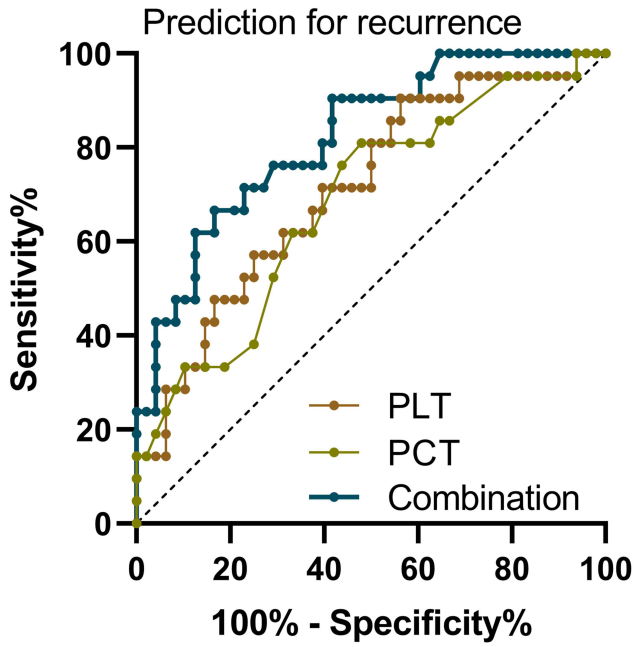

Figure 4 ROC analysis for the predictive values of PLT and PCT and their combined test for recurrence during the one-year follow-up after the surgery in intrauterine adhesions (IUA) patients.

MPV and PDW did not show any significant differences between the admission values and those at the time of recurrence (Figure 5C and D). Thus, it can be concluded that PLT and PCT dynamically increase in IUA patients with recurrence after surgery.

Table 4 Predictive Values of PLT, PCT and Their Combined Test for Recurrence During the One year of Follow-up After the Surgery in Intrauterine Adhesions (IUA) Patients

	Cut-off Value	AUC (95% CI)	p	Sensitivity (%)	Specificity (%)	Youden Index
PLT	227.8 × 10^9/L	0.71 (0.58–0.84)	0.005	80.95	50	0.31
PCT	0.235%	0.69 (0.55–0.82)	0.0150	76.19	56.25	0.32
Combination	–	0.82 (0.72–0.92)	< 0.001	76.19	70.83	0.47

Note: Logit (Combination) = 0.012 × PLT + 11.11 × PCT.
Abbreviation: CI, confidence interval.

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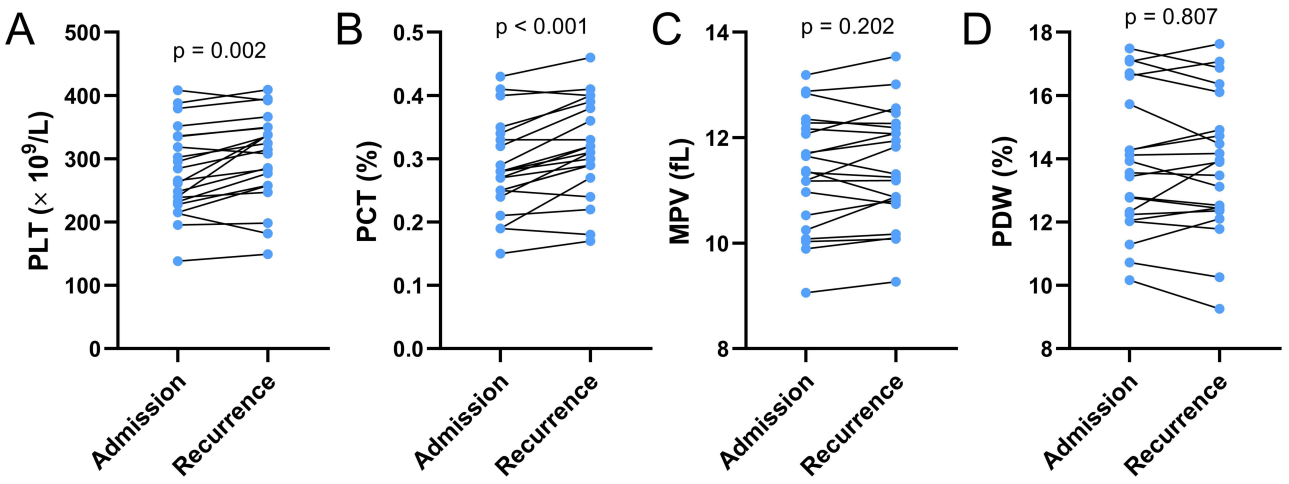

Figure 5 Comparisons of platelet count (PLT, (**A**)), platelet crit (PCT, (**B**)), mean platelet volume (MPV, (**C**)), and platelet distribution width (PDW, (**D**)) at the time of admission and recurrence in women with intrauterine adhesions (IUA) who had postoperative recurrence (RC, n = 21) during the one year of follow-up after the surgery. A box plot was used to show the data, and p values were calculated by paired *t*-test.

Discussion

In China, IUA are prevalent and can significantly impact women's reproductive health, which leads to substantial medical expenses, exhibits poor treatment outcomes, and frequently recurs post-treatment. Timely diagnosis of IUA is imperative, as they exert a considerable influence on the physical and psychological well-being of women in their childbearing years. At present, the preoperative evaluation of IUA by ultrasound, MRI, and HSG is insufficient.[22–24] Therefore, it is of significance to identify the biomarker for IUA diagnosis.

Platelets are circulating anucleate cells that are crucial in wound healing, thrombosis, hemostasis, and inflammation. Platelets contribute to severe bleeding, thrombotic disorders, and cardiovascular diseases, such as myocardial infarction and atherosclerosis.[25] Platelet-related parameters commonly include PLT, MPV, PCT, and PDW. PLT is a routine indicator of blood tests that reflects the total amount of platelets in recent peripheral blood samples; MPV demonstrates the proliferation of bone marrow megakaryocytes and platelet production; PCT overall reflects the quantity and size of platelets, while PDW reflects the consistency of platelets and may serve as a marker of platelet activation.[19,26] Many studies suggest that platelet-related parameters have predictive value for short-term and long-term status of cardiovascular and cerebrovascular acute and chronic bleeding, as well as ischemic diseases.[27,28] In recent years, platelet-related indicators have been used to monitor the activity of chronic diseases, such as malignant tumors, atherosclerosis, and autoimmune diseases. The potential for long-term alterations in the activity involved in the development of IUA after injury, along with the extensive participation of platelets across various stages of IUA formation, suggests that platelet-related parameters may serve as indicators of the progression of IUA. We analyzed and compared the platelet-related parameters in healthy women and IUA patients. It was found that PLT and PCT increased while MPV and PDW had no difference in IUA patients compared to healthy women. These findings indicated that PLT and PCT were positively associated with IUA. The ROC analysis furthermore demonstrated that PLT and PCT could predict the occurrence of IUA; significantly, the combination of PLT and PCT could more effectively predict the occurrence of IUA. Therefore, the predictive value of PLT and PCT for IUA occurrence expanded the function of platelets.

The most common and effective clinical treatment for uterine adhesions is hysteroscopic adhesion lysis. This procedure can significantly restore the normal volume and shape of the uterus.[29] Studies have found that the recurrence rate after surgery ranges from 3% to 24%, with the highest rates reaching 20–63%.[30–33] In our recruited IUA patients, the percentage of IUA patients with recurrence was 30%, which was consistent with the reported incidence rate. In clinical practice, patients with IUA had a higher recurrence rate, especially in moderate to severe cases, with a comprehensive recurrence rate exceeding 60%. Our analysis showed that the percentage of patients with severe IUA was higher in the recurrence group, consistent with previous findings. It was also found that abortion time contributed to IUA recurrence

after surgery. However, more evidence is needed to determine whether the platelet-related parameters could predict the recurrence of IUA.

The IUA patients were divided into non-recurrence and recurrence groups according to the follow-ups. Subsequently, the PLT and PCT were analyzed and compared among the two groups. The result showed that PLT and PCT increased, while MPV and PDW did not significantly increase in IUA patients with recurrence. These findings indicated that PLT and PCT also could predict the IUA recurrence after surgery. The subsequent ROC analysis presented that PLT and PCT could convincingly predict the recurrence of IUA with high sensitivity. The AUC of ROC for the combination of PLT and PCT in the prediction of recurrence was higher than the single parameters. Collectively, it was concluded that PLT, PCT, or their combination could effectively predict the recurrence of IUA after surgery. To validate the dynamic changes of platelet-related parameters in IUA patients, the preoperative and postoperative platelet-related parameters were compared. It was found that PLT and PCT significantly increased in IUA patients after recurrence compared to pre-operation. Similarly, there was no significant difference in MPV and PDW among IUA patients after surgery. These findings demonstrated that the increase of PLT and PCT was positively associated with the occurrence and recurrence of IUA.

Ultrasound imaging, particularly 3D ultrasound, has become a key non-invasive, cost-effective tool for diagnosing IUA.[34] It provides clear panoramic images of the uterine cavity and quantifies adhesions, allowing for better preoperative and postoperative management.[34] Ultrasound can guide surgeries, improve safety, reduce recurrence risks, and minimize patient discomfort, making it an essential part of IUA diagnosis and treatment.[34] Integrating the newly proposed classification systems for IUAs, such as the simplified descriptive system for better communication and the comprehensive Urman-Vitale system that includes symptoms, imaging, and postoperative outcomes, could provide a strong framework for assessing IUAs in hypertensive patients.[35,36] This approach would improve fertility predictions and enable more tailored treatment plans, ultimately enhancing surgical outcomes and long-term reproductive health in this high-risk group.

Based on our findings, the combination of PLT and PCT enhanced the diagnostic utility of platelet-related parameters for IUA, improving AUC, specificity, and sensitivity. This non-invasive approach allows early detection, enabling timely intervention and better treatment planning. Additionally, using PLT and PCT to predict postoperative recurrence helps identify high-risk patients, allowing for tailored follow-up care and preventive measures. The combined markers serve as more effective diagnostic and prognostic tools for IUA occurrence and recurrence, supporting personalized management and improving long-term outcomes. When combined with IUA classification, they offer a comprehensive approach to assess recurrence risk, guide personalized treatment, and improve fertility outcomes. Larger studies are needed to validate this combined approach and confirm its clinical utility, ultimately providing more targeted and personalized care for diverse populations. In our study, we observed the predictive values of PLT and PCT in relation to the occurrence and recurrence of IUA post-surgery. However, our study still has some limitations. Specifically, due to the small sample size of IUA patients and limited recurrent cases, the risk factor analysis may lack sufficient statistical power, leading to inconclusive results. This limitation, along with potential confounders, should be considered when interpreting the findings. Larger studies with better control of confounders are needed to draw more definitive conclusions. Moreover, the control group comprised women with unknown intrauterine anatomy, rather than patients suspected of having intrauterine adhesions who were confirmed to have normal findings on hysteroscopic examination. This approach was adopted due to practical constraints; however, future studies may benefit from including a control group with documented normal intrauterine anatomy to better align with the IUA patient cohort. Additionally, the difference in PLT and PCT between the recurrent IUA patients at admission and recurrence stages was also not convincing.

Conclusion

PLT and PCT levels are higher in patients with IUA and are further increased in those with recurrent cases. PLT and PCT exhibit positive correlations with IUA recurrence and can be utilized for diagnosing IUA as well as predicting its recurrence after surgery.

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Disclosure

The authors have no competing interest to declare in this work.

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