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ORIGINAL RESEARCH

Effects of Acupuncture on Uterine Hemodynamics and Early-Phase Pain Relief in Primary Dysmenorrhea: A Retrospective Cohort Study

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Background: Primary dysmenorrhea is fundamentally driven by uterine ischemia resulting from excessive vascular resistance. While acupuncture is theorized to improve perfusion, high-quality evidence controlling for pharmacological confounders is limited. This study aimed to evaluate the hemodynamic effects and longitudinal analgesic efficacy of the "Regulating Ren and Unblocking Du" acupuncture protocol.

Methods: This retrospective cohort study analyzed data from 286 patients treated between 2020 and 2024. To minimize selection bias, a 1:1 Propensity Score Matching (PSM) algorithm was applied to balance baseline covariates, including medication regimen (NSAIDs vs. hormonal therapy), disease severity, and age at menarche. The final matched cohort included 158 patients (79 pairs). The intervention group received acupuncture plus conventional medication, while the control group received medication alone. Primary outcomes included uterine artery Doppler indices (Pulsatility Index [PI], Resistance Index [RI], S/D ratio) and Visual Analogue Scale (VAS) pain scores assessed at 1, 3, and 6 months.

Results: Post-treatment, the acupuncture group exhibited significantly lower vascular resistance compared to controls, with a mean difference of −0.54 (95% CI: −0.66 to −0.42) for PI and −1.7 for the S/D ratio ($p < 0.001$). Clinically, acupuncture provided superior rapid analgesia; at 1 month, VAS scores were significantly lower in the intervention group compared to controls ($p < 0.001$). This advantage persisted at 3 months but converged by 6 months ($p = 0.32$), indicating a diminishing differential effect over time. Subgroup analyses revealed enhanced efficacy in patients aged <30 years or with a disease duration <5 years. Minor adverse events occurred in 6.3% of acupuncture recipients.

Conclusion: After rigorously adjusting for confounders, acupuncture was associated with reduced uterine arterial resistance. Clinically, it offers a distinct "window of opportunity" for rapid symptom control in the early treatment phase, particularly for younger patients.

Plain Language Summary: This study evaluated whether adding a specific acupuncture technique, called "Regulating Ren and Unblocking Du" to usual medication improves uterine blood flow and pain in women with menstrual cramps without underlying disease. In this review of 158 patients, one group received acupuncture plus medication and the other received medication alone. The acupuncture group showed greater improvement in uterine blood flow and greater pain reduction in the short term up to three months, especially in younger patients and those with a shorter pain history. However, the added benefit of acupuncture diminished after six months. Acupuncture is safe, with only minor side effects such as mild bruising or temporary dizziness. In conclusion, this acupuncture approach can enhance short-term blood flow and pain relief when combined with conventional treatment; however, its effects may not be sustained long-term without ongoing sessions.

Keywords: primary dysmenorrhea, acupuncture, uterine blood flow, pain relief, retrospective study

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Introduction

Primary dysmenorrhea, characterized by recurrent menstrual cramping without pelvic pathology, affects up to 91% of reproductive-age women.[1,2] Its pathophysiology involves excessive prostaglandin F2α (PGF2α) synthesis, inducing myometrial hypercontractility and subsequent uterine ischemia.[3] Doppler ultrasound studies indicate that elevated uterine artery resistance indices, specifically the pulsatility index (PI) and resistance index (RI), correlate with reduced tissue perfusion and increased pain severity.[4,5] These hemodynamic alterations highlight potential therapeutic targets for improving microcirculation in dysmenorrhea management.

While nonsteroidal anti-inflammatory drugs (NSAIDs) and hormonal contraceptives remain first-line treatments, 20–30% of patients experience suboptimal responses or tolerate them poorly due to gastrointestinal or cardiovascular risks.[6,7] Moreover, these therapies primarily manage symptoms rather than directly targeting vascular resistance. Acupuncture is increasingly recognized as a potential alternative therapy. Clinical evidence suggests it may modulate pain via endogenous opioids and the suppression of inflammatory mediators.[8–10] Additionally, needling specific acupoints may decrease uterine artery resistance indices, potentially improving endometrial perfusion and reducing ischemia-related pain.[11,12]

Despite this potential, a critical gap remains: while specialized acupuncture protocols—such as the "Regulating Ren and Unblocking Du" technique—are theorized to harmonize uterine blood flow, empirical evidence is largely restricted to subjective pain outcomes.[13,14] There is a lack of quantitative Doppler ultrasound data evaluating how these specific meridian-based protocols affect uterine artery hemodynamics in clinical practice. Therefore, this retrospective cohort study aims to evaluate whether the "Regulating Ren and Unblocking Du" protocol is associated with improvements in uterine artery resistance indices (PI, RI, and systolic/diastolic [S/D] ratio) and early-phase pain relief. By investigating both quantitative Doppler metrics and longitudinal pain scores, this study seeks to further clarify the clinical utility of this adjunctive therapy.

Materials and Methods

Study Design

This single-center retrospective cohort study analyzed electronic medical records of patients with primary dysmenorrhea from the gynecology department of The Second Affiliated Hospital of Shaanxi University of Chinese Medicine between January 2020 and December 2024. Data were extracted from the hospital's standardized electronic database, which included demographics, treatment protocols, ultrasound examinations, and follow-up records. Patients were categorized into two groups: the intervention group received conventional medication combined with "Regulating Ren and Unblocking Du" acupuncture. To ensure adequate therapeutic dosage, the completion of at least 8 acupuncture sessions per treatment course was established as the strictly defined minimum exposure criterion for inclusion in the intervention group, while the control group received conventional medication alone (NSAIDs or hormonal therapy). The study was approved by the Institutional Ethics Committee of The Second Affiliated Hospital of Shaanxi University of Chinese Medicine (Approval No. LW2025007-9), and the requirement for informed consent was waived due to the anonymized retrospective nature of the data.

Participants

Participants were selected from female patients aged 18–40 years diagnosed with primary dysmenorrhea according to the International Federation of Gynecology and Obstetrics (FIGO) criteria for cyclic pelvic pain unrelated to organic pathology.[15] The strict inclusion criteria were defined as follows: (1) completion of uterine artery Doppler ultrasound within one month before treatment initiation; (2) availability of complete baseline and follow-up records, including visual analogue scale (VAS) scores for pain intensity and menstrual symptom duration; and (3) specifically for the intervention cohort, fulfillment of the minimum exposure criterion of ≥8 acupuncture sessions.

The exclusion criteria comprised: (1) secondary dysmenorrhea (eg., endometriosis, uterine fibroids, or pelvic inflammatory disease confirmed by laparoscopy or imaging); (2) comorbid cardiovascular diseases, cerebrovascular disorders, or coagulation abnormalities (eg., thrombocytopenia or anticoagulant therapy); (3) use of other acupuncture

therapies or herbal medicine within three months prior to enrollment; and (4) missing ultrasound data or incomplete follow-up evaluations. To ensure diagnostic accuracy, secondary dysmenorrhea cases were rigorously excluded through cross-referencing surgical records, imaging reports, and histopathological findings.

Interventions

Intervention Group

Participants in the intervention group received conventional pharmacological therapy combined with the "Regulating Ren and Unblocking Du" acupuncture protocol. Conventional medication included NSAIDs (eg., ibuprofen) or hormonal therapy (eg., combined oral contraceptives) prescribed based on clinical guidelines. The acupuncture protocol targeted specific acupoints based on Chinese edition of the WHO Standard Acupuncture Point Locations in the Western Pacific Region:[16]

Ren Mai (Conception Vessel): Guanyuan (CV4, located 3 cun inferior to the umbilicus), Zhongji (CV3, 1 cun inferior to CV4).

Du Mai (Governor Vessel): Mingmen (GV4, at the lumbar spine level between L2 and L3), Yaoyangguan (GV3, at the lumbar spine level between L4 and L5).

Adjunctive acupoints: Sanyinjiao (SP6, 3 cun superior to the medial malleolus), Xuehai (SP10, on the medial thigh 2 cun above the medial superior border of the patella).

Acupuncture Procedure

Sterile disposable stainless steel needles (0.25 × 40 mm) were inserted perpendicularly to a depth of 10–25 mm, depending on the acupoint location. A balanced reinforcement-reduction technique was applied to achieve the deqi sensation. For the purpose of this study, deqi was operationally defined as a composite subjective sensation comprising soreness, numbness, heaviness, or distension reported by the patient around the acupoint, frequently accompanied by a specific biomechanical sensation of resistance or "needle grasp" perceived by the administering acupuncturist. Needles were retained for 30 minutes per session, administered 3 times weekly over 4 weeks (total ≥8 sessions). All procedures were performed by licensed acupuncturists with ≥5 years of clinical experience, trained in standardized protocols to ensure consistency.

Control Group

The control group received conventional pharmacological therapy alone without acupuncture. Based on patient preference, symptom severity, and clinical contraindications, participants were prescribed either a primary regimen of NSAIDs (predominantly ibuprofen or naproxen) or hormonal therapy (specifically combined oral contraceptives). Patients receiving a concurrent combination of both as their primary maintenance therapy were not included in this cohort. Medication dosages and administration schedules strictly followed institutional guidelines for primary dysmenorrhea management.

Data Collection

Primary Outcomes

Endometrial blood flow parameters were assessed via transvaginal Doppler ultrasound (Voluson E10, GE Healthcare) performed by certified sonographers. To minimize cycle-dependent hemodynamic variability, all baseline examinations were strictly scheduled during the follicular phase (days 5–11 of the menstrual cycle). Pulsatility index (PI), resistance index (RI), and systolic/diastolic velocity ratio (S/D) of the uterine arteries were measured bilaterally and averaged for analysis. Baseline ultrasound data were collected within one month before treatment initiation, and follow-up measurements were obtained 1–3 days after the final acupuncture session (intervention group) or 4 weeks after medication initiation (control group).

Pain intensity was evaluated using the visual analogue scale (VAS, 0–10 cm).[17] Baseline VAS scores were extracted from standardized patient-reported outcome forms recorded during the initial consultation. Post-treatment VAS assessments were collected at three time points: Short-term: 1 month after treatment completion (covering 1–2 menstrual cycles); Mid-term: 3 months post-treatment; Long-term: 6 months post-treatment. Scores were obtained from follow-up clinic visit records or telehealth consultations. Patients without documented VAS scores at all three time points were excluded to ensure longitudinal data consistency.

Secondary Outcomes

Menstrual symptom duration (hours per cycle) and analgesic medication use frequency (doses per cycle) were calculated based on self-reported pain diaries and pharmacy dispensing records. To address pharmacological heterogeneity, the primary maintenance medication regimen was categorized as either NSAID-based (eg., ibuprofen, naproxen) or hormonal therapy-based (eg., combined oral contraceptives), based on the dominant prescription filled during the study period.

Adverse events (AEs) were defined as any clinical notes indicating localized bruising (subcutaneous hemorrhage ≥5 mm at needle sites) or dizziness (eg., terms like "lightheadedness," "nausea," or "diaphoresis" recorded within 24 hours post-treatment).[18] Severe AEs included infections, syncope, or hospitalization directly linked to treatment. For the control group, AEs related to conventional medication (eg., gastrointestinal symptoms, headaches) were extracted from prescription logs and progress notes using standardized ICD-10 codes.[19]

Covariates

Demographic and clinical covariates included age, body mass index (BMI), disease duration, age at menarche (years), and menstrual cycle regularity (21–35 days). Gynecological history was scrutinized for specific menstrual characteristics, specifically the presence of menstrual clots, defined as patient-reported observation of clots >1 cm in diameter during at least 50% of recent cycles, a clinical marker often associated with higher prostaglandin levels and increased pain severity.[20] Additionally, uterine position (anteverted vs. retroverted) was extracted from the baseline ultrasound reports, as uterine retroversion is a recognized anatomical factor that may exacerbate pelvic congestion and dysmenorrhea symptoms.[21] These variables were extracted from electronic health records and baseline assessments.

Statistical Analysis

Data analysis was performed using SPSS version 26.0 and R software version 4.3.4. Continuous variables were summarized as mean ± standard deviation or median [interquartile range] based on normality assessed via Shapiro–Wilk tests, while categorical variables were expressed as frequencies and percentages. To rigorously control for selection bias, a 1:1 nearest-neighbor Propensity Score Matching (PSM) algorithm with a caliper of 0.02 was implemented using a multivariate logistic regression model that incorporated age, BMI, disease duration, age at menarche, presence of clots, baseline hemodynamic indices, and medication regimen; covariate balance was validated by Standardized Mean Differences (SMD) < 0.10. In the matched cohort, between-group comparisons employed independent samples t-tests, Mann–Whitney *U*-tests, or Chi-square/Fisher's exact tests as appropriate. Longitudinal trajectories of VAS scores and secondary outcomes were evaluated using linear mixed-effects models with random intercepts to account for repeated measures, incorporating group-by-time interaction terms. The robustness of these findings was verified through sensitivity analyses comparing complete-case (CC) data with multiple imputation (MI) (20 datasets). Additionally, relationships between hemodynamic changes and pain relief were quantified using Spearman's rank correlation coefficients, and subgroup heterogeneity was assessed using generalized linear models with interaction terms, with statistical significance defined as a two-tailed p-value < 0.05. As a retrospective study, the sample size was determined by the availability of eligible electronic medical records rather than an a priori calculation; however, a post-hoc power analysis indicated that the matched cohort of 79 pairs provided >80% statistical power to detect the observed mean difference of −1.8 in VAS scores at 1 month, assuming an alpha error of 0.05. Furthermore, to quantitatively assess the robustness of our findings to unmeasured confounding, we calculated the E-value for the primary clinical outcome (VAS score at 1 month).

Results

Patient Screening and Baseline Characteristics

From January 2020 to December 2024, 286 patients were screened. After excluding 38 patients (secondary dysmenorrhea [n=18], coagulation disorders [n=12], incomplete data [n=8]), 248 patients were included in the pre-matched analysis (Intervention: n=85; Control: n=163). In the pre-matched cohort, baseline differences were observed (Table 1). The intervention group exhibited longer disease duration, higher baseline VAS scores, earlier age at menarche, and a higher prevalence of menstrual blood clots compared to the control group (all $p < 0.05$). Additionally, the proportion of patients receiving hormonal therapy was higher in the intervention group ($p = 0.015$).

Table 1 Demographic, Clinical, and Hemodynamic Characteristics of the Study Population Before and After Propensity Score Matching (PSM)

Variable	Before PSM				After PSM			
	Intervention (n=85)	Control (n=163)	SMD	p-Value	Intervention (n=79)	Control (n=79)	SMD	p-Value
Demographics								
Age (years), mean ± SD	26.9 ± 4.3	25.4 ± 4.6	0.334	0.012	26.7 ± 4.2	26.5 ± 4.1	0.048	0.765
BMI (kg/m^2), mean ± SD	22.5 ± 3.2	22.9 ± 3.4	0.121	0.354	22.4 ± 3.1	22.6 ± 3.0	0.065	0.682
Gynecological History								
Age at Menarche (years)	12.8 ± 1.1	13.2 ± 1.3	0.33	0.035	12.9 ± 1.2	13.0 ± 1.2	0.083	0.612
Disease duration (years), median [IQR]	5.0 [3.0–8.0]	3.0 [2.0–6.0]	0.412	0.003	4.0 [2.0–7.0]	4.0 [3.0–7.5]	0.052	0.814
Regular menstrual cycle, n (%)	72 (84.7%)	135 (82.8%)	0.051	0.702	67 (84.8%)	66 (83.5%)	0.036	0.824
Parity (≥1), n (%)	18 (21.2%)	29 (17.8%)	0.085	0.518	17 (21.5%)	15 (19.0%)	0.062	0.698
Uterine Position (Retroverted), n (%)	28 (32.9%)	45 (27.6%)	0.115	0.385	25 (31.6%)	23 (29.1%)	0.054	0.738
Clinical Baseline								
Baseline VAS score, mean ± SD	7.7 ± 1.2	7.2 ± 1.4	0.384	0.006	7.6 ± 1.3	7.5 ± 1.2	0.08	0.621
Presence of Clots, n (%)	55 (64.7%)	81 (49.7%)	0.306	0.028	50 (63.3%)	48 (60.8%)	0.052	0.745
Baseline Hemodynamics								
Uterine Artery PI	3.10 ± 0.44	3.05 ± 0.46	0.111	0.402	3.12 ± 0.45	3.08 ± 0.42	0.091	0.578
Uterine Artery RI	0.83 ± 0.06	0.81 ± 0.08	0.281	0.058	0.83 ± 0.06	0.82 ± 0.07	0.076	0.615
Medication Regimen								
NSAIDs, n (%)	50 (58.8%)	121 (74.2%)	0.331	0.015	49 (62.0%)	48 (60.8%)	0.025	0.873
Hormonal Therapy, n (%)	35 (41.2%)	42 (25.8%)	0.331	0.015	30 (38.0%)	31 (39.2%)	0.025	0.873
Comorbidities & Lifestyle								
Chronic hypertension, n (%)	3 (3.5%)	4 (2.5%)	0.06	0.645	2 (2.5%)	2 (2.5%)	0	1
Type 2 diabetes, n (%)	2 (2.4%)	3 (1.8%)	0.042	0.76	2 (2.5%)	2 (2.5%)	0	1
Family history, n (%)	23 (27.1%)	40 (24.5%)	0.059	0.662	21 (26.6%)	20 (25.3%)	0.029	0.854
Current smoking, n (%)	6 (7.1%)	10 (6.1%)	0.04	0.768	6 (7.6%)	5 (6.3%)	0.05	0.754
Alcohol use (≥1/week), n (%)	10 (11.8%)	18 (11.0%)	0.025	0.862	9 (11.4%)	8 (10.1%)	0.042	0.795

Notes: Statistical notes: Data presented as mean ± SD, median [IQR], or n (%). p-values calculated via *t*-test, Mann–Whitney *U*-test, or Chi-square/Fisher's exact test. Covariate balance was assessed using SMD (threshold < 0.10). Definitions: Medication Regimen: Primary maintenance therapy (NSAID vs. Hormonal). Clots: Patient-reported clots >1 cm in ≥50% of cycles. Hemodynamics: Measured during the follicular phase. Retroverted: Posteriorly tilted uterus on ultrasound.
Abbreviations: PSM, propensity score matching; SMD, standardized mean difference; PI, pulsatility index; RI, resistance index; VAS, visual analogue scale.

A 1:1 nearest-neighbor PSM algorithm (caliper 0.02) was applied to adjust for covariates. This process yielded 79 patient pairs (n=158) (Figure 1). Following PSM, baseline demographic, clinical, and hemodynamic characteristics did not differ significantly between the two groups, with all SMDs < 0.10. Regarding treatment adherence, patients in the matched intervention group completed a median of 11 acupuncture sessions (interquartile range: 10–12).

Changes in Endometrial Blood Flow Parameters

At baseline, uterine artery Doppler indices did not differ significantly between the groups (Table 1). Post-treatment evaluations showed that the intervention group had lower vascular resistance compared to the control group. Specifically, post-treatment PI (Mean Difference: −0.54, 95% CI: −0.66 to −0.42, $p < 0.001$) and RI (Mean Difference: −0.07, 95% CI: −0.09 to −0.05, $p < 0.001$) were significantly lower in the intervention group. Additionally, the post-treatment S/D ratio was lower in the intervention group (Mean Difference: −1.7, 95% CI: −2.0 to −1.4, $p < 0.001$), while post-treatment diastolic velocity was significantly higher (10.5 ± 3.0 vs. 9.1 ± 2.4 cm/s; $p < 0.001$) (Table 2 and Figure 2).

Pain Relief Outcomes

Longitudinal analysis of VAS scores demonstrated a significant group-by-time interaction ($p < 0.001$). At 1 month post-treatment, the intervention group reported significantly lower VAS scores compared to the control group (4.5 ± 1.1 vs. 6.3 ± 1.4), with a mean difference of −1.8 (95% CI: −2.2 to −1.4; $p < 0.001$). The difference between groups remained

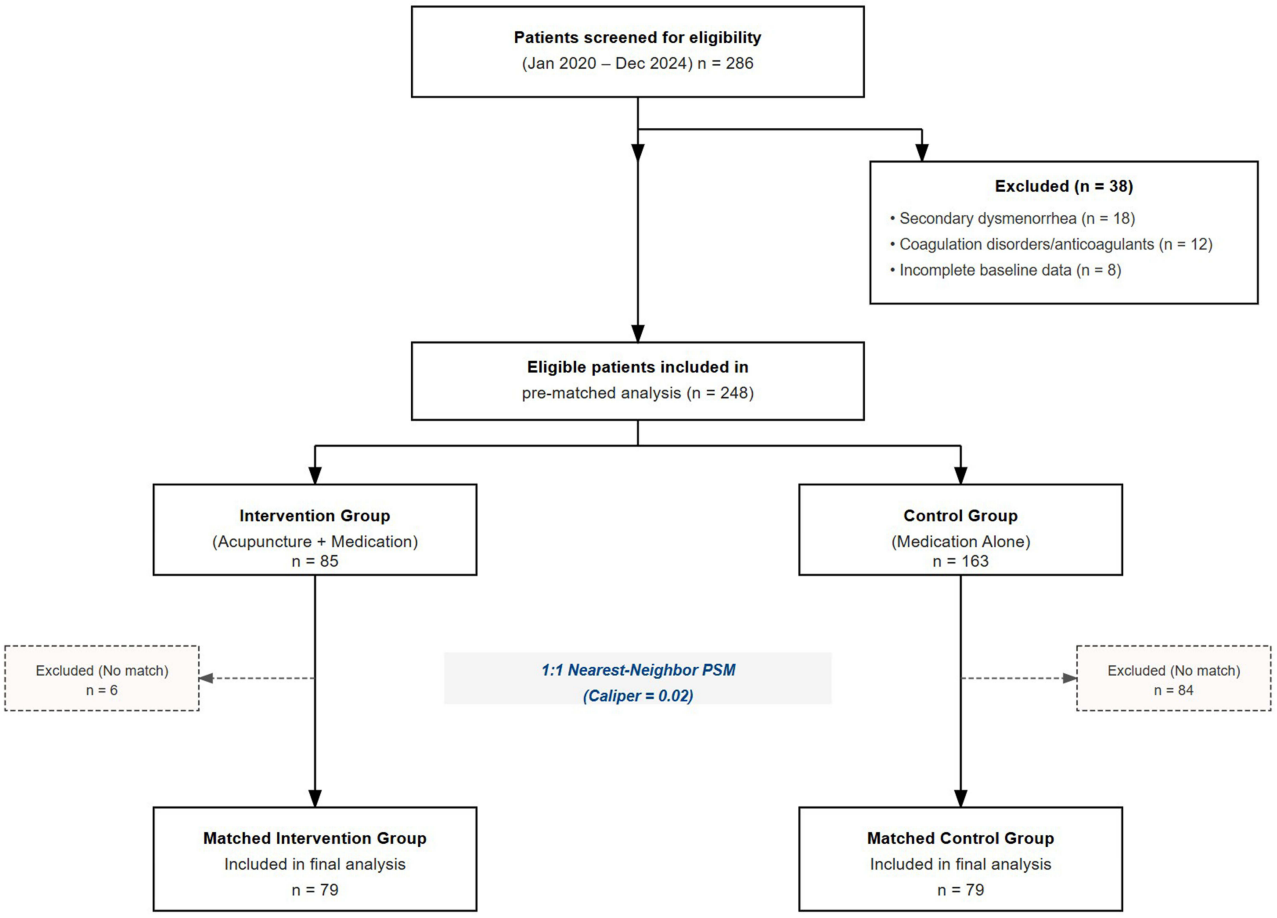

Figure 1 Flowchart of patient screening, eligibility assessment, propensity score matching process, and final cohort inclusion.

significant at 3 months (Mean Difference: −2.3, 95% CI: −2.7 to −1.9; p < 0.001). However, at the 6-month follow-up, VAS scores did not differ significantly between the two groups (4.9 ± 1.2 vs. 5.1 ± 1.3; p = 0.320) (Table 3 and Figure 3).

Duration of Symptoms and Frequency of Drug Use

At baseline, symptom duration and analgesic use did not differ significantly between the two groups (Table 4 and Figure 4). At 1 month post-treatment, the intervention group had a significantly shorter duration of menstrual symptoms compared to the control group (15.2 ± 3.2 vs. 15.8 ± 3.5 hours/cycle; Mean Difference: −0.6, 95% CI: −1.1 to −0.1; p < 0.001). Similarly, analgesic use was significantly lower in the intervention group at 1 month (4.1 ± 1.1 vs. 4.5 ± 1.3 doses/cycle; Mean Difference: −0.4, 95% CI: −0.7 to −0.1; p < 0.001). These differences between

Table 2 Comparison of Uterine Artery Doppler Indices Before and After Intervention

Parameter	Intervention Group (n=79)		Control Group (n=79)		Group Difference	
	Baseline	Post-Treatment	Baseline	Post-Treatment	Mean Diff (95% CI)	p-Value
Pulsatility Index (PI)	3.12 ± 0.45	2.31 ± 0.39	3.08 ± 0.42	2.85 ± 0.40	−0.54 (−0.66 to −0.42)	<0.001
Resistance Index (RI)	0.83 ± 0.06	0.71 ± 0.05	0.82 ± 0.07	0.78 ± 0.06	−0.07 (−0.09 to −0.05)	<0.001
S/D Ratio	6.5 ± 1.2	4.1 ± 0.9	6.4 ± 1.1	5.8 ± 1.0	−1.7 (−2.0 to −1.4)	<0.001
Diastolic Velocity (cm/s)	8.2 ± 2.1	10.5 ± 3.0	8.4 ± 2.3	9.1 ± 2.4	1.4 (0.6 to 2.2)	<0.001

Notes: Statistical notes: Data expressed as mean ± SD. Comparisons: Between-group differences at the post-treatment time point were analyzed using independent t-tests. Baseline values did not differ significantly (p > 0.05) via PSM.
Abbreviations: S/D, systolic/diastolic velocity ratio; CI, confidence interval; Diff, difference.

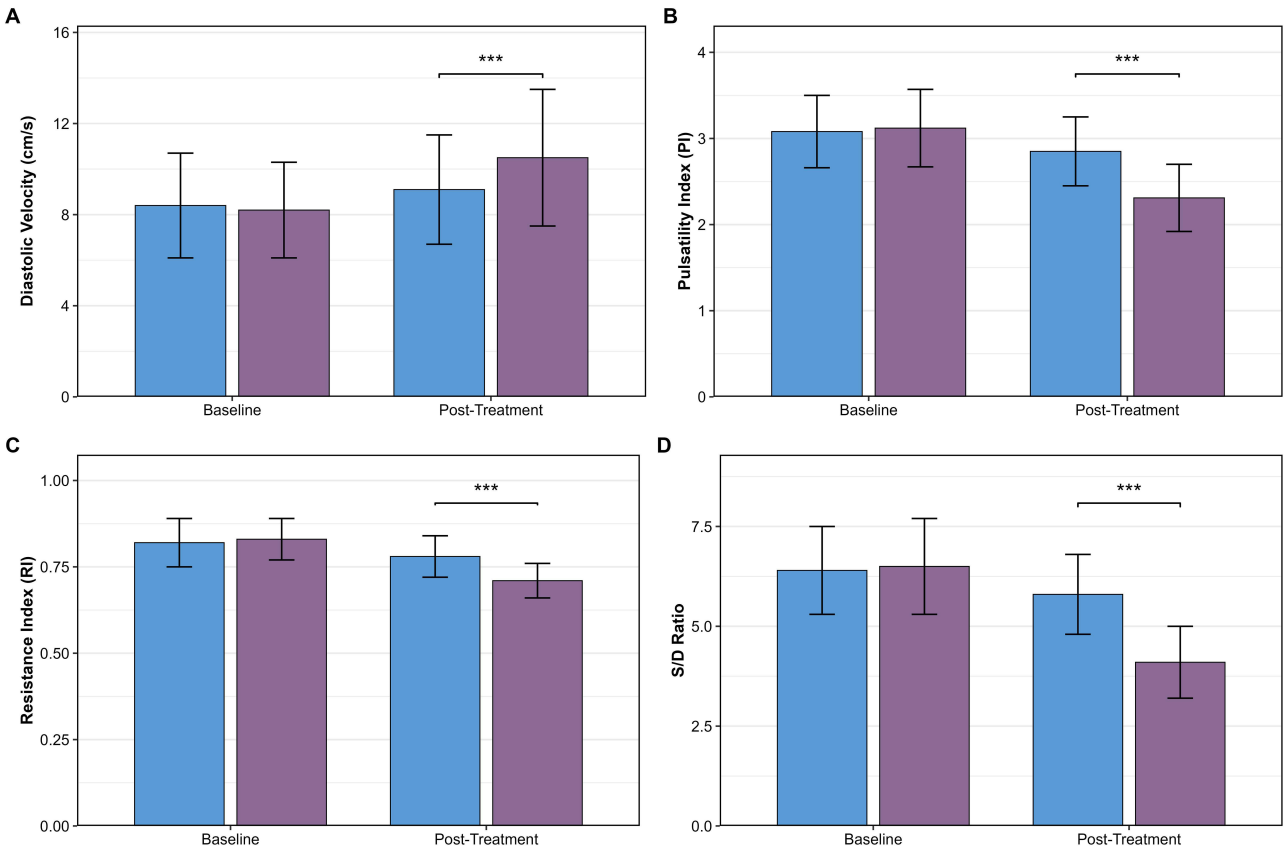

Figure 2 Comparison of Uterine Artery Doppler Indices Before and After Intervention. Bar graphs showing changes in (**A**) Pulsatility Index (PI), (**B**) Resistance Index (RI), (**C**) S/D Ratio, and (**D**) Diastolic Velocity (cm/s) comparing baseline and post-treatment values. Blue bars represent the control group and purple bars represent the intervention group. Error bars represent standard deviations. Between-group differences with p-values are shown for each parameter. *** $p < 0.001$.

groups remained significant at 3 months post-treatment ($p < 0.001$ for both outcomes). However, at the 6-month follow-up, symptom duration (12.7 ± 2.3 vs. 12.9 ± 2.5 hours/cycle; $p = 0.562$) and analgesic use (3.8 ± 1.1 vs. 3.8 ± 1.3 doses/cycle; $p = 0.953$) did not differ significantly between the groups (Table 4).

Correlation Analysis

A correlation analysis was performed to evaluate the relationship between the changes in uterine artery indices and the changes in VAS scores (Table 5 and Figure 5). A positive correlation was observed between the magnitude of PI reduction (ΔPI) and VAS reduction (ΔVAS) (Spearman's $r = 0.52$, 95% CI: 0.43–0.61; $p < 0.001$). Significant positive

Table 3 Longitudinal Changes in Visual Analogue Scale (VAS) Scores

Timepoint	Intervention Group (n=79)	Control Group (n=79)	Mean Difference (95% CI)	p-Value
Baseline	7.6 ± 1.3	7.5 ± 1.2	0.1 (−0.3 to 0.5)	0.621
1 Month Post-treatment	4.5 ± 1.1	6.3 ± 1.4	−1.8 (−2.2 to −1.4)	<0.001
Change from Baseline (Δ)	−3.1 ± 1.0	−1.2 ± 0.9	—	—
3 Months Post-treatment	3.6 ± 1.0	5.9 ± 1.3	−2.3 (−2.7 to −1.9)	<0.001
6 Months Post-treatment	4.9 ± 1.2	5.1 ± 1.3	−0.2 (−0.6 to 0.2)	0.320

Notes: Statistical notes: Data expressed as mean ± SD. Analysis: Group comparisons at each time point utilized independent t-tests. Longitudinal interaction effects (Group × Time) were confirmed significant ($p < 0.001$) using linear mixed-effects models. A negative mean difference indicates lower pain intensity in the intervention group.
Abbreviations: VAS, visual analogue scale (0–10); CI, confidence interval.

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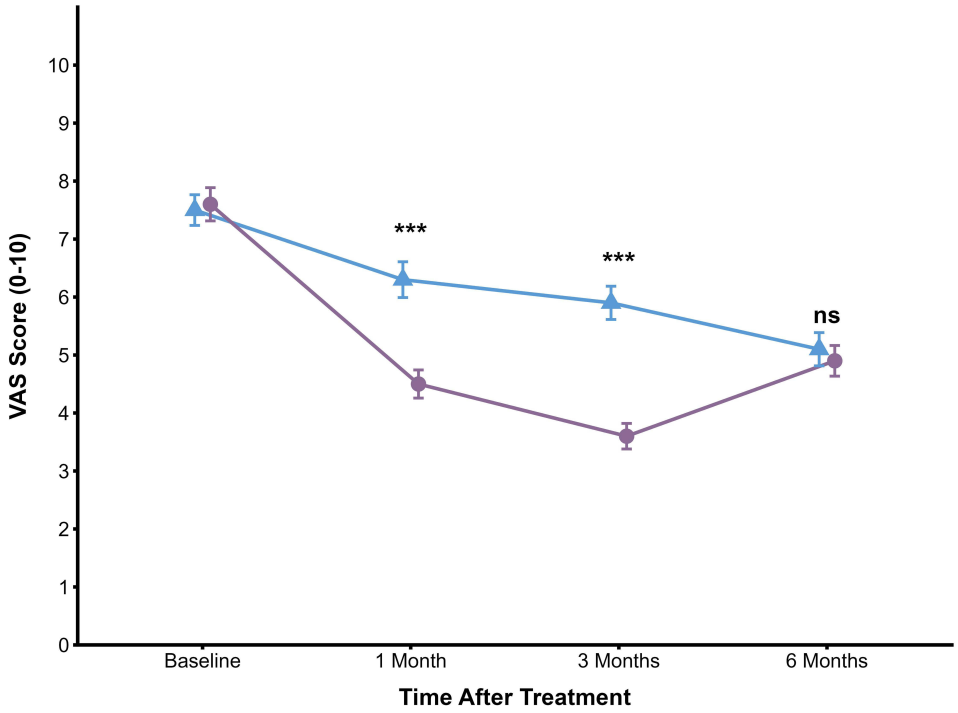

Figure 3 Changes in Visual Analogue Scale (VAS) Scores Over Time. Line graph showing changes in pain intensity across four time points (baseline, 1 month, 3 months, and 6 months). Blue triangles represent the control group and purple circles represent the intervention group. Error bars represent 95% confidence intervals. Linear mixed-effects models revealed a significant group × time interaction ($p < 0.001$). *** $p < 0.001$ vs. control group; ns, not significant.

correlations were also observed between ΔRI and ΔVAS ($r = 0.48$, 95% CI: 0.38–0.58; $p < 0.001$), as well as between the ΔS/D ratio and ΔVAS ($r = 0.45$, 95% CI: 0.35–0.55; $p < 0.001$).

Subgroup Analysis

Subgroup analyses indicated that age and disease duration had significant interaction effects with the intervention ($p = 0.013$ and $p = 0.038$, respectively) (Table 6). For age, the reduction in PI was greater in patients aged <30 years (Mean Difference in ΔPI: −0.34, 95% CI: −0.41 to −0.27) compared to those aged ≥30 years (Mean Difference in ΔPI: −0.09, 95% CI: −0.15 to −0.03). Regarding disease duration, the reduction in VAS scores was

Table 4 Changes in Symptom Duration and Analgesic Use Frequency

Outcome	Timepoint	Intervention Group (n=79)	Control Group (n=79)	Mean Difference (95% CI)	p-Value
Symptom Duration (hours/cycle)	Baseline	18.5 ± 4.1	18.2 ± 3.8	0.3 (−0.5 to 1.1)	0.511
	1 month post-treatment	15.2 ± 3.2	15.8 ± 3.5	−0.6 (−1.1 to −0.1)	<0.001
	3 months post-treatment	12.9 ± 2.7	13.9 ± 3.3	−1.0 (−1.6 to −0.4)	<0.001
	6 months post-treatment	12.7 ± 2.3	12.9 ± 2.5	−0.2 (−0.9 to 0.5)	0.562
Analgesic Use (doses/cycle)	Baseline	5.2 ± 1.8	5.1 ± 1.6	0.1 (−0.3 to 0.5)	0.625
	1 month post-treatment	4.1 ± 1.1	4.5 ± 1.3	−0.4 (−0.7 to −0.1)	<0.001
	3 months post-treatment	3.9 ± 0.9	4.2 ± 1.2	−0.3 (−0.6 to −0.0)	<0.001
	6 months post-treatment	3.8 ± 1.1	3.8 ± 1.3	0.0 (−0.4 to 0.4)	0.953

Notes: Statistical notes: Data expressed as mean ± SD. Comparisons: Between-group Mean Differences were calculated using independent t-tests at each time point. A negative mean difference indicates shorter symptom duration or fewer analgesic doses in the intervention group.
Abbreviation: CI, confidence interval.

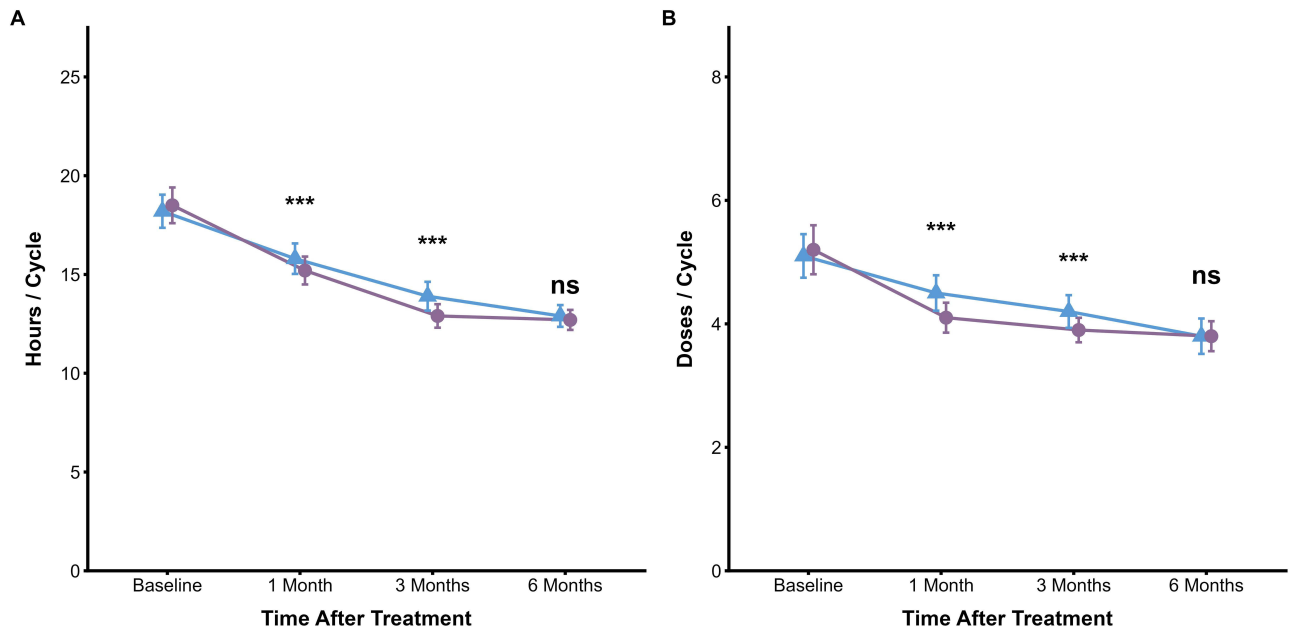

Figure 4 Changes in secondary outcomes over time. Line graphs showing changes in (**A**) symptom duration (Hours/Cycle) and (**B**) analgesic use (Doses/Cycle) across four time points. Blue triangles represent the control group and purple circles represent the intervention group. Error bars represent 95% confidence intervals. Between-group mean differences were assessed at each time point: *** $p < 0.001$ vs. control group; ns, not significant.

greater in patients with a disease duration <5 years (Mean Difference in ΔVAS: −3.3, 95% CI: −3.7 to −2.9) compared to patients with a duration ≥5 years (Mean Difference in ΔVAS: −2.3, 95% CI: −2.8 to −1.8).

Safety Assessment

In the intervention group, 5 out of 79 participants (6.3%) reported AEs, including localized subcutaneous bruising (n=3) and dizziness (n=2). All events resolved without medical intervention. No severe AEs were recorded. In the control group, 0 out of 79 participants reported AEs. The overall incidence of documented AEs did not differ significantly between the two groups ($p = 0.058$) (Table 7).

Sensitivity Analyses

Sensitivity analyses were performed using both CC and MI datasets. In the MI analysis (n=79 per group), VAS scores were significantly lower in the intervention group compared to the control group at 1 month (4.5 vs. 6.3; $p < 0.001$) and 3 months (3.6 vs. 5.9; $p < 0.001$). At 6 months, VAS scores did not differ significantly between the groups ($p = 0.320$). Similar statistical results were observed in the CC analysis (Intervention n=68; Control n=71) (Table 8). Additionally, the E-value sensitivity analysis yielded an E-value of 13.5 for the point estimate of the primary outcome (VAS at 1 month), with a lower confidence limit E-value of 7.2.

Table 5 Correlation Coefficients Between Hemodynamic Changes and Pain Relief (Δ)

Hemodynamic Parameter	Correlation with ΔVAS	95% CI	p-Value
ΔPulsatility Index (PI)	r = 0.52	0.43–0.61	<0.001
ΔResistance Index (RI)	r = 0.48	0.38–0.58	<0.001
ΔS/D Ratio	r = 0.45	0.35–0.55	<0.001

Notes: Spearman's rank correlation coefficients reported due to non-normal distribution of ΔPI/ΔVAS (Shapiro–Wilk $p < 0.05$).
Abbreviations: Δ, change from baseline to 6 months; CI, confidence interval.

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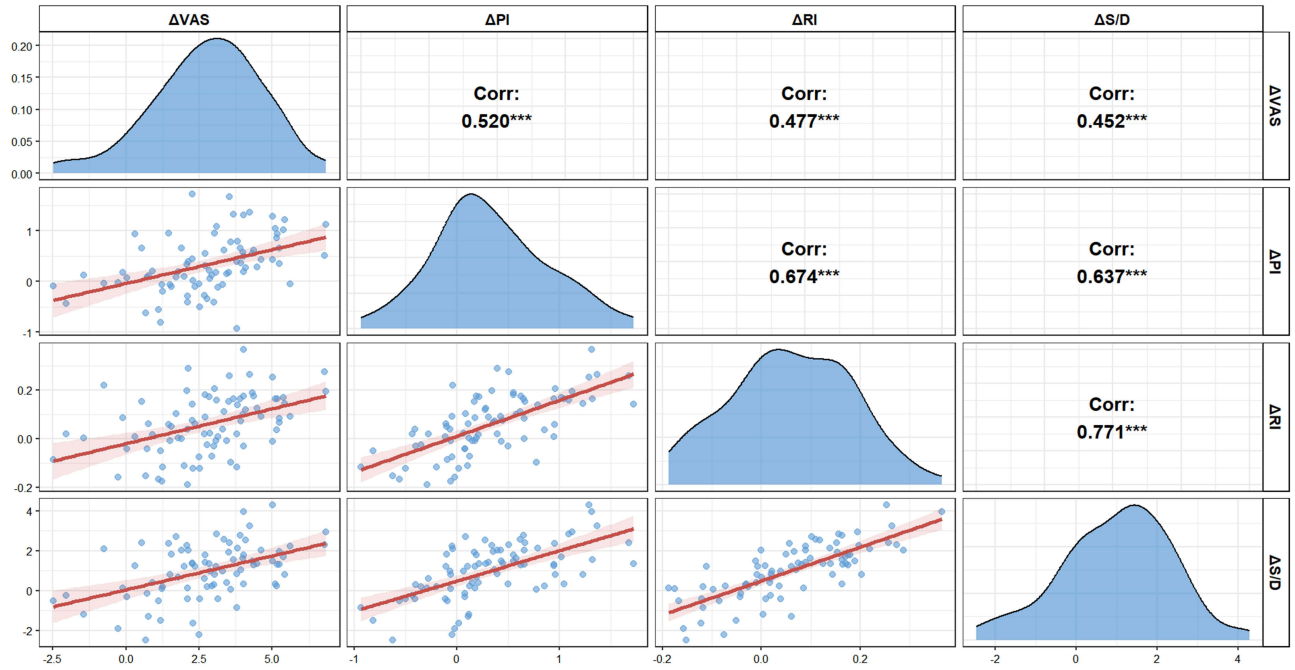

Figure 5 Correlation matrix showing relationships between changes in hemodynamic parameters and pain scores. The matrix displays scatterplots with fitted regression lines and 95% confidence bands (lower diagonal), distribution density histograms (diagonal), and Spearman's rank correlation coefficients (upper diagonal) for changes in Visual Analogue Scale (ΔVAS), Pulsatility Index (ΔPI), Resistance Index (ΔRI), and Systolic/Diastolic ratio (ΔS/D). *** $p < 0.001$.

Discussion

This retrospective cohort study, rigorously adjusted via PSM, suggests that the "Regulating Ren and Unblocking Du" acupuncture protocol, when combined with conventional pharmacological therapy, is associated with improved endometrial blood flow and reduced pain in patients with primary dysmenorrhea. By effectively balancing measured baseline confounders such as medication type and disease severity, our analysis helps to clarify the potential hemodynamic

Table 6 Subgroup Analysis of Treatment Effects by Age and Disease Duration

Subgroup	Intervention Group	Control Group	Mean Difference (95% CI)	p-Value	Interaction p
Age					0.013
<30 years (n=128)	ΔPI: −0.92 ± 0.21	ΔPI: −0.58 ± 0.19	−0.34 (−0.41 to −0.27)	<0.001	
≥30 years (n=70)	ΔPI: −0.61 ± 0.18	ΔPI: −0.52 ± 0.16	−0.09 (−0.15 to −0.03)	0.002	
Disease Duration					0.038
<5 years (n=202)	ΔVAS: −5.1 ± 1.0	ΔVAS: −1.8 ± 0.9	−3.3 (−3.7 to −2.9)	<0.001	
≥5 years (n=196)	ΔVAS: −3.8 ± 1.2	ΔVAS: −1.5 ± 1.1	−2.3 (−2.8 to −1.8)	<0.001	

Notes: Statistical notes: Interaction effects tested via generalized linear models with group × subgroup terms. All models adjusted for baseline BMI and menstrual cycle regularity.
Abbreviations: ΔPI, change in pulsatility index; ΔVAS, change in visual analogue scale.

Table 7 Adverse Events in the Intervention and Control Groups

Event Type	Intervention Group (n=79)	Control Group (n=79)	Statistics	p-Value
Local Bruising	3 (3.8%)	0 (0.0%)	FET	0.245
Dizziness	2 (2.5%)	0 (0.0%)	FET	0.497
Total Minor Events	5 (6.3%)	0 (0.0%)	FET	0.058
Severe Events	0 (0.0%)	0 (0.0%)	—	—

Notes: Statistical notes: Data expressed as frequency (%).
Abbreviation: FET, Fisher's exact test.

Table 8 Sensitivity Analysis of VAS Outcomes: Complete-Case vs. Multiple Imputation

Timepoint	Complete-Case Analysis		Multiple Imputation Analysis	
	Int (n=68)	Ctrl (n=71)	Intervention (n=79)	Control (n=79)
Baseline VAS	7.6 ± 1.3	7.5 ± 1.2	7.6 ± 1.3	7.5 ± 1.2
1 Month Post-treatment	4.4 ± 1.0	6.2 ± 1.3	4.5 ± 1.1	6.3 ± 1.4
Between-Group Δ (95% CI)	−1.8 (−2.2 to −1.4)	p < 0.001	−1.8 (−2.2 to −1.4)	p < 0.001
3 Months Post-treatment	3.5 ± 1.0	5.8 ± 1.4	3.6 ± 1.0	5.9 ± 1.3
Between-Group Δ (95% CI)	−2.3 (−2.7 to −1.9)	p < 0.001	−2.3 (−2.7 to −1.9)	p < 0.001
6 Months Post-treatment	4.8 ± 1.2	5.0 ± 1.4	4.9 ± 1.2	5.1 ± 1.3
Between-Group Δ (95% CI)	−0.2 (−0.6 to 0.2)	p = 0.35	−0.2 (−0.6 to 0.2)	p = 0.32

Notes: Statistical notes: Complete-case analysis included only participants with VAS data at all timepoints. Multiple imputation used fully conditional specification (FCS) with predictive mean matching (20 imputations). Between-group differences adjusted for baseline VAS and covariates (BMI, disease duration).
Abbreviations: VAS, visual analogue scale; CI, confidence interval; Δ, change from baseline.

contribution of acupuncture. The intervention group demonstrated pronounced reductions in uterine artery resistance indices, including PI, RI, and S/D ratio, which correlated strongly with decreased VAS scores and shorter menstrual pain duration. These findings align with emerging research highlighting acupuncture's potential dual role in modulating vascular function and pain pathways,[22] yet they also reveal a distinct temporal pattern characterized by rapid initial relief followed by a convergence of outcomes by six months post-treatment.

The observed hemodynamic improvements suggest that acupuncture may enhance endometrial perfusion by potentially reducing vascular resistance. This hypothesized mechanism is consistent with prior studies demonstrating that needling acupoints such as Guanyuan (CV4) and Sanyinjiao (SP6) increases uterine artery diastolic velocity, thereby mitigating ischemia-induced pain.[13] However, our study uniquely emphasizes the "Regulating Ren and Unblocking Du" protocol's focus on the Conception Vessel (Ren Mai) and Governor Vessel (Du Mai), meridians traditionally associated with reproductive health and Qi circulation. From a neurophysiological perspective, targeting GV3 (Yaoyangguan) and GV4 (Mingmen), located in the lumbosacral region, may induce segmental neuromodulation. This may inhibit excessive sympathetic outflow to the uterine arteries, thereby relieving vasospasm and restoring perfusion, a hypothesis supported by neuroimaging studies showing acupuncture-induced activation of the hypothalamic-pituitary-adrenal axis.[23]

Acupuncture has been shown to be effective in primary dysmenorrhea, supported by a large number of studies.[9,18,24] For instance, a 2018 study by Shetty et al demonstrated that acupuncture at SP6 significantly reduced pain intensity, as measured by the VAS, in patients with primary dysmenorrhea.[25] Our results demonstrated sustained pain relief in the intervention group at 6 months (ΔVAS >3 points), though the effect magnitude was less pronounced than the durable benefits reported in chronic pain populations by MacPherson et al[26] This divergence may reflect differences in pathophysiology (cyclic vs. persistent pain) and control interventions (active pharmacotherapy vs. sham/no treatment). Rather than indicating a failure of acupuncture, the gradual convergence of VAS scores between groups suggests that acupuncture may provide a critical "clinical window of opportunity." It appears to accelerate symptom control in the early cycles, when pharmacological agents alone may be slow to achieve maximal efficacy, thereby potentially breaking the "pain-ischemia-spasm" cycle rapidly. While the persistent hemodynamic improvements (eg., PI reduction) suggest acupuncture's biological durability, the clinical parity at six months implies that pharmacological accumulation eventually matches the initial burst of relief provided by acupuncture. Further studies should explore whether extended maintenance sessions enhance long-term efficacy in dysmenorrhea.[27] In our cohort, both groups exhibited comparable pain scores at six months, indicating that the superior additive benefit of acupuncture over conventional medication alone diminished over time. This temporal pattern suggests that while acupuncture provides vital short-term enhancements in pain relief, its effects may not persist without sustained intervention. These findings highlight the potential need for maintenance acupuncture sessions or integrative strategies combining acupuncture with behavioral therapies to prolong therapeutic benefits. Importantly, sensitivity analyses using multiple imputation and complete-case approaches confirmed the consistency of these trends, reinforcing that missing data did not substantially influence the conclusions.

The reduction in analgesic use within the intervention group highlights acupuncture's potential to decrease reliance on NSAIDs, which are associated with gastrointestinal and cardiovascular risks.[6,10] A cohort study found that integrating acupuncture with NSAIDs reduced medication use compared to NSAIDs alone, aligning with our findings.[28] Mechanistically, improved uterine perfusion may facilitate the rapid "washout" of local inflammatory metabolites and prostaglandins, thereby reducing the threshold for nociceptor activation. Additionally, acupuncture may suppress prostaglandin synthesis through the downregulation of cyclooxygenase-2 (COX-2) expression, as demonstrated in animal models.[29] Furthermore, the inclusion of Xuehai (SP10), an acupoint linked to blood stasis resolution, may enhance microcirculation and reduce inflammatory mediators, synergizing with pharmacological therapies to amplify pain relief.[30]

Exploratory subgroup analyses revealed that younger patients (<30 years) and those with shorter disease duration (<5 years) experienced greater hemodynamic and pain improvements. This age-dependent response may reflect preserved vascular elasticity and neuronal plasticity in younger individuals, allowing for more effective modulation of uterine blood flow.[31] Similarly, patients with shorter disease duration likely have less entrenched central sensitization, a phenomenon observed in chronic pain conditions where prolonged nociceptive input leads to irreversible neural remodeling.[32] These insights advocate for early intervention with acupuncture to maximize therapeutic outcomes, a strategy supported by the WHO's guidelines recommending acupuncture as a therapy for dysmenorrhea, including adolescent populations.[33]

The safety profile of acupuncture further strengthens its clinical utility. Only 6.1% of participants reported minor adverse events, such as localized bruising or transient dizziness, consistent with large-scale registries documenting acupuncture's favorable safety record.[9] In contrast, the control group's lack of documented medication-related adverse events may underestimate risks, as retrospective studies often fail to capture subjective symptoms like nausea or headaches. Prospective trials with active AE monitoring are needed to clarify this discrepancy.

Despite its strengths, this study has limitations. First, the retrospective design introduces selection bias and limits the control over unmeasured confounders. Although propensity score matching rigorously adjusts for measured covariates, it does not eliminate the possibility of residual confounding from unmeasured variables. However, our E-value sensitivity analysis demonstrated that an unmeasured confounder would need an exceptionally strong association (risk ratio > 7.2) with both the intervention and the outcome to completely nullify the observed analgesic benefits. Since such a magnitude of unmeasured confounding is highly improbable in realistic clinical settings, our core findings remain highly robust despite the observational nature of the study. Second, reliance on electronic health records limited our ability to assess subjective outcomes, such as quality of life or psychological distress, which are critical to comprehensive pain management. Third, the real-world clinical setting inherently precluded the implementation of blinding or sham acupuncture controls; thus, we cannot entirely isolate the specific physiological effects of the acupuncture protocol from potential non-specific placebo responses. Fourth, the single-center setting restricts generalizability, particularly to populations with diverse cultural or socioeconomic backgrounds. Fifth, our follow-up was restricted to six months due to the retrospective design, as real-world patients rarely return for extended routine monitoring once their symptoms improve. Consequently, the sustainability of the hemodynamic effects beyond this time point remains uncharacterized. Future multicenter prospective studies, ideally incorporating sham controls, extended follow-up periods (>6 months), and biomarkers like serum prostaglandins or inflammatory cytokines, could further validate our clinical findings and elucidate the underlying biochemical pathways.

Conclusion

In this retrospective cohort study, adding the "Regulating Ren and Unblocking Du" acupuncture protocol to conventional therapy was associated with rapid improvements in endometrial hemodynamics and early-phase pain control in primary dysmenorrhea. Mechanistically, targeting specific lumbosacral (eg., GV3, GV4) and lower abdominal acupoints may induce segmental neuromodulation, which aligns with our observation of reduced uterine vascular resistance. While exploratory analyses suggest this adjunctive approach particularly benefits younger patients, the clinical superiority over medication alone wanes over a six-month period. These findings underscore the value of integrating meridian-based acupuncture with standard care for rapid, hemodynamically supported symptom management, while highlighting the potential need for ongoing maintenance sessions to sustain long-term benefits.

Abbreviations

AEs, Adverse Events; BMI, Body Mass Index; CI, Confidence Interval; COX-2, Cyclooxygenase-2; CV, Conception Vessel (Ren Mai); GV, Governor Vessel (Du Mai); LMM, Linear Mixed-Effects Models; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs; PD, Primary Dysmenorrhea; PI, Pulsatility Index; PSM, Propensity Score Matching; RI, Resistance Index; S/D, Systolic/Diastolic velocity ratio; SD, Standard Deviation; SMD, Standardized Mean Difference; TCM, Traditional Chinese Medicine; VAS, Visual Analogue Scale.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was performed in accordance with the Declaration of Helsinki. Ethical approval was granted by the Institutional Ethics Committee of The Second Affiliated Hospital of Shaanxi University of Chinese Medicine (Approval No. LW2025007-9). The requirement for informed consent was waived by the Institutional Ethics Committee due to the retrospective and anonymized nature of the study.

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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The authors declare that they have no competing interests in this work.

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