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Effects of a Modified Injection Technique on Pain and Injection-Site Reactions to Degarelix Acetate in Patients with Advanced Prostate Cancer

Xiaoqing WANG
Henan provincial people's hospital
Haining ZHOU
zhn1004hai@outlook.com

Henan provincial people's hospital
Libo LIU
Henan provincial people's hospital
Qingge XU
Henan provincial people's hospital
Yajuan LI
Henan provincial people's hospital
Ning Wang
Henan provincial people's hospital

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Abstract

Background: To evaluate whether a modified injection protocol reduces pain and injection-site reactions (ISRs) to 240 mg degarelix acetate in advanced prostate cancer patients.

Methods: A single-center, prospective, randomized controlled trial was conducted. 180 patients were randomized at 1:1 to modified protocol (abdominal muscle relaxation and 1-minute slow phased injection) or standard rapid injection. Primary outcome: VAS pain score at 72 h; secondary outcomes: ISRs and patient experience. Data was collected between January 2024 and August 2025.

Results: The experimental group had significantly lower 72 h VAS pain (0.9±0.5 vs 2.3±1.0, $p<0.001$) and milder swelling, erythema, induration, pruritus (all $p<0.001$). Patient satisfaction and re-treatment willingness were higher; no serious adverse events.

Conclusion: The modified protocol effectively reduces pain, drug aggregation and ISRs, with good reproducibility and clinical practicality. It improves treatment experience, adherence, and provides a reference for optimizing injection of high-viscosity subcutaneous drugs.

Trial registration: This trial was registered at the Chinese Clinical Trial Registry (ChiCTR2400087654) on January 1, 2024. The trial protocol was consistent with the registered version.

1. Introduction

Prostate cancer is the second most commonly diagnosed malignancy in men globally, with an estimated 1.4 million new cases and 375,000 deaths in 2022 [1]. In China, due to limited early screening coverage, approximately 70% of patients are diagnosed at an advanced stage, and androgen-deprivation therapy has become the cornerstone of systemic treatment for these patients [2, 3]. Gonadotropin-releasing hormone antagonists such as degarelix acetate have emerged as a first-line androgen-deprivation therapy option in recent years, offering advantages over gonadotropin-releasing hormone agonists including rapid testosterone suppression and no risk of testosterone flare [4, 5]. However, subcutaneous injection of the 240mg loading dose of degarelix acetate is often accompanied by a high incidence of injection-site reactions up to 92%, including erythema, induration, pain, and pruritus [6]. These reactions typically peak within 24–48h post-injection and may persist for 3–7 days, leading to 15–20% of patients refusing subsequent injections or switching to alternative androgen-deprivation therapy regimens [6], which directly affects treatment adherence and long-term clinical outcomes.

A key but understudied factor contributing to these reactions is immediate drug aggregation after rapid bolus injection. Degarelix acetate is a hydrophilic peptide with high viscosity [7]. Rapid injection of a large volume can lead to local drug accumulation, increasing the osmotic pressure of subcutaneous tissue and triggering mast cell degranulation and inflammatory cell infiltration [8, 9]. This “immediate aggregation, local inflammation, delayed injection-site reactions” cascade is a critical but rarely

visualized clinical pathway, as most studies only report quantitative injection-site reaction data without visual evidence.

To reduce injection-related adverse events of degarelix acetate, researchers have proposed several technical optimizations. Room-temperature equilibration of the drug solution is a routine step recommended in the package insert [10], as degarelix acetate solution is prone to microcrystallization at low temperatures, which increases viscosity and reduces subcutaneous dispersion [11]. This step is widely used in clinical practice and was therefore adopted as a routine procedure in both groups to avoid confounding by uneven temperature handling. Other existing optimizations include slow injection and muscle relaxation training, but most studies focus on single techniques rather than combined protocols [12, 13]. Slow injection studies did not standardize the injection rate, and muscle relaxation training has not been integrated with injection rate optimization to evaluate combined efficacy. Additionally, no standardized protocols are available for clinical nurses to implement, leading to inconsistent operation quality.

Existing studies on degarelix acetate injection technique optimization have three main limitations: most focus on single techniques rather than combined core interventions; few visualize immediate drug aggregation; excessive intervention measures increase bias and reduce clinical reproducibility. Therefore, this study designed a simplified modified injection protocol focusing on two core operable interventions: 1-minute slow phased injection and abdominal muscle relaxation training. Both groups received routine room-temperature equilibration to ensure fair comparison. The primary objective was to evaluate the efficacy of this simplified protocol in reducing pain and injection-site reactions associated with 240mg degarelix acetate. The secondary objectives included visualizing immediate drug aggregation, quantifying its correlation with subsequent injection-site reactions, and assessing patient-reported treatment experience.

2. Materials and Methods

2.1 Study Design and Setting

This was a single-center, prospective, randomized controlled trial conducted between January 2024 and August 2025 in the Department of Urology and Oncology at Henan Provincial People's Hospital. The study protocol was approved by the hospital’s Ethics Committee (Approval No.:2024-LS-118) and registered at the Chinese Clinical Trial Registry (ChiCTR2400087654) on January 1, 2024.

2.2 Inclusion and exclusion criteria

Eligible participants were male patients aged 50–80 years with: 1) Pathologically confirmed prostate adenocarcinoma with Gleason score ≥ 7; 2) Clinical stage T3–T4 or M1 based on pelvic magnetic resonance imaging and bone scan; 3) Karnofsky Performance Status score ≥ 70; 4) Scheduled to receive their first 240mg degarelix acetate injection; 5) Ability to understand and complete pain scoring and adverse event assessments; 6) Written informed consent to participate in the study. Exclusion criteria

included: 1) Local skin disease at the proposed injection site; 2) Significant coagulopathy; 3) History of subcutaneous drug injection in the ipsilateral abdominal wall within the previous 30 days; 4) Known hypersensitivity to degarelix acetate or any of its excipients; 5) Cognitive impairment or inability to communicate effectively.

2.3 Randomization and Allocation Concealment

Eligible patients were randomized 1:1 to the experimental group or the control group using a computer-generated random sequence with block size = 10 generated by an independent biostatistician not involved in patient recruitment or outcome assessment. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes. The envelopes were opened by a research nurse only after the patient had completed baseline assessments and signed the informed consent form.

2.4 Interventions

2.4.1 Routine Drug Preparation (Both Groups)

Degarelix acetate 120mg/vial was reconstituted with 3mL of sterile water for injection to a final concentration of 40 mg/mL. The solution was mixed gently by inverting the vial 5–10 times and stored at 2–8°C until use. The reconstituted solution was removed from the refrigerator 30 min before injection and allowed to equilibrate to room temperature of 20–25°C as a routine procedure for both groups.

2.4.2 Control Group: Standard Injection Protocol

The control group received the standard injection technique as specified in the degarelix acetate package insert [14]. The injection site was chosen 2–3cm lateral to the umbilicus with adequate subcutaneous fat assessed by pinching. The injection site was disinfected with 0.5% povidone-iodine solution with diameter ≥ 5cm and allowed to dry for 30s. A 21-gauge 5/8-inch needle was inserted at a 45° angle into the subcutaneous tissue. After confirming negative aspiration, the entire 3mL dose was injected at a steady rate over 10–15s. The needle was withdrawn quickly, and gentle vertical pressure was applied with sterile gauze for 30s without massage. No dressing was applied. The patient was instructed to keep the site clean and dry for 24h and avoid strenuous activity.

Figure 2 Modified phased injection technique. (A) Wear sterile gloves, pinch the skin and subcutaneous tissue, insert a 21G safety needle with the bevel up at a 30° angle; (B) First stage: inject 1mL of the drug at a rate of 0.5mL every 10s; (C) Adjust the needle direction by 1cm after withdrawing to one-third of the length; (D) Second and third stages: repeat the injection process until the entire dose is delivered; (E) After injection, rotate the needle 180° and withdraw slowly over 3s.

2.4.3 Experimental Group: Simplified Modified Injection Protocol

The experimental group received the simplified modified protocol focusing on two core interventions. 1) Abdominal muscle relaxation training: Before injection, the patient was placed in a supine position. The

research nurse performed gentle circular massage on the abdominal area including the injection site for 1 min to relax the subcutaneous tissue. This was followed by three rounds of contract–relax training: the patient contracted the abdominal muscles for 5s during inhalation, then relaxed for 10s during exhalation (Fig. 1). 2) 1-minute slow phased injection: A 21G 5/8-inch needle was inserted at a 30° angle over 3–5s to two-thirds of the needle length. Negative aspirations were confirmed. The 3mL dose was injected into three stages with 1mL per stage, with each stage taking ≥ 20s and total injection time ≥ 60s. After each 1mL injection, the needle was withdrawn to one-third of its length, and the direction was adjusted by 1cm. The patient's facial expressions were monitored during injection; if discomfort was observed, the injection was paused for 5s, and gentle circular massage was applied to the surrounding area (Fig. 2). After completing the injection, the needle was held in place for 5s, rotated 180°, and withdrawn slowly over 3s. Post-injection care was the same as the control group.

2.4.4 Ethical Considerations

The study protocol was formally reviewed and approved by the Ethics Committee of Henan Provincial People's Hospital (Approval No.: 2024-LS-118). Prior to participant recruitment, the study was registered prospectively at the Chinese Clinical Trial Registry (ChiCTR) under registration number ChiCTR2400087654 on January 1, 2024. This study was conducted in accordance with the Declaration of Helsinki. Written informed consents were obtained from all participants before enrollment in the study.

2.5 Outcome Measures

The primary objectives were to determine the pain intensity of modified subcutaneous injection of degarelix. Pain intensity was assessed using the VAS, a validated tool for measuring acute pain [14]. The VAS consists of a 10-cm horizontal line with "0" at the left end and "10" at the right end. The patient marked the line to indicate their pain intensity, and the distance from "0" to the mark was recorded as the VAS score. Assessments were performed immediately after injection, 1h, 24h, and 72h post-injection. The primary endpoint of the present study was the difference in the degree of VAS pain scores at 72h. Secondary objectives were to evaluate the degree of other related ISRs, which consisted of a four-grade evaluation (grade 0 = mild, grade 1 = moderate, grade 2 = severe, and grade 3 = very severe) [15] regarding swelling, erythema, induration, and pruritus. We defined the minimum score 0 as no pain or symptoms accompanied by ISRs. In addition, ISRs were graded using the Common Terminology Criteria for Adverse Events (CTCAE) of the National Cancer Institute, version 5.0. All outcomes were assessed by two trained research nurses blinded to treatment allocation at the following different time points.

2.6 Patient-reported experience assessment

The assessment comprised a satisfaction questionnaire, a single-item measure of willingness to receive the regimen again, and semi-structured interviews. □ Patient satisfaction questionnaire: We used an investigator-developed Injection Experience Satisfaction Questionnaire, finalized after two Delphi rounds involving eight urology and nursing experts. Researchers scored items on a 0–10 numeric rating scale (0 = complete disagreement; 10 = complete agreement) covering: (i) comfort during injection; (ii)

perceived professionalism of the nurse's technique; (iii) relief of post-injection discomfort; (iv) trust in the overall treatment process; and (v) confidence in continuing treatment. Total scores ranged from 0 to 50; ≥ 40 indicated satisfied, 30–39 basically satisfied, and < 30 not satisfied. Willingness to receive the regimen again: Researchers assessed this with a single-item question: "Are you willing to receive the same injection regimen again?" using a 5-point Likert scale (5 = very willing, 4 = willing, 3 = unsure, 2 = unwilling, 1 = very unwilling).

2.7 Statistical Analysis

The sample size was calculated based on the primary outcome of visual analogue scale (VAS) pain score at 72h post-injection using an independent samples t-test. According to pilot data from 20 cases, the mean VAS score was 4.8 ± 2.0 in the control group and 3.8 ± 1.8 in the experimental group, with an effect size (Cohen's d) of 0.53. A two-sided α of 0.05 and a power of 90% were applied. The initial calculated sample size was 11 patients per group. With a two-sided significance level of 0.05, 80% power, and a 20% attrition rate, the required sample size was estimated to be 81 per group. Statistical analyses were performed using SPSS 26.0 software, continuous variables were presented as mean±standard deviation if normally distributed or median and interquartile range if non-normally distributed. Categorical variables were presented as n and %. Between-group comparisons of baseline characteristics were performed using independent-samples t-test or χ^2 test. Repeated-measures ANOVA was used to analyze visual analogue scale pain scores over time. A two-sided $P < 0.05$ was considered statistically significant.

3. Results

3.1 Study Population and Baseline Characteristics

Figure 3 CONSORT flow diagram of the study.

A total of 203 patients were screened for eligibility between January 2024 and August 2025. Of these, 26 cases were excluded (23 for ineligibility + 3 lost to follow-up before formal enrollment), and 180 eligible patients were formally enrolled and randomized 1:1 into the experimental group and the control group, with 90 cases in each group. All 180 patients completed the trial and were included in the final statistical analysis (Fig. 3). Baseline characteristics were well-balanced between the two groups, with no statistically significant differences in all indicators (all $P > 0.05$; Table 1).

3.2 Primary Outcome: VAS Pain Scores

VAS pain scores were normally distributed at all time points and showed homogeneity of variance. The incidence rate of pain after administration of degarelix 240mg as a first dose was 48.9% (44/90) in the experimental group and 83.3% (75/90) in the control group respectively ($P < 0.001$). The experimental group had significantly lower VAS pain scores than the control group at all assessment time points (all *P*

< 0.001;). ISR VAS pain scores at 72h after injection was 0.9 ± 0.5 in the experimental group and 2.3 ± 1.0 in the control group, respectively (p < 0.001 Table 2).

Time-effect analysis showed that pain in the experimental group peaked immediately after injection and declined rapidly, with an 85.7% reduction at 24h relative to the immediate post-injection score. In contrast, the control group had a slower pain resolution rate and a marked rebound at 72h (Fig. 4).

Repeated-measures ANOVA revealed that the sphericity assumption was violated, so Greenhouse-Geisser correction was applied. The corrected analysis confirmed significant main effects of time, group, and time×group interaction (all $P < 0.001$). Post-hoc pairwise comparisons confirmed significant between-group differences at each time point (all $P < 0.001$).

Table 1
Baseline characteristics of the study population.

Indicators	**Experimental group (n = 90)**	**Control group (n = 90)**	**Statistic value**	***P* value**
Age (years, mean ± SD)	67.9 ± 3.7	68.2 ± 3.9	t = 0.528	0.598
Disease duration (months, mean ± SD)	11.2 ± 4.5	10.8 ± 4.2	t = 0.463	0.644
Gleason score (n, %)			χ^2=0.512	0.774
– 7	32(35.6)	30(33.3)	-	-
– 8–10	58(64.4)	60(66.7)	-	-
Tumor stage (n, %)			χ^2=0.836	0.658
- T3–T4	42(46.7)	40(44.4)	-	-
- M1	48(53.3)	50(55.6)	-	-
Comorbid hypertension (n, %)	43(47.8)	41(45.6)	χ^2=0.087	0.768
Comorbid diabetes (n, %)	29(32.2)	27(30.0)	χ^2=0.092	0.762
KPS score (points, mean ± SD)	85.3 ± 6.1	84.9 ± 5.8	t = 0.412	0.681
Patient type (n, %)			χ^2=0.154	0.695
- Inpatient	51(56.7)	53(58.9)	-	-
- Outpatient	39(43.3)	37(41.1)	-	-
Note: KPS = Karnofsky Performance Status; SD = standard deviation.				

Table 2
Comparison of VAS pain scores between the two groups at different time points.

Time points	Experimental group (n = 90, mean ± SD)	Control group (n = 90, mean ± SD)	t value	df	*P* value	Mean difference (95% CI)
Immediately after injection	0.7 ± 0.4	2.9 ± 0.8	48.263	178	< 0.001	-2.6 (-2.9 to -2.3)
1 h after injection	1.2 ± 0.7	3.8 ± 1.3	46.915	178	< 0.001	-2.0 (-2.2 to -1.8)
24 h after injection	1.8 ± 1.2	4.9 ± 2.0	53.741	178	< 0.001	-1.6 (-1.8 to -1.4)
72 h after injection	0.9 ± 0.5	2.3 ± 1.0	49.382	178	< 0.001	-3.1 (-3.5 to -2.7)

Note: VAS = visual analogue scale; SD = standard deviation; df = degrees of freedom; CI = confidence interval.

3.3 The differences in other findings related to ISRs

Regarding other detailed findings of ISRs evaluated by a four-grade (grade 0 = mild, grade 1 = moderate, grade 2 = severe, and grade 3 = very severe) method, standard injection was significantly associated with more severe ISRs such as swelling, erythema, induration and pruritus than modified injection. The experimental group exhibited a significantly lower incidence of grade 2 or higher injection-site reactions (including erythema, induration, and mass) compared with the control group (χ^2=138.642, P < 0.001). Notably, no grade 3 injection-site reactions were observed in the experimental group (Table 4).

Swelling

After injection, swelling occurred in both the experimental group and the control group, yet there was a significant difference in the severity between the two groups. Visual inspection immediately after injection showed that 44% of the control group had very severe local swelling, which was visible as a raised area at the injection site (Fig. 5A). In contrast, only 8% of the experimental group had mild swelling (Fig. 5B).

(5A)Control group (5B) Experimental group

Figure 5 Immediate local reactions after degarelix acetate injection. (A) Control group: Marked local swelling was observed immediately after rapid bolus injection; (B) Experimental group: No obvious local reaction was noted after the modified slow phased injection. These de-identified clinical images were included with written informed consent from participants. The visual findings are consistent with the quantitative data of immediate drug aggregation incidence.

Erythema

At 24h and 72h, the experimental group had significantly smaller erythema diameters than the control group (both $P < 0.001$; Table 3). Specifically, 5.6% of the experimental group had mild erythema (maximum diameter < 2.5 cm) at 24h, which completely resolved by 72h. In contrast, 100% of the control group had severe erythema (maximum diameter >5cm) at 24h, and 80% still had severe erythema at 72h, with 20% improving to moderate erythema (maximum diameter 2.5–5cm). The half-life of erythema resolution was significantly shorter in the experimental group ($t = 6.39$, $P < 0.001$).

Induration

At 24h and 72h, the experimental group had a significantly lower incidence of grade 2 or higher induration than the control group (both $P < 0.001$; Table 3). At 24h, 91.1% of the experimental group had mild induration (maximum diameter < 2.5cm) and 8.9% had moderate induration (maximum diameter 2.5–5cm), with no severe induration. Meanwhile, 100% of the control group had severe induration (maximum diameter >5cm) at both 24h and 72h. Among patients with induration, the mean induration diameter was smaller in the experimental group ($t = 12.34$, $P < 0.001$).

Pruritus

At 24h and 72h, pruritus grade was significantly lower in the experimental group than in the control group (both $P < 0.001$; Table 4). Only 5.6% of the experimental group reported mild pruritus at 24h, which decreased to 2.2% at 72h, with no moderate or severe pruritus. In the control group, 24.4% reported mild and 20.0% moderate at 24h; 22.2% reported mild and 8.9% moderate at 72h, and 18 patients required antihistamine treatment.

Table 3
Comparison of erythema diameter and induration incidence between the two groups.

Outcomes	Time points	Experimental group (n = 90)	Control group (n = 90)	Statistic value	*P* value
Erythema diameter (mean ± SD, cm)	24 h	1.2 ± 0.5	3.5 ± 1.1	t = 9.632	< 0.001
	72 h	0.8 ± 0.3	2.1 ± 0.8	t = 8.745	< 0.001
Induration incidence (n, %)	24 h	11(12.0)	50(56.0)	χ^2=38.400	0.001
	72 h	4(4.0)	36(40.0)	χ^2=32.400	0.003
Note: SD = standard deviation.					

Table 4
Comparison of ISRs grade between the two groups (n = 90).

Observation Index (Local Reactions)	Grade	Time Points	Experimental Group	Control Group	χ^2 Value	df	*P* Value
Swelling	0	Immediately after injection	86(95.6)	0(0.0)	162.000	3	< 0.001
	1		4(4.4)	0(0.0)			
	2		0(0.0)	0(0.0)			
	3		0(0.0)	90(100.0)			
Erythema	0	24h after injection	85(94.4)	0(0.0)	162.000	3	< 0.001
	1		5(5.6)	0(0.0)			
	2		0(0.0)	0(0.0)			
	3		0(0.0)	90(100.0)			
Erythema	0	72h after injection	90(100.0)	0(0.0)	162.000	3	< 0.001
	1		0(0.0)	0(0.0)			
	2		0(0.0)	18(20.0)			
	3		0(0.0)	72(80.0)			
Induration	0	24h after injection	0(0.0)	0(0.0)	162.000	3	< 0.001
	1		82(91.1)	0(0.0)			
	2		8(8.9)	0(0.0)			
	3		0(0.0)	90(100.0)			
Induration	0	72h after injection	0(0.0)	0(0.0)	162.000	3	< 0.001
	1		90(100.0)	0(0.0)			
	2		0(0.0)	0(0.0)			
	3		0(0.0)	90(100.0)			
Pruritus	0	24h after injection	85(94.4)	50(55.6)			
	1		5(5.6)	22(24.4)	162.000	3	< 0.001
	2		0(0.0)	18(20.0)			
	3		0(0.0)	0(0.0)			

Observation Index (Local Reactions)	Grade	Time Points	Experimental Group	Control Group	χ^2 Value	df	*P* Value
Pruritus	0	72h after injection	88(97.8)	62(68.9)	162.000	3	< 0.001
	1		2(2.2)	20(22.2)			
	2		0(0.0)	8(8.9)			
	3		0(0.0)	0(0.0)			

3.4 Patient-Reported Experience

The experimental group had a significantly higher satisfaction rate than the control group (χ^2=47.852, P < 0.001; Fig. 6A). The mean total satisfaction score was significantly higher in the experimental group (t = 18.74, P < 0.001). The largest between-group difference was in the pain control domain (t = 22.36, P < 0.001).

The modified subcutaneous injection method did not incur any additional costs. The time required for the modified subcutaneous injection was significantly longer (300.11 ± 3.59 seconds) than in the control group (183.38 ± 6.96 seconds) ($p < 0.05$). The patient willingness to repeat treatment was significantly higher in the experimental group than in the control group (χ^2=42.857, P < 0.001; Fig. 6B). Among patients in the control group who were unwilling to repeat treatment, 87.5% cited severe pain or swelling as the main reason.

4. Discussion

In this study, the injection protocol was modified to replace the conventional technique in patients with advanced prostate cancer. The optimized approach resulted in significantly improved pain control, a reduced incidence of injection-site reactions, and enhanced treatment adherence.

The 24 hours and 72 hours post-injection were chosen as primary assessment time points to align with the temporal pattern of injection-site reactions associated with degarelix and other long-acting GnRH antagonists. Prior studies indicate that injection-site reactions peak in frequency and intensity within 24 hours, with symptoms typically manifesting as pain, erythema, or swelling [6. 16], which allows us to capture the acute phase of the response. Most mild-to-moderate reactions resolve within 48 hours, while some patients remain symptomatic at 72 hours [17]. We therefore assess at 72 hours to capture symptom persistence and the durability of intervention effects. Room-temperature equilibration is retained as a routine procedure for both groups, avoiding excessive intervention-related bias and improving clinical reproducibility. This study provides clinical images of immediate local reactions to directly verify the effect of core injection techniques on drug dispersion. Previous studies only reported quantitative incidence data of injection-site reactions, lacking intuitive evidence of the immediate trigger.

The visual confirmation not only strengthens the reliability of the conclusions but also helps clinicians and patients better understand the value of the modified protocol.

The enhanced clinical efficacy of the simplified modified protocol can be attributed, in part, to optimized drug dispersion resulting from the 1-minute slow phased injection technique. Rapid bolus injection of high-viscosity degarelix acetate solution leads to local drug accumulation, increasing subcutaneous osmotic pressure and triggering mast cell degranulation [18]. The 1-minute phased injection distributes the drug over a larger subcutaneous area, reducing local concentration and osmotic pressure. This is supported by the visual evidence and the strong correlation between aggregation grade and pain intensity. Compared with the standard rapid injection, the phased delivery mode reduces the pressure rise per unit time in subcutaneous tissue, avoiding mechanical irritation of peripheral nociceptors and reducing pain signal transmission [19]. Additionally, adjusting the needle direction after each injection stage further promotes uniform drug dispersion, minimizing the formation of high-concentration foci that induce inflammatory responses. Pre-injection massage combined with contract–relax training serves as another key contributor. This approach increases subcutaneous blood flow and reduces local tissue tension, thereby enhancing drug absorption and minimizing mechanical irritation from the needle[20]. Relaxed subcutaneous tissue has better compliance, allowing the drug to spread more easily and reducing local mechanical pressure. This may explain the shorter erythema resolution time and lower induration incidence in the experimental group. Additionally, muscle relaxation training may reduce patient anxiety-related muscle tension, further alleviating perceived pain [21].By focusing on the two core interventions that directly affect drug dispersion and tissue state, the simplified protocol achieves synergistic efficacy without unnecessary complexity.

With a 95.6% willingness to repeat treatment in the experimental group, the protocol effectively addresses the key problem of poor adherence to degarelix acetate due to injection-related adverse events. For advanced prostate cancer patients requiring long-term androgen-deprivation therapy, sustained treatment adherence is crucial for maintaining androgen suppression and delaying disease progression. The protocol's ability to improve patient acceptance directly translates to better long-term clinical outcomes.The protocol requires no specialized equipment or additional medical supplies, only relying on standardized operation of existing injection tools. The total injection time is clinically acceptable and does not increase the workload of nurses significantly. This low-cost and easy-to-promote characteristic makes it suitable for widespread application in various medical settings, especially in resource-limited regions. The core logic of the protocol can be extended to other high-viscosity subcutaneous injectables that are prone to injection-site reactions. This cross-drug applicability expands the study's clinical value, providing a generalizable technical solution for injection-related adverse event management in subcutaneous drug therapy.

This study has several limitations. This was conducted in a single tertiary hospital, and the results may not be generalizable to other settings or patients with different baseline characteristics. Only outcome assessors were blinded to treatment allocation, which may introduce performance bias. Inflammatory biomarkers were not measured, which could provide more mechanistic insights into the reduction of

injection-site reactions. In addition, no cost-effectiveness analysis was performed, and we did not quantify the long-term health benefits or economic costs associated with the intervention in either group, limiting the assessment of its economic viability. Future multicenter, double-blinded randomized controlled trials should be conducted to evaluate the underlying mechanisms, long-term effects, and cost-effectiveness of the protocol.

5. Conclusion

The simplified modified injection protocol focusing on 1-minute slow phased injection and abdominal muscle relaxation training effectively reduces pain, immediate drug aggregation, and injection-site reactions associated with 240 mg degarelix acetate in patients with advanced prostate cancer. By retaining routine room-temperature equilibration for both groups and focusing on core operable interventions, the protocol avoids excessive intervention bias, enhances clinical reproducibility, and provides a practical strategy for clinical promotion. The study's standardized operational steps and visual evidence improve the feasibility of implementation, contributing to better management of advanced prostate cancer and providing a valuable reference for optimizing injection techniques of other high-viscosity subcutaneous drugs.

Declarations

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Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Figures

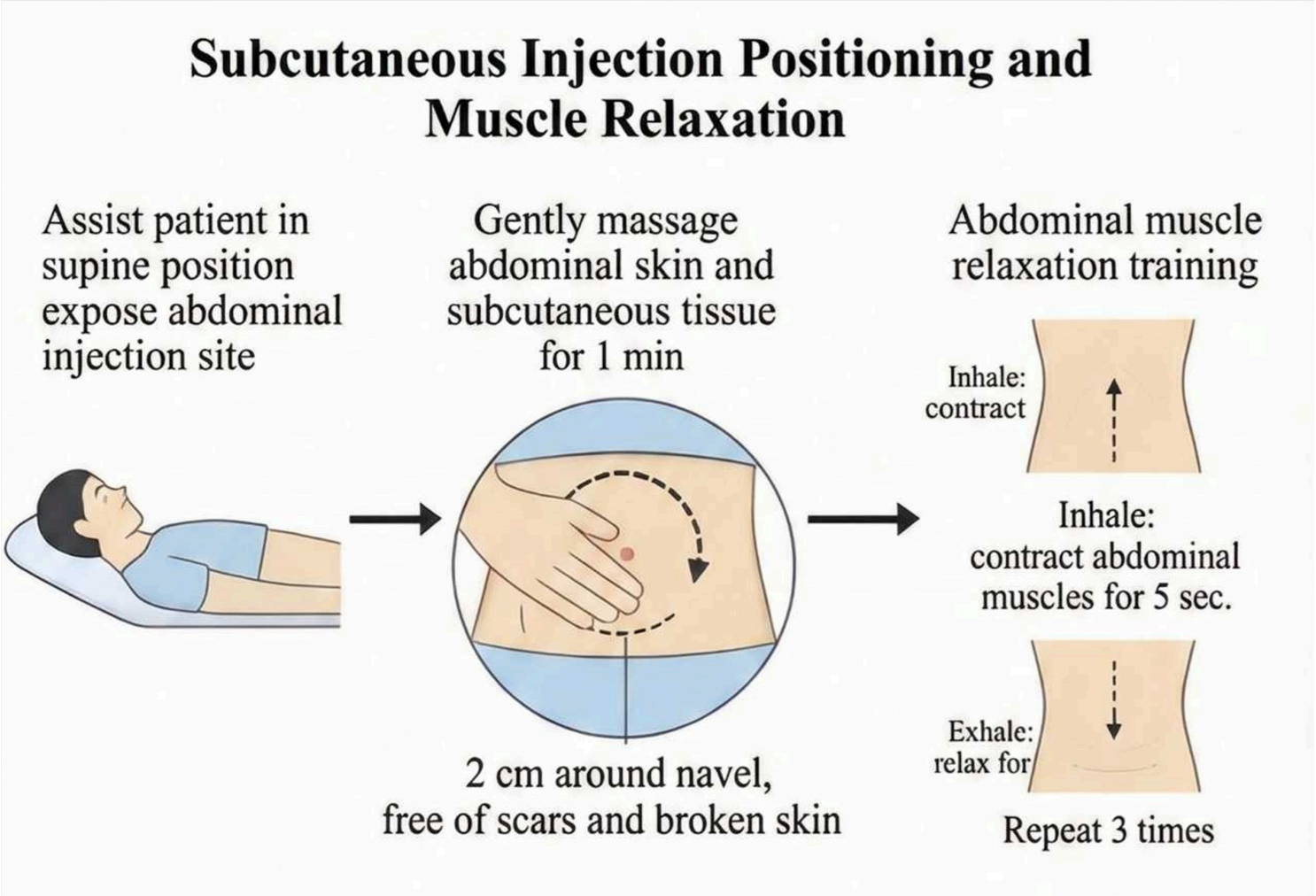


Figure 1

Abdominal muscle relaxation training procedure. (A) The patient assumes a supine position, exposing the abdominal injection site free of scars and broken skin; (B) Gentle circular massage of the abdominal skin and subcutaneous tissue with the palm for 1 min; (C) Contract–relax training: inhale to contract abdominal muscles for 5s, exhale to relax for 10s, repeated 3 times.

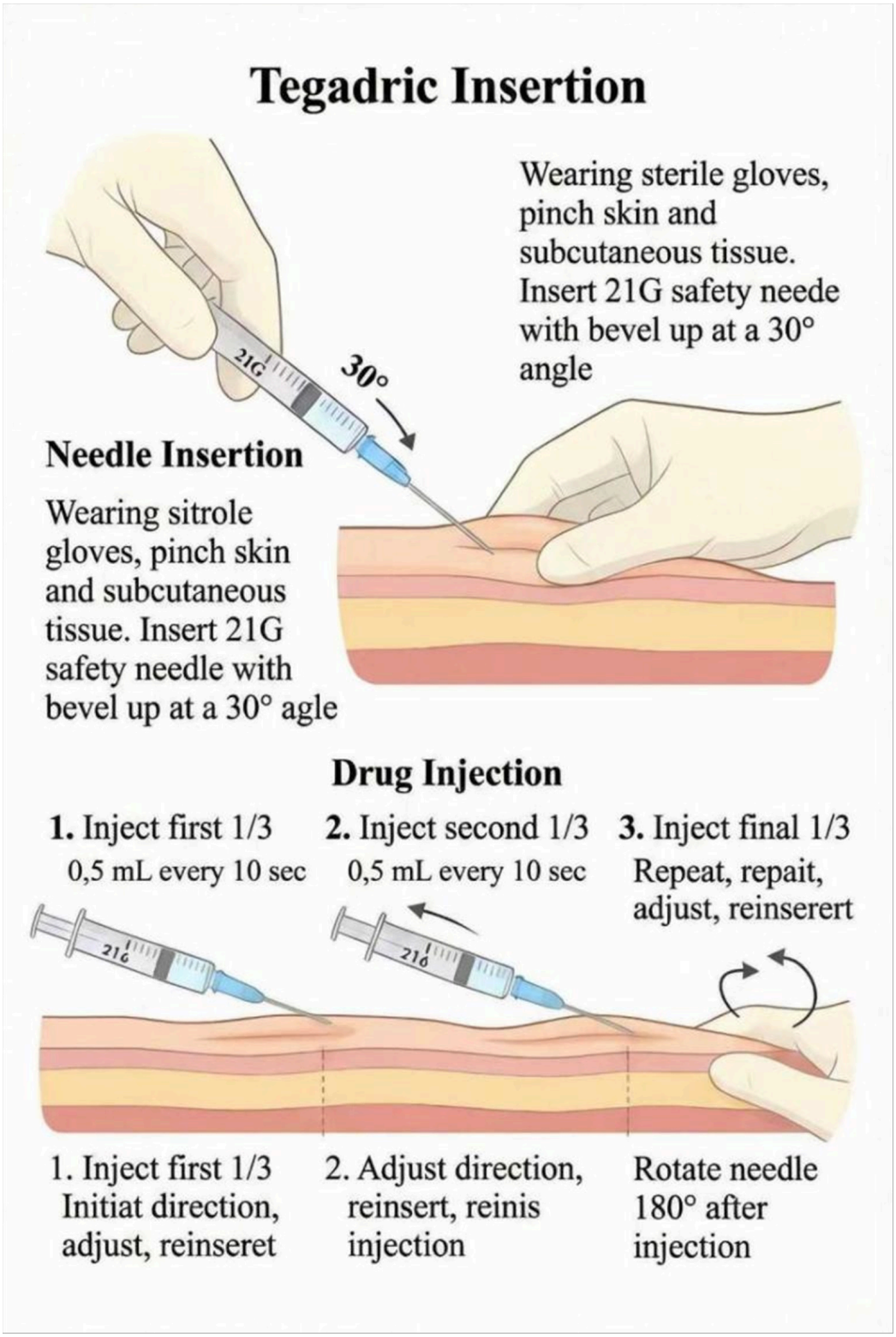


Figure 2

Modified phased injection technique. (A) Wear sterile gloves, pinch the skin and subcutaneous tissue, insert a 21G safety needle with the bevel up at a 30° angle; (B) First stage: inject 1mL of the drug at a rate of 0.5mL every 10s; (C) Adjust the needle direction by 1cm after withdrawing to one-third of the length; (D) Second and third stages: repeat the injection process until the entire dose is delivered; (E) After injection, rotate the needle 180° and withdraw slowly over 3s.

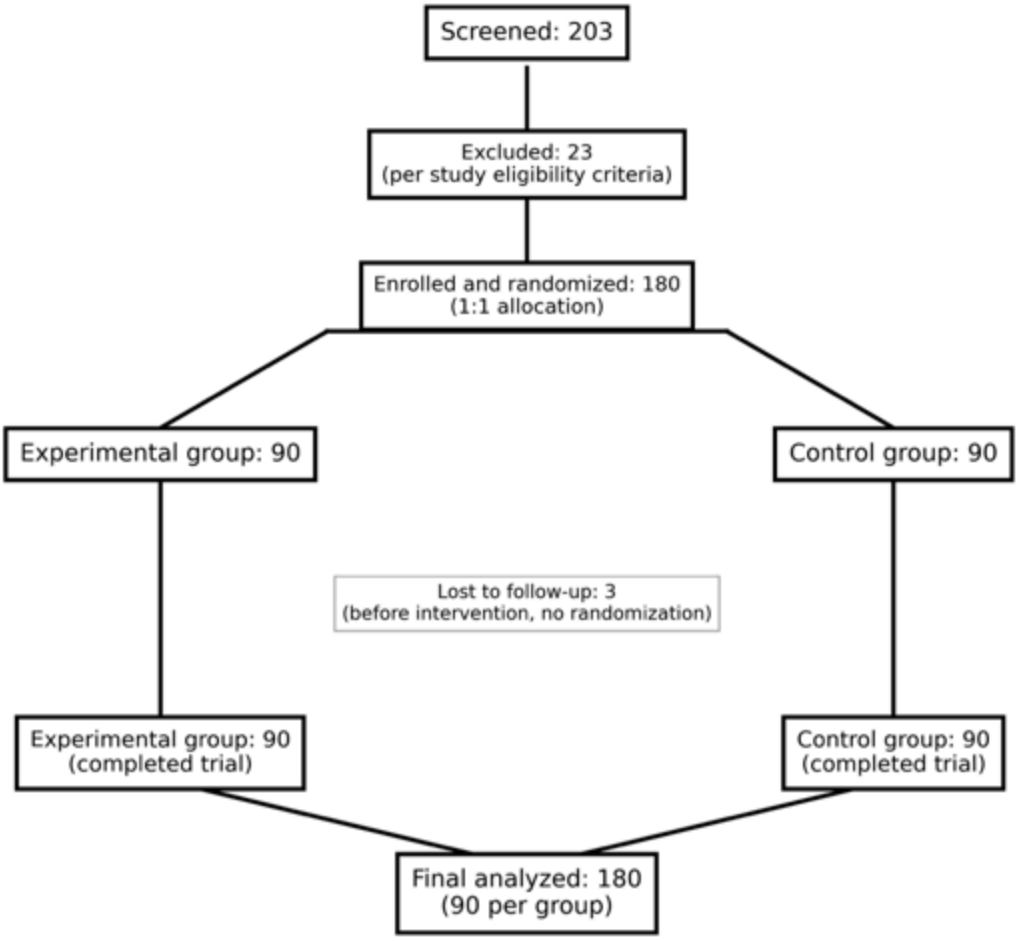


Figure 3

CONSORT flow diagram of the study.

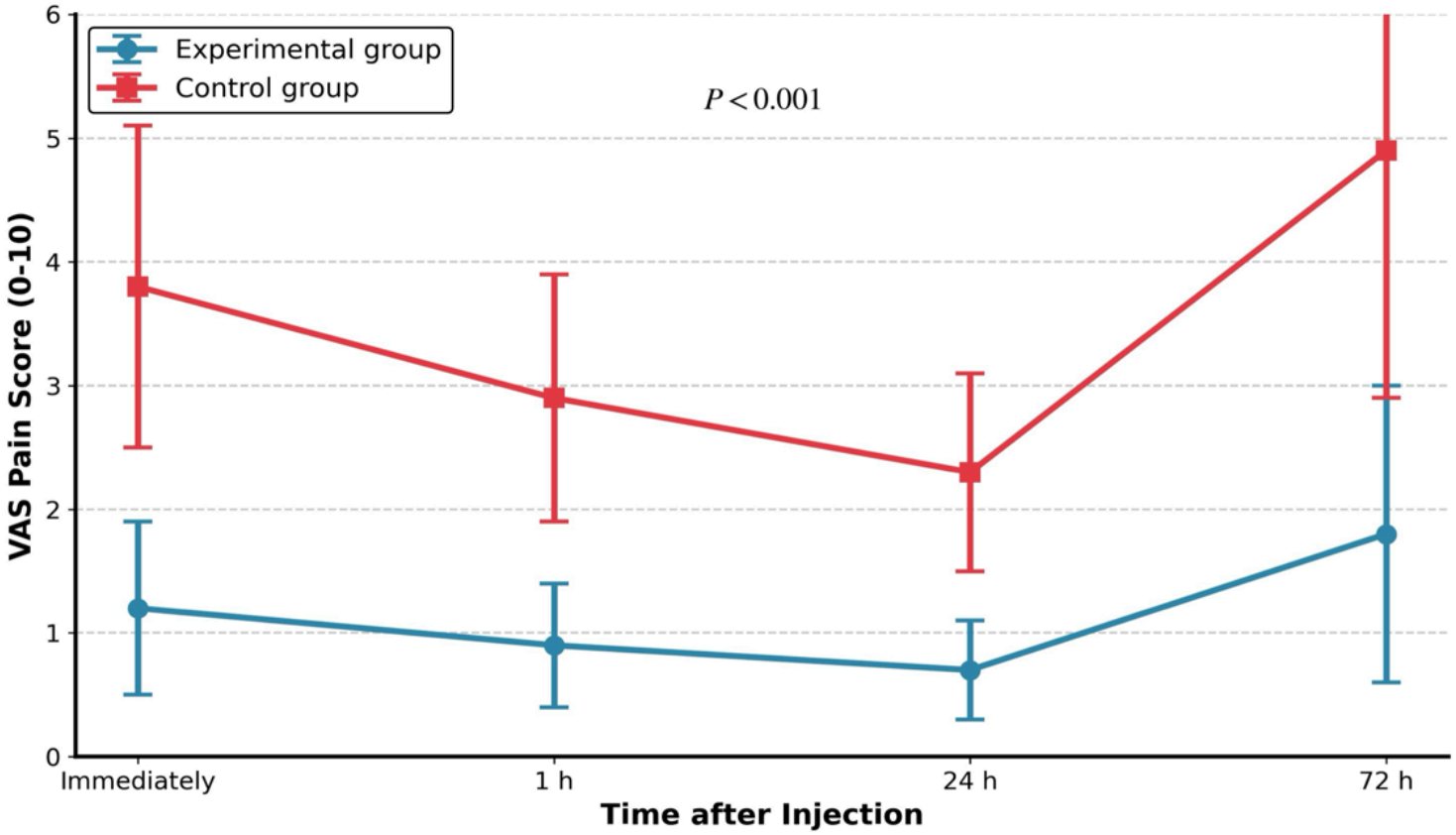
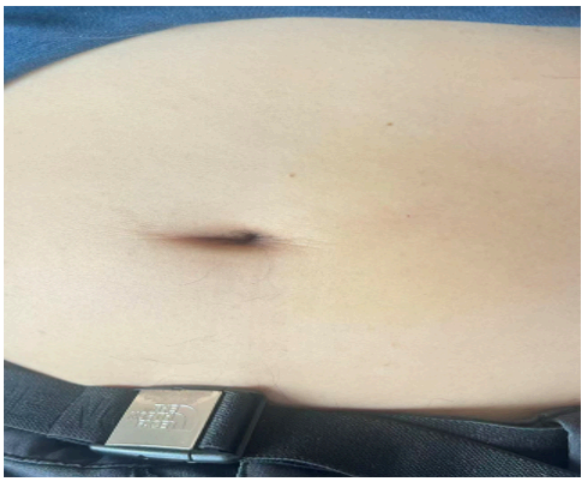


Figure 4

Dynamic changes in VAS pain scores between the two groups over time. Data are presented as mean±SD. *P*<0.001 vs control group at the same time point.



(5A)Control group



(5B) Experimental group

Figure 5

Immediate local reactions after degarelix acetate injection. (A) Control group: Marked local swelling was observed immediately after rapid bolus injection; (B) Experimental group: No obvious local reaction was noted after the modified slow phased injection. These de-identified clinical images were included with written informed consent from participants. The visual findings are consistent with the quantitative data of immediate drug aggregation incidence.

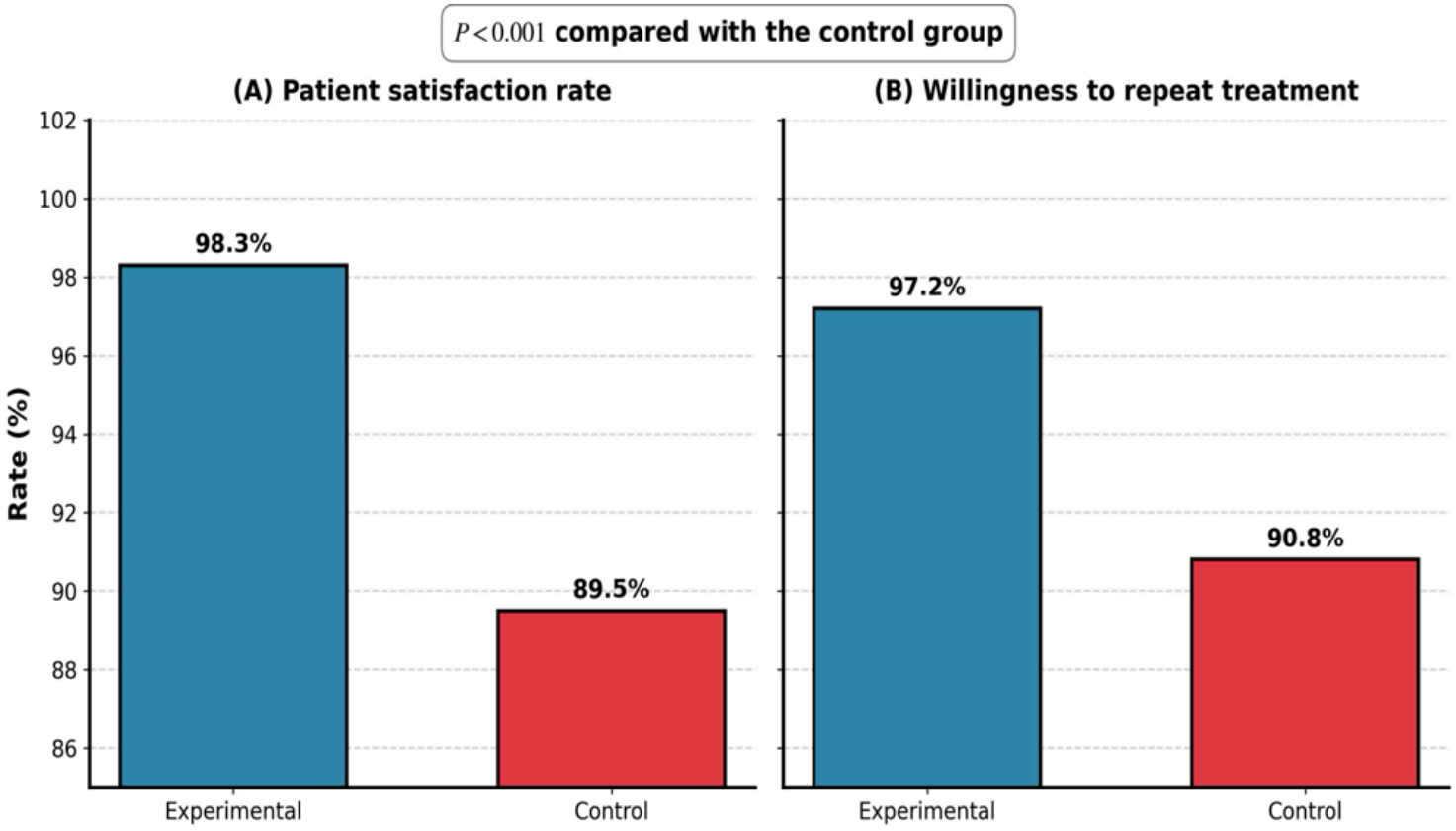


Figure 6

Comparison of patient-reported outcomes between the two groups. (A) Patient satisfaction rate; (B) Willingness to receive repeat treatment. Data are presented as n and %. *P*<0.001 vs control group.