

Original Article

A retrospective cohort study on the improvement of urodynamic parameters and NIH-CPSI scores with Relin granules in BPH patients with high prostatitis-like symptom scores

Xiaoming Xu^{1*}, Jihui Qu^{2*}, Xiaokai Hu³

¹Department of Urologic Surgery, Ningbo Hospital of Integrated Traditional Chinese and Western Medicine, Ningbo 315000, Zhejiang, China; ²Department of Urologic Surgery, Tianjin Medical University Baodi Hospital, Tianjin 301800, China; ³Teaching and Research Section of Traditional Chinese Medicine, Qilu Medical University, Zibo 255300, Shandong, China. *Co-first authors.

Received March 30, 2026; Accepted June 22, 2026; Epub July 15, 2026; Published July 30, 2026

Abstract: Objective: To investigate the efficacy of Relin Granules combined with conventional therapy in improving urodynamic parameters, symptom scores, and inflammatory biomarkers in patients with benign prostatic hyperplasia (BPH) who have high prostatitis-like symptoms. Methods: This retrospective cohort study enrolled 132 BPH patients with a National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) total score ≥ 15 who were treated between January 2023 and January 2025. Among them, 44 patients received conventional therapy plus Relin Granules (4 g tid, 12 weeks), and 88 received conventional therapy alone. Conventional treatment included the α -blocker tamsulosin and, in some patients, the 5 α -reductase inhibitor finasteride. The primary outcomes were changes in NIH-CPSI, International Prostate Symptom Score (IPSS), and urodynamic parameters. Results: After 12 weeks, the combination group showed significantly greater improvements in NIH-CPSI total score (adjusted difference -4.3, $P < 0.001$), pain domain (-1.9, $P < 0.001$) and quality of life domain (-1.4, $P < 0.001$), while the urinary symptom domain did not differ significantly ($P = 0.056$). Compared with the conventional group, the combination group had a greater reduction in IPSS total score (adjusted difference -2.1, $P = 0.004$). No significant differences were observed in maximum flow rate (Qmax, adjusted difference 0.8 mL/s, $P = 0.342$) or postvoid residual volume (PVR, 3.2 mL, $P = 0.415$). The combination group showed significantly greater reductions in serum tumor necrosis factor- α (TNF- α) (adjusted difference -3.28 pg/mL, $P < 0.001$) and urinary prostatic exosomal protein (PSEP) (-0.15 ng/mg, $P = 0.007$), and a greater increase in interleukin-10 (IL-10) (1.89 pg/mL, $P = 0.012$). Adverse event rates were similar ($\chi^2 = 0.254$, $P = 0.614$). Conclusion: In BPH patients with high prostatitis-like symptoms, adding Relin Granules to conventional therapy was associated with alleviation of pain, improvement in quality of life and lower urinary tract symptoms (LUTS), potentially through anti-inflammatory mechanisms, with good safety.

Keywords: Chronic prostatitis, Relin granules, urodynamics, national institutes of health chronic prostatitis symptom index, inflammation

Introduction

Benign prostatic hyperplasia (BPH) is the most prevalent benign urological condition in middle-aged and elderly men. Bladder outlet obstruction secondary to BPH is a primary cause of lower urinary tract symptoms (LUTS) [1]. However, it has been found in clinical practice that the severity of symptoms in BPH patients is not completely parallel to obstructive indicators such as prostate volume enlargement,

suggesting the existence of more complex pathophysiological mechanisms [2]. Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and BPH share considerable symptomatic overlap. The two often coexist, constituting a “BPH inflammatory phenotype” characterized by chronic inflammation. Its core symptom assessment relies on the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) [4]. For such patients, conventional drug treatment represented by α -blockers and

5 α -reductase inhibitors can improve urinary obstruction, but the relief of prostatitis-like pain and discomfort, as measured by NIH-CPSI score, is often limited, which has become a difficulty in clinical treatment [5, 6].

Current treatment strategies for BPH with concomitant significant prostatitis-like symptoms have clear limitations. On the one hand, conventional western medicine treatment focuses on alleviating mechanical obstruction, and it is insufficient to intervene in the accompanying inflammatory state and symptom dimensions such as nerve sensitization mediated by it [7-9]. On the other hand, although traditional Chinese medicine (TCM) has accumulated rich clinical experience in the treatment of chronic prostatitis, in which proprietary drugs such as Relin Granules are widely used in urinary tract infection and lower Jiao damp-heat syndrome (a TCM term), whether it can provide additional improvement in symptoms on the basis of conventional treatment in the context of BPH, especially for patients with high NIH-CPSI score characteristics, still lacks high-quality evidence support from real-world clinical practice [10-12]. Existing studies mostly focus on the evaluation of the effect of monotherapy or surgery. The efficacy mode of integrated traditional Chinese and Western medicine intervention for such complex symptom phenotypes, especially its possible differential impact on subjective symptom scores and objective urodynamic parameters, has not been systematically explored [13-15]. Therefore, it is of great significance to clarify the additional therapeutic value of Relin Granules for such patients for optimizing clinical decision-making.

By comparing the difference between combination therapy and conventional therapy alone, this study is expected to provide a new evidence-based basis for clinical management of such intractable patients, and explore its potential path of action.

Data and methods

General information, sample size calculation and patient screening process

This study was a single-center, retrospective cohort study designed to evaluate treatment efficacy in a real-world clinical setting. The study protocol was reviewed and approved by

the Ethics Review Committee of Tianjin Medical University Baodi Hospital of Integrated Traditional Chinese and Western Medicine (Approval Number: [2023] Ethics No. 003). The requirement for written informed consent specific to this study was waived by the ethics committee owing to its retrospective design. However, all patients had provided written consent for treatment and for the use of their anonymized medical data for research purposes at the time of clinical registration, in compliance with our hospital's privacy policy.

The study cohort was derived from male patients with LUTS who attended the Urology Outpatient Department of our hospital between January 2023 and January 2025. A total of 132 patients meeting all inclusion criteria were included. Among these, 44 patients received Relin Granules in addition to conventional treatment (Relin Granules combination group), and 88 patients received only conventional western medicine treatment (conventional therapy group). This grouping ratio of approximately 1:2 reflects real-world clinical practice, where relatively few BPH patients opt to receive Chinese medicine treatment alongside conventional therapy.

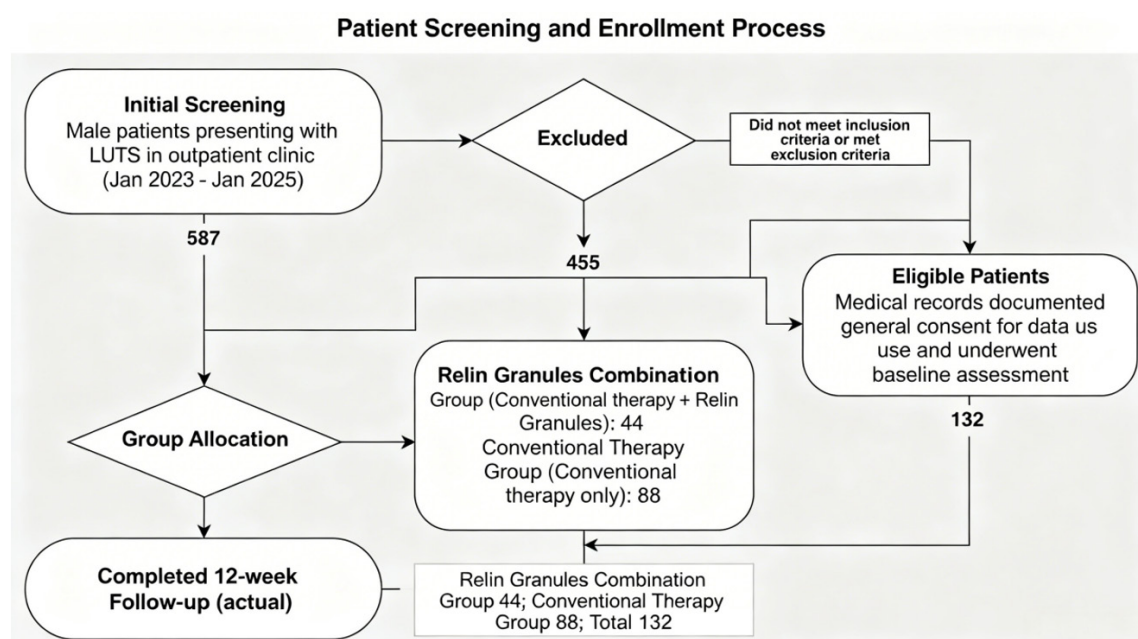
The sample size was estimated based on the change in the NIH-CPSI total score from baseline to 12 weeks of treatment. Using PASS 15.0 software (NCSS, LLC), and referencing previous literature on NIH-CPSI score changes in BPH patients with inflammatory symptoms, we hypothesized that the conventional therapy group would achieve a mean decrease of 6.0 points (SD=4.0 points). We expected that the Relin Granules combination group would achieve a mean decrease of 9.0 points (i.e., an additional 3.0-point reduction). With a two-sided significance level $\alpha=0.05$ and power $(1-\beta)=80\%$, and accounting for a potential 15% rate of incomplete data in a retrospective design, the required sample size was 126 patients. The final inclusion of 132 patients met and slightly exceeded this requirement, ensuring adequate statistical power.

The patient screening and enrollment process is summarized in **Table 1** and **Figure 1**.

Inclusion criteria: (1) Male patients aged between 50 and 80 years; (2) Clinical diagnosis of BPH: prostate volume measured by transab-

Table 1. Patient screening and enrollment process

Stage	Description	Number
Initial Screening	Male patients presenting with LUTS in outpatient clinic (Jan 2023 - Jan 2025)	587
Excluded	Did not meet inclusion criteria or met exclusion criteria	455
Eligible Patients	Medical records documented general consent for data use and underwent baseline assessment	132
Group Allocation	Relin Granules Combination Group (Conventional therapy + Relin Granules)	44
	Conventional Therapy Group (Conventional therapy only)	88
Completed 12-week Follow-up (actual)	Completed all follow-up assessments; data included in final analysis	Relin Granules Combination Group 44; Conventional Therapy Group 88; Total 132


Figure 1. Patient screening and enrollment process.

dominal ultrasound >30 mL, and IPSS >7 points; (3) Presence of significant prostatitis-like symptoms, defined as NIH-CPSI total score ≥ 15 points, consistent with the scale's threshold for moderate-to-severe symptoms. Patients with very severe symptoms (NIH-CPSI ≥ 25) were not excluded and were eligible for enrollment; (4) Complete medical records available for the 12-week treatment and follow-up period.

Exclusion Criteria: (1) Patients diagnosed or suspected of having prostate cancer or bladder tumor based on digital rectal examination, abnormal serum prostate-specific antigen (PSA) levels (above age-specific upper reference limits), or prostate biopsy. (2) Patients

with urethral stricture, neurogenic bladder, bladder stones, or a history of prostate or bladder neck surgery. (3) Use of antibiotics, non-steroidal anti-inflammatory drugs, or other Chinese proprietary medicines (e.g., Qianlie Shutong, Wenglitong) for prostate-related symptoms within 4 weeks prior to enrollment, which could affect baseline assessment. (4) Severe cardiac, hepatic, or renal insufficiency (defined as New York Heart Association functional class III-IV, Child-Pugh class B/C, or estimated glomerular filtration rate < 30 mL/min/1.73 m²). (5) Those who are known to be allergic to any component of Relin Granules. (6) Those who suffer from mental illness or cognitive impairment and cannot cooperate to complete the questionnaire and follow-up.

Research methods

(1) Therapeutic intervention plan: All enrolled patients received conventional western medicine treatment based on the “Chinese guidelines for the diagnosis and treatment of benign prostatic hyperplasia”. The basic medication was tamsulosin hydrochloride sustained-release capsules (Astellas Pharma, specification: 0.2 mg), 0.2 mg, taken orally once daily at bedtime. Finasteride (5 mg once daily) was added at the discretion of the treating urologist, generally for patients with prostate volume >40 mL or IPSS >19 points, in accordance with the Chinese guidelines for diagnosis and treatment of benign prostatic hyperplasia. Its use was recorded and included as a covariate in all adjusted analyses.

On the basis of conventional treatment, the Relin Granules combination group was added with Relin Granules (Jiangxi Jiminxinxin Pharmaceutical Co., Ltd., Guoyao Zhunzi z3602-0064). The usage is 1 bag (4 g) each time, three times a day, taken with about 200 mL warm boiled water, and taken after meals. The treatment lasted for 12 weeks. The study drugs were uniformly provided by the hospital pharmacy, and the batch number was recorded. Patients were reminded to keep empty drug containers, and medication compliance during the 4 weeks was assessed through pill counts and structured interviews at each follow-up visit. Compliance was defined as taking more than 80% of the prescribed dose.

The choice to add Relin Granules was made by the treating urologist based on clinical presentation—usually when patients reported bothersome pelvic pain or discomfort not adequately controlled by α -blockers alone—and after discussing the off-label use of a Chinese patent medicine with the patient. This treatment assignment therefore reflects real-world clinical decision-making but may introduce confounding factors. We addressed this by adjusting for key baseline covariates (age, prostate volume, hypertension, diabetes, finasteride use) in the main analyses. Propensity score matching was not employed because the modest sample size would have resulted in a substantial loss of cases and reduced statistical power, and because multivariable adjustment is considered appropriate for estimating treat-

ment effects in observational studies of this size.

(2) Study design and follow-up points: This study used a retrospective cohort design, and patients were not randomized. Treatment groups were determined based on actual prescriptions documented in medical records. Outcome data were extracted from the hospital's electronic medical record system at baseline and at the 12-week follow-up visit (end of treatment).

(3) Bias control: To minimize measurement bias, outcome assessors were blinded to treatment allocation. Specifically, technicians performing uroflowmetry and transabdominal ultrasound for residual urine measurement, as well as laboratory technicians measuring serum inflammatory markers, were unaware of the patients' treatment group assignments. Research assistants extracting NIH-CPSI and IPSS data from medical records used standardized data extraction forms to ensure consistency.

Observation indices

(1) NIH-CPSI total score: This scale is the gold-standard tool for assessing symptom severity and quality of life impact in CP/CPPS [15]. It comprises three domains: pain or discomfort (4 items, score range 0-21), urinary symptoms (2 items, score range 0-10), and quality of life impact (3 items, score range 0-12). The total score ranges from 0 to 43, with higher scores indicating more severe symptoms. The change in its total score served as the primary basis for evaluating the effect of Relin Granules on improving prostatitis-like core symptoms.

(2) Secondary efficacy indicators: ① IPSS and quality of life (QoL): IPSS is a standardized scale to assess the severity of LUTS caused by BPH, including 7 symptom problems (total score 0-35 points), and the QoL single-item score (0-6 points) reflects the degree to which symptoms are bothersome in daily life. ② Maximum urine flow rate (Qmax): Qmax was measured using a urodynamic analyzer when the patient reported a strong desire to void. The measurement was repeated three times, and the highest value was recorded (unit: mL/s). This indicator directly reflects the improvement of bladder outlet obstruction.

Post-void residual urine volume (PVR): the patient underwent transabdominal bladder ultrasound immediately after measuring Qmax. The three diameter lines of the bladder were measured, and the volume was calculated according to the ellipsoid formula (length × width × height × 0.52) as PVR (unit: mL).

(3) Exploratory biomarkers (serum and urine): To explore the potential mechanism of action, we collected fasting venous blood and random urine samples from patients at baseline and 12 weeks of treatment. ① Serum inflammatory cytokines: Levels of tumor necrosis factor- α (TNF- α) were measured using a human TNF- α Quantikine ELISA kit (R&D Systems, Minneapolis, MN, USA, Cat# DTA00D; detection limit 0.5 pg/mL; intra-assay CV <4.5%, inter-assay CV <7.2%). Interleukin-10 (IL-10) was measured using a human IL-10 Quantikine ELISA kit (R&D Systems, Cat# D1000B; detection limit 0.5 pg/mL; intra-assay CV <3.1%, inter-assay CV <7.5%). All assays were performed according to the manufacturer's instructions. ② Urinary prostatic exosomal protein (PSEP): PSEP concentration in random mid-stream urine was determined using a human PSEP ELISA kit (Cusabio, Wuhan, China, Cat# CSB-EL018097HU; detection limit 0.078 ng/mL; intra-assay CV <8%, inter-assay CV <10%). To correct for urine dilution, the PSEP concentration (ng/mL) was divided by the urine creatinine concentration (mg/dL) measured by the Jaffé kinetic method on an automated chemistry analyzer and multiplied by 100, yielding a PSEP-to-creatinine ratio (ng/mg).

(4) Safety indicators: All adverse events (AEs) occurred during the whole study period were recorded, including their occurrence time, severity, correlation with the study drug, treatment measures and outcome. At the same time, routine blood, liver function (alanine aminotransferase, aspartate aminotransferase) and renal function (serum creatinine) were detected at baseline and 12 weeks of treatment, and laboratory abnormalities were monitored.

Statistical methods

All statistical analyses were performed using R language (version 4.3.1) and SPSS statistical software (version 26.0, IBM). Continuous variables are described as mean ± standard deviation

or median (interquartile range) according to their distribution.

Normality of continuous variables was assessed using the Shapiro-Wilk test. For baseline characteristics, independent-samples t-test was used for normally distributed variables, Mann-Whitney U test for non-normally distributed variables, and chi-square test or Fisher's exact test for categorical variables. It should be clearly pointed out that these univariate comparisons are only used for descriptive characterization of the sample at baseline and not to infer post-treatment balance between groups. The core causal inference of this study is based on multivariable linear mixed models (LMM) controlling for pre-specified potential confounders. All adjusted LMMs included the following fixed-effect covariates: treatment group, time point (as a categorical variable: baseline, 4 weeks, 8 weeks, 12 weeks), the group × time interaction term, age (continuous), prostate volume (continuous), body mass index (continuous), comorbid hypertension (yes/no), comorbid diabetes (yes/no), and concomitant finasteride use (yes/no). The random effect was the individual patient identifier as a random intercept. The t-test results in the tables are provided only for descriptive interpretation at single follow-up time points and should not be interpreted as adjusted effect estimates.

The main analysis method is linear mixed model (LMM), which is a standard and powerful tool for processing repeated measurement data. We will construct the model with NIH-CPSI total score (as the main analysis) and secondary continuous outcome indicators (IPSS, QoL, Qmax, PVR, TNF- α , IL-10, and adjusted PSEP) as dependent variables.

Fixed effect: it will be included in the treatment group (Relin Granules combination group vs. conventional therapy group), the assessment time point (as a categorical variable: baseline, 4 weeks, 8 weeks, 12 weeks), and the crucial interaction term between the group and the time point. The significance of the interaction term directly tests whether there is a difference in the trajectory of symptoms or indicators over time between the two groups, that is, whether the treatment is effective.

Random effect: the individual identifier of the included patients was taken as the random

Table 2. Baseline demographic and clinical characteristics of patients

Characteristic	Relin Granules Combination Group (n=44)	Conventional Therapy Group (n=88)	Statistic	P
Age (years)	67.2 ± 6.8	66.6 ± 7.1	t=0.461	0.646
Body Mass Index (kg/m ²)	24.8 ± 3.1	25.1 ± 2.9	t=-0.556	0.579
Current Smoker, n (%)	11 (25.0)	26 (29.5)	χ ² =0.318	0.573
Comorbid Hypertension, n (%)	22 (50.0)	39 (44.3)	χ ² =0.414	0.52
Comorbid Diabetes, n (%)	9 (20.5)	14 (15.9)	χ ² =0.446	0.504
Prostate Volume (mL), Mean ± SD	50.3 ± 18.7	47.9 ± 17.2	t=0.742	0.46
Serum Total PSA (ng/mL), Median (IQR)	2.8 (1.6-4.5)	2.5 (1.4-4.1)	Z=0.791	0.429
Concomitant Finasteride Use, n (%)	10 (22.7)	30 (34.1)	χ ² =1.875	0.171
NIH-CPSI Score, Mean ± SD				
Total Score	23.6 ± 5.2	22.9 ± 4.8	t=0.774	0.44
Pain Domain	7.8 ± 2.1	7.4 ± 2.3	t=0.955	0.341
Urinary Symptoms Domain	6.6 ± 1.8	6.3 ± 1.7	t=0.931	0.353
Quality of Life Domain	9.2 ± 2.5	9.1 ± 2.4	t=0.223	0.824
IPSS Score, Mean ± SD				
Total Score	21.8 ± 5.6	20.9 ± 5.9	t=0.833	0.406
Quality of Life Item	4.2 ± 1.1	4.0 ± 1.0	t=1.043	0.299
Urodynamic Parameters, Mean ± SD				
Qmax (mL/s)	9.4 ± 2.8	9.8 ± 3.1	t=-0.732	0.466
PVR (mL)	68.3 ± 32.5	62.9 ± 29.8	t=0.935	0.352
Serum Biomarkers, Mean ± SD				
TNF-α (pg/mL)	18.42 ± 6.37	17.89 ± 5.94	t=0.473	0.637
IL-10 (pg/mL)	5.23 ± 2.11	5.41 ± 2.08	t=-0.463	0.644
Urinary Biomarker, Mean ± SD				
PSEP/Creatinine (ng/mg)	0.89 ± 0.31	0.85 ± 0.28	t=0.735	0.464

Note: Values are presented as mean ± standard deviation, median (interquartile range), or number (percentage). NIH-CPSI, National Institutes of Health Chronic Prostatitis Symptom Index; IPSS, International Prostate Symptom Score; Qmax, maximum urinary flow rate; PVR, post-void residual volume; TNF-α, tumor necrosis factor-alpha; IL-10, interleukin-10; PSEP, prostatic exosomal protein; PSA, prostate-specific antigen.

intercept to consider the correlation between multiple measurements of the same patient.

Missing data processing: under the assumption that the data are missing at random (MAR), the linear mixed model can provide effective parameter estimation by using all available data, which is better than the method of analyzing only the completers.

For the main outcome, we presented the adjusted estimated marginal means and their 95% confidence interval (CI) of the total NIH-CPSI score for both groups, calculated based on the linear mixed model at 12 weeks of treatment, and drew the curve of the estimated marginal mean of the two groups over time to visually show the difference in efficacy.

In safety analysis, categorical data will be compared by chi-square test or Fisher's exact test.

All hypothesis tests were two-sided, and *P* values <0.05 were considered statistically significant.

Results

Baseline demographic and clinical characteristics

All 132 enrolled patients (100%) completed the 12-week treatment and follow-up protocol: 44 in the Relin Granules combination group and 88 in the conventional therapy group. The baseline demographic and clinical characteristics of the two groups were comparable, with no statistically significant differences observed in any variable (all *P*>0.05), as detailed in **Table 2**. The mean age of patients was 66.8 years, the mean prostate volume was 48.7 mL, and the mean NIH-CPSI total score was 23.2 points, confirm-

Relin granules for BPH patients with prostatitis-like symptoms: a cohort study

Table 3. Comparison of NIH-CPSI score changes before and after treatment (Mean $\pm$ SD) and linear mixed model analysis results

Indicator	Time Point	Relin Granules Combination Group (n=44)	Conventional Therapy Group (n=88)	t	P
NIH-CPSI Total Score	Baseline	23.6 $\pm$ 5.2	22.9 $\pm$ 4.8	0.768	0.444
	4 weeks	17.3 $\pm$ 4.9	18.8 $\pm$ 4.5	-1.752	0.082
	8 weeks	12.7 $\pm$ 4.1	15.4 $\pm$ 4.3	-3.453	<0.001
	12 weeks	10.2 $\pm$ 3.8	13.8 $\pm$ 4.0	-4.955	<0.001
Pain Domain Score	Baseline	7.8 $\pm$ 2.1	7.4 $\pm$ 2.3	0.969	0.334
	12 weeks	2.1 $\pm$ 1.4	3.8 $\pm$ 1.9	-5.260	<0.001
Urinary Symptoms Domain Score	Baseline	6.6 $\pm$ 1.8	6.3 $\pm$ 1.7	0.937	0.35
	12 weeks	3.0 $\pm$ 1.2	3.7 $\pm$ 1.3	-2.991	0.003
Quality of Life Domain Score	Baseline	9.2 $\pm$ 2.5	9.1 $\pm$ 2.4	0.223	0.824
	12 weeks	4.8 $\pm$ 1.6	6.1 $\pm$ 1.8	-4.055	<0.001

Note: NIH-CPSI, National Institutes of Health Chronic Prostatitis Symptom Index.

Table 4. Comparison of changes in secondary efficacy indicators before and after treatment (Mean $\pm$ SD)

Indicator	Time Point	Relin Granules Combination Group (n=44)	Conventional Therapy Group (n=88)	t	P (t-test)
IPSS Total Score	Baseline	21.8 $\pm$ 5.6	20.9 $\pm$ 5.9	0.840	0.402
	12 weeks	11.2 $\pm$ 4.7	13.3 $\pm$ 5.1	-2.288	0.024
QoL Single Item Score	Baseline	4.2 $\pm$ 1.1	4.0 $\pm$ 1.0	1.047	0.297
	12 weeks	2.1 $\pm$ 0.9	2.7 $\pm$ 0.8	-3.895	<0.001
Qmax (mL/s)	Baseline	9.4 $\pm$ 2.8	9.8 $\pm$ 3.1	-0.721	0.472
	12 weeks	12.8 $\pm$ 3.5	12.1 $\pm$ 3.7	1.043	0.299
PVR (mL)	Baseline	68.3 $\pm$ 32.5	62.9 $\pm$ 29.8	0.952	0.343
	12 weeks	35.6 $\pm$ 25.1	32.4 $\pm$ 22.8	0.735	0.464

Note: IPSS, International Prostate Symptom Score; Qmax, maximum urinary flow rate; PVR, post-void residual volume.

Table 5. Changes in exploratory biomarker levels before and after treatment (Mean $\pm$ SD)

Biomarker	Time Point	Relin Granules Combination Group (n=44)	Conventional Therapy Group (n=88)	t	P (t-test)
Serum TNF- α (pg/mL)	Baseline	18.42 $\pm$ 6.37	17.89 $\pm$ 5.94	0.472	0.638
	12 weeks	11.25 $\pm$ 4.82	14.53 $\pm$ 5.16	-3.517	<0.001
Serum IL-10 (pg/mL)	Baseline	5.23 $\pm$ 2.11	5.41 $\pm$ 2.08	-0.466	0.642
	12 weeks	6.89 $\pm$ 2.45	5.82 $\pm$ 2.20	2.536	0.012
Urinary PSEP/Creatinine (ng/mg)	Baseline	0.89 $\pm$ 0.31	0.85 $\pm$ 0.28	0.746	0.457
	12 weeks	0.61 $\pm$ 0.25	0.73 $\pm$ 0.26	-2.531	0.012

Note: TNF- α , tumor necrosis factor-alpha; IL-10, interleukin-10; PSEP, prostatic exosomal protein.

ing the successful recruitment of a BPH population with significant prostatitis-like symptoms.

Main efficacy outcome: NIH-CPSI score change

The NIH-CPSI scores at baseline and after 4, 8, and 12 weeks of treatment are presented in **Table 3**. By week 12, the NIH-CPSI total score had decreased significantly in both groups, but

the reduction was more pronounced in the Relin Granules combination group. The mean total score at week 12 was 10.2 $\pm$ 3.8 in the combination group versus 13.8 $\pm$ 4.0 in the conventional therapy group ($P < 0.001$). The linear mixed model, adjusting for age, body mass index, prostate volume, hypertension, diabetes, and concomitant finasteride use, confirmed a significantly greater reduction in the

Table 6. Incidence of adverse events during treatment [n (%)]

Adverse Event Type	Relin Granules Combination Group (n=44)	Conventional Therapy Group (n=88)	Statistic	P
Any Adverse Event	9 (20.5)	15 (17.0)	$\chi^2=0.229$ (Fisher)	0.614
Dizziness	1 (2.3)	4 (4.5)	- (Fisher)	0.667
Orthostatic Hypotension	0 (0)	2 (2.3)	- (Fisher)	0.552
Ejaculatory Dysfunction	1 (2.3)	3 (3.4)	- (Fisher)	1
Gastrointestinal Discomfort (Diarrhea/Abdominal Bloating)	5 (11.4)	1 (1.1)	- (Fisher)	0.013
Fatigue	2 (4.5)	3 (3.4)	- (Fisher)	0.671
Other	0 (0)	2 (2.3)	- (Fisher)	0.552
Adverse Event Leading to Discontinuation	1 (2.3)	1 (1.1)	- (Fisher)	0.562

Table 7. Key results of sensitivity analysis (Worst-Case Imputation)

Analysis Scenario	Relin Granules Combination Group (n=44)	Conventional Therapy Group (n=88)	t	P
Completer Analysis (Primary Analysis)	-13.4 $\pm$ 5.8	-9.1 $\pm$ 5.2	-4.308	<0.001
Worst-Case Imputation Analysis	-12.1 $\pm$ 6.3	-8.3 $\pm$ 5.6	-3.523	<0.001

Table 8. Summary of linear mixed model results for primary and secondary outcomes at week 12

Outcome	Estimated Marginal Mean (95% CI) - Relin Granules Group	Estimated Marginal Mean (95% CI) - Conventional Group	Adjusted Between-Group Difference (95% CI)	P (treatment effect at week 12)	P (group $\times$ time interaction)
NIH-CPSI total score	9.9 (8.9-10.9)	14.2 (13.2-15.2)	-4.3 (-5.8 to -2.8)	<0.001	0.008
NIH-CPSI pain domain	2.0 (1.5-2.5)	3.9 (3.4-4.4)	-1.9 (-2.6 to -1.2)	<0.001	0.004
NIH-CPSI urinary symptoms	3.1 (2.7-3.5)	3.9 (3.5-4.3)	-0.8 (-1.4 to -0.2)	0.056	0.09
NIH-CPSI QoL domain	4.7 (4.1-5.3)	6.1 (5.5-6.7)	-1.4 (-2.0 to -0.8)	<0.001	0.01
IPSS total score	11.1 (9.9-12.3)	13.2 (12.0-14.4)	-2.1 (-3.6 to -0.6)	0.004	0.19
QoL single item	2.0 (1.7-2.3)	2.6 (2.3-2.9)	-0.6 (-0.9 to -0.3)	<0.001	0.08
Qmax (mL/s)	12.7 (11.6-13.8)	11.9 (10.8-13.0)	0.8 (-0.8 to 2.4)	0.342	0.56
PVR (mL)	36.5 (28.9-44.1)	33.3 (25.7-40.9)	3.2 (-4.5 to 10.9)	0.415	0.48
Serum TNF- α (pg/mL)	11.0 (9.4-12.6)	14.3 (12.7-15.9)	-3.28 (-4.82 to -1.74)	<0.001	0.003
Serum IL-10 (pg/mL)	6.9 (5.9-7.9)	5.0 (4.0-6.0)	1.89 (0.41-3.37)	0.012	0.18
Urinary PSEP/creatinine (ng/mg)	0.60 (0.52-0.68)	0.75 (0.67-0.83)	-0.15 (-0.26 to -0.04)	0.007	0.02

combination group. At week 12, the estimated marginal mean (95% CI) for the NIH-CPSI total score was 9.9 (8.9-10.9) in the combination group versus 14.2 (13.2-15.2) in the conventional group, yielding an adjusted between-group difference of -4.3 (95% CI: -5.8 to -2.8; $P<0.001$). The group $\times$ time interaction term was statistically significant ($P=0.008$), indicating that the trajectories of symptom improvement differed between the two groups over the 12-week period. Analysis of the NIH-CPSI sub-domains at week 12 revealed that the combination group had significantly lower scores in all three domains: pain (2.1 ± 1.4 vs. 3.8 ± 1.9 , $P<0.001$), urinary symptoms (3.0 ± 1.2 vs. 3.7 ± 1.3 , $P=0.003$), and quality of life (4.8 ± 1.6 vs. 6.1 ± 1.8 , $P<0.001$). For the pain domain, the LMM-estimated marginal mean at week 12

was 2.0 (1.5-2.5) in the combination group versus 3.9 (3.4-4.4) in the conventional group (adjusted difference -1.9, 95% CI: -2.6 to -1.2, $P<0.001$). For the urinary symptom domain, the adjusted difference was -0.8 (95% CI: -1.4 to -0.2, $P=0.056$). For the quality-of-life domain, the adjusted difference was -1.4 (95% CI: -2.0 to -0.8, $P<0.001$). The complete linear mixed model results for all primary and secondary outcomes at week 12 are summarized in **Table 8**.

Secondary efficacy outcomes

IPSS, QoL scores, and urodynamic parameters: As shown in **Table 4** and **Figure 2**, the IPSS total score and QoL single-item score improved significantly in both groups. At week 12, the IPSS

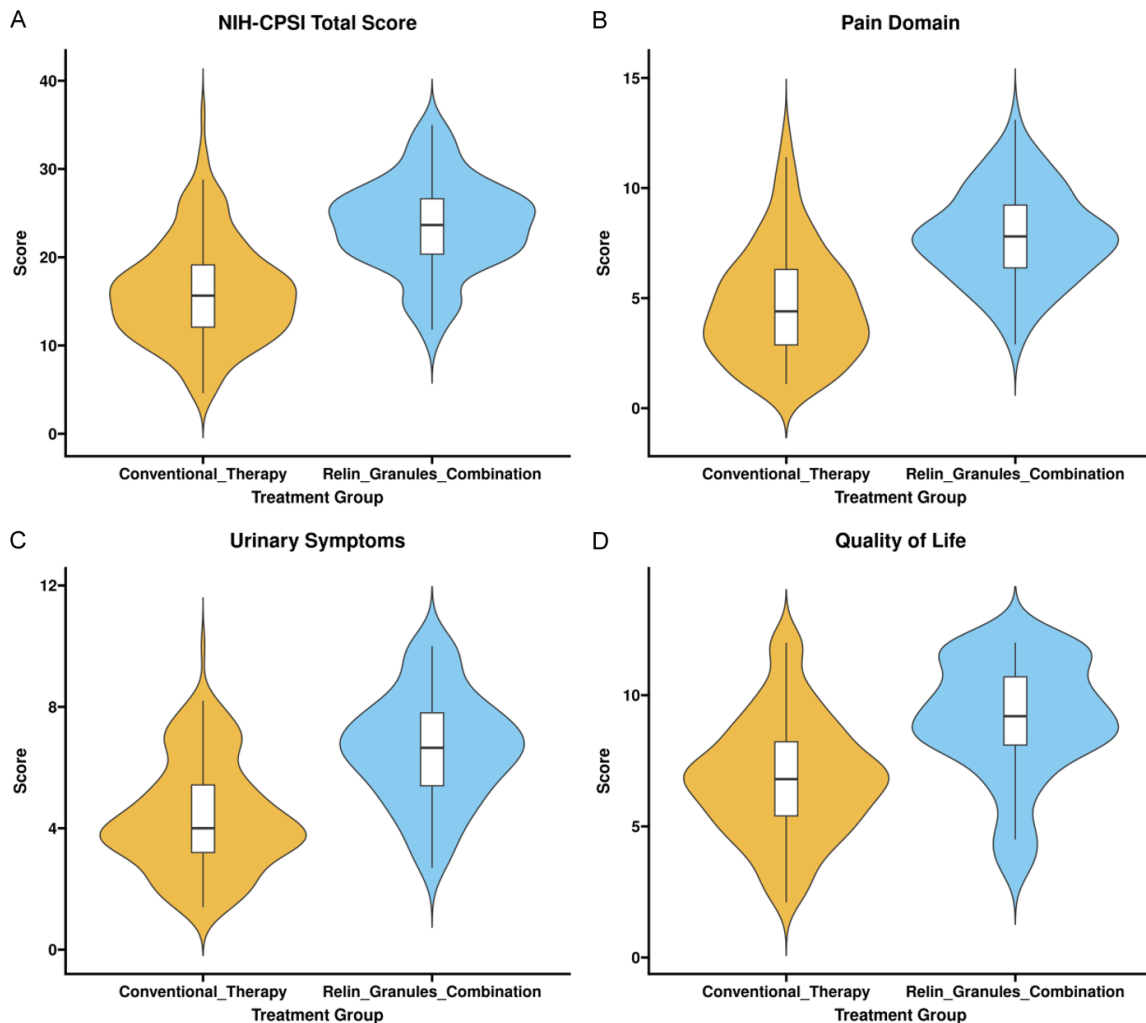


Figure 2. Comparison of changes in secondary efficacy indicators.

total score was significantly lower in the combination group (11.2 ± 4.7) compared with the conventional therapy group (13.3 ± 5.1 ; $P=0.024$). The LMM analysis confirmed this benefit: the estimated marginal mean IPSS total score at week 12 was 11.1 (9.9-12.3) in the combination group versus 13.2 (12.0-14.4) in the conventional group, with an adjusted between-group difference of -2.1 (95% CI: -3.6 to -0.6; $P=0.004$). The group $\times$ time interaction for IPSS was not significant ($P=0.19$), suggesting that the rate of improvement over time did not differ significantly between groups, but the overall treatment effect at 12 weeks favored the combination group. A similar, more significant benefit was observed for the QoL single-item score (2.1 ± 0.9 vs. 2.7 ± 0.8 , $P<0.001$). For the IPSS QoL single-item score, the LMM-estimated adjusted difference at week 12 was

-0.6 (95% CI: -0.9 to -0.3; $P<0.001$) in favor of the combination group. Regarding objective urodynamic parameters, both groups experienced significant improvements in Qmax and PVR from baseline. However, the 12-week values for Qmax (12.8 ± 3.5 vs. 12.1 ± 3.7 mL/s, $P=0.299$) and PVR (35.6 ± 25.1 vs. 32.4 ± 22.8 mL, $P=0.464$) did not differ significantly between groups. For urodynamic parameters, LMM analysis showed no significant treatment effect. The adjusted between-group difference for Qmax was 0.8 mL/s (95% CI: -0.8 to 2.4; $P=0.342$), and for PVR was 3.2 mL (95% CI: -4.5 to 10.9; $P=0.415$). The group $\times$ time interaction terms were also non-significant (Qmax: $P=0.56$; PVR: $P=0.48$).

Exploratory biomarkers: The changes in exploratory biomarkers are summarized in **Table 5**

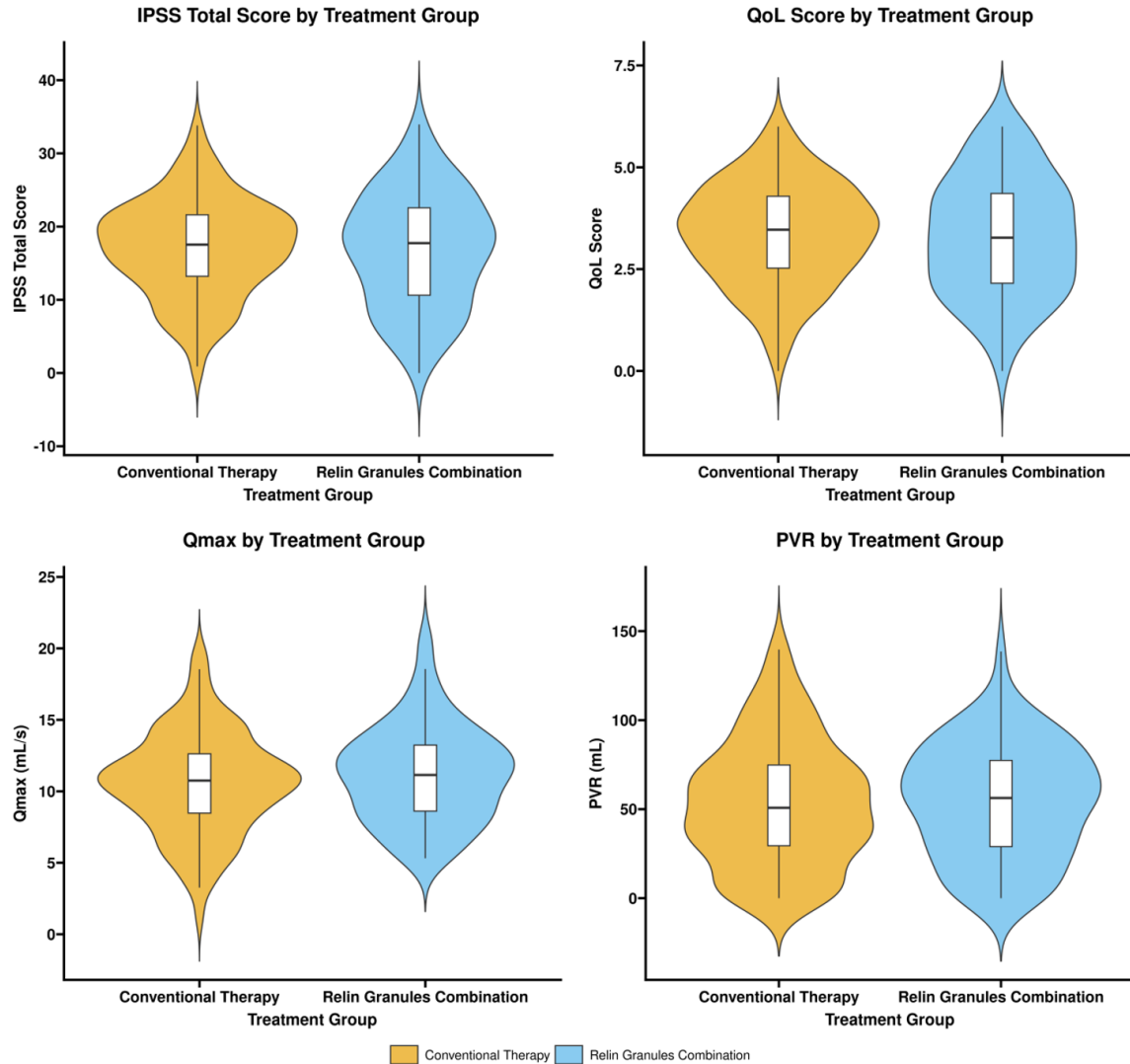


Figure 3. Changes in exploratory biomarker levels.

and depicted in **Figure 3**. After 12 weeks, the serum level of the pro-inflammatory cytokine TNF- α decreased significantly more in the Relin Granules combination group (11.25 ± 4.82 pg/mL) than in the conventional therapy group (14.53 ± 5.16 pg/mL; $P < 0.001$). LMM analysis yielded an adjusted between-group difference for TNF- α of -3.28 pg/mL (95% CI: -4.82 to -1.74 ; $P < 0.001$). For IL-10, the adjusted difference was 1.89 pg/mL (95% CI: 0.41 to 3.37 ; $P = 0.012$). For urinary PSEP/creatinine, the adjusted difference was -0.15 ng/mg (95% CI: -0.26 to -0.04 ; $P = 0.007$). The group $\times$ time interactions were significant for TNF- α ($P = 0.003$) and PSEP ($P = 0.02$), but not for IL-10 ($P = 0.18$). Concurrently, serum levels of the anti-inflammatory cytokine IL-10 were signifi-

cantly higher in the combination group at week 12 (6.89 ± 2.45 vs. 5.82 ± 2.20 pg/mL; $P = 0.012$). The reduction in the urinary biomarker PSEP/creatinine was also significantly greater in the combination group (0.61 ± 0.25 ng/mg) compared to the conventional group (0.73 ± 0.26 ng/mg; $P = 0.012$).

Safety analysis

The incidence of adverse events is detailed in **Table 6**. During the 12-week treatment period, 9 patients (20.5%) in the combination group and 15 patients (17.0%) in the conventional therapy group reported at least one adverse event, with no significant difference in the overall incidence ($P = 0.614$). The most common

adverse event in the combination group was mild gastrointestinal discomfort (diarrhea or abdominal bloating), reported in 5 patients (11.4%), which was significantly more frequent than in the conventional therapy group (1 patient, 1.1%; $P=0.013$). All gastrointestinal events were transient and resolved spontaneously. One patient in each group discontinued treatment due to an adverse event ($P=0.562$).

Sensitivity and subgroup analyses

The robustness of the primary outcome was confirmed by a sensitivity analysis using worst-case imputation for missing data (**Table 7**). Even under this conservative assumption, the improvement in the NIH-CPSI total score remained significantly greater in the Relin Granules combination group (-12.1 ± 6.3 points) than in the conventional therapy group (-8.3 ± 5.6 points; $P<0.001$).

Furthermore, a pre-specified subgroup analysis was conducted to examine the consistency of the treatment effect across baseline symptom severity. Patients were divided into those with a baseline NIH-CPSI total score <25 and those with a score ≥ 25 . At week 12, the significant between-group difference favoring the combination therapy was observed in both subgroups. The adjusted between-group difference in the NIH-CPSI total score change was -4.1 points (95% CI, -6.5 to -1.7) in the mild-to-moderate subgroup and -4.5 points (95% CI, -7.3 to -1.7) in the severe subgroup, with no significant interaction between treatment and baseline severity (P for interaction $=0.42$). An additional analysis testing the interaction between treatment group and concomitant finasteride use showed that the efficacy of Relin Granules was consistent regardless of finasteride co-administration (P for interaction $=0.68$).

Discussion

The purpose of this study was to evaluate the additional efficacy of the Chinese patent medicine Relin Granules in BPH patients with high prostatitis-like symptoms who had a limited response to conventional treatment in a real-world clinical setting. The results showed that after 12 weeks of treatment, the patients in the Relin Granules combination group achieved more significant relief of core chronic prostatitis symptoms, especially pain and quality of life

[16-18]. At the same time, biomarkers reflecting systemic and local inflammatory state of prostate also showed a more favorable trend. However, no additional advantage of combination therapy was observed in the improvement of objective urodynamic parameters. These findings together paint a picture: for BPH patients with significant inflammatory phenotype, the addition of Relin Granules may reduce the burden of symptoms mainly by regulating inflammation related pathways, rather than directly acting on the mechanical obstruction of bladder outlet.

In this study, the improvement of the NIH-CPSI total score, pain and quality of life subdomain scores in the combination group were significantly better than those in the conventional therapy group. This result is consistent with previous reports on significant relief of pain symptoms in patients after prostate surgery, although the magnitude of pain relief with combination therapy was smaller than that achieved with invasive surgery [19, 20]. The reason may be that the symptoms of BPH related LUTS and CP/CPPS are highly overlapped, while traditional α -blockers or 5 α -reductase inhibitors have limited effect on the improvement of inflammatory symptoms with pain as the core [21, 22]. Relin Granules, as a kind of Chinese patent medicine with the effects of clearing heat and dampness, removing blood stasis and promoting lymphatic circulation, its potential mechanism of reducing pain may involve the regulation of the local inflammatory microenvironment of the prostate. The changes in biomarkers observed in this study provide indirect support for this, indicating that its efficacy may be partly due to the correction of abnormal immune or inflammatory response, thus directly alleviating the pain and discomfort of patients.

In terms of the overall LUTS assessed by the IPSS, the combination therapy also showed advantages, but there was no significant difference in the improvement degree between the two groups in the two key urodynamic indicators of Qmax and PVR. This phenomenon - where subjective symptom relief is not fully synchronized with objective obstructive parameters - is not rare in the study of patients with BPH complicated with inflammation [23]. It suggests that the severity of symptoms perceived

by patients, especially the symptoms of urinary storage period, such as urgent urination and nocturia, may be affected by a variety of factors, such as inflammation of the prostate and bladder neck and nerve sensitization, rather than just physical obstruction caused by gland enlargement [24]. Therefore, Relin Granules may improve patients' voiding symptoms by reducing tissue edema and nerve excitability through non-mechanical pathways, even if the absolute increase of urinary flow rate does not increase. This further emphasizes that for BPH patients with pain and irritating symptoms, the treatment strategy should go beyond simple "shrinking glands" or "expanding channels", and should take into account the multiple pathophysiological processes behind the symptoms [25].

The analysis results of exploratory biomarkers provide a potential biological explanation for the above clinical observations. In the combination group, the serum levels of TNF- α decreased more significantly, while the levels of IL-10 increased. At the same time, the urine levels of PSEP, a potential marker related to prostate histological inflammation, also decreased more significantly. The consistent changes of these three indicators strongly suggest that the efficacy of Relin Granules may be related to systemic and local anti-inflammatory effects on the prostate. Previous studies have confirmed that histological inflammation is one of the important driving factors of BPH progress and symptoms, and the degree of inflammatory cell infiltration is positively correlated with the symptom score of patients. Therefore, the improvement of symptoms observed in this study, especially the relief of pain, is likely to be partly due to the inhibition of drugs on classic or non-classic inflammatory pathways such as NLRP3 inflammasome, which reduces the release of inflammatory mediators, thereby reducing tissue damage and nerve stimulation [26, 27]. This provides a new perspective for understanding the role of traditional Chinese medicine compound in multi-target regulation of complex disease states. It must be noted that Relin Granules are a multi-herb formulation, and the key active ingredients (e.g., specific flavonoids, alkaloids) that mediate the observed effects on TNF- α and IL-10 were not isolated or characterized in this study. Furthermore, the ability of these components

to directly modulate inflammatory responses in prostate epithelial cells or macrophages has not been tested in vitro. Thus, the mechanistic link between Relin Granule intake and the biomarker changes remain at the level of clinical association. Dedicated phytochemical analysis and cell-based experiments using prostate epithelial cell lines stimulated with inflammatory cytokines are warranted to pinpoint the active molecules and their intracellular targets.

The results of sensitivity analysis and subgroup analysis supported the robustness of the main conclusions of this study. Even under the assumption of considering the worst case (i.e., no efficacy in all patients lost to follow-up), the advantages of combination therapy in the main outcome still exist. In addition, regardless of the baseline symptom burden of patients, the trend of additional benefits brought by Relin Granules was consistent, and no significant heterogeneity in the treatment effect was found. This indicates that for BPH patients who meet the inclusion criteria of this study (i.e., NIH-CPSI total score ≥ 15), the addition of Relin Granules may be a generally beneficial complementary treatment strategy [28]. The universality and safety of this kind of curative effect together constitute the realistic basis for its popularization and application in clinical practice. The spectrum of adverse events showed that the combined treatment did not significantly increase the overall risk, and the main new adverse reactions were mild gastrointestinal reactions, which was consistent with the known characteristics of many Chinese patent medicines, and the incidence was within the acceptable range [29, 30]. Notably, mild gastrointestinal discomfort occurred more often with the addition of Relin Granules, a finding consistent with the known adverse effect profile of this Chinese patent medicine. However, all events were mild and self-limited, and the absolute increase in risk must be weighed against the notable improvement in pain and quality of life.

Of course, this study has several limitations. First, the non-randomized retrospective cohort design may be subject to unmeasured confounding. Although we adjusted for known important confounders using multivariate models and described the clinical rationale for prescribing Relin Granules, residual confounding

by indication cannot be excluded. Propensity score matching was not used because of the limited sample size, but future prospective randomized trials are needed to fully address selection bias. Second, the absence of blinding in this retrospective study precludes exclusion of a placebo effect, particularly for subjective patient-reported outcomes such as NIH-CPSI pain and IPSS scores. The observed dissociation between pronounced subjective improvement and lack of additive benefit on objective urodynamic measures, together with the corresponding changes in inflammatory biomarkers, provides some reassurance against a pure placebo response; nevertheless, a double-blind, randomized, placebo-controlled trial is necessary to definitively establish the specific efficacy of Relin Granules beyond expectation effects. Third, although we observed favorable changes in serum TNF- α , IL-10, and urinary PSEP, our study did not directly examine prostate tissue infiltration of inflammatory cells (e.g., macrophages, T-cell subsets) or key inflammasome/NF- κ B pathway activation. Therefore, it remains unclear whether Relin Granules directly inhibit intraprostatic inflammation or primarily modulate systemic immune responses. Future studies incorporating prostate biopsy specimens or animal models with pathway-specific inhibitors are needed to clarify the causal relationship between the observed biomarker changes and symptom improvement. Finally, the single-center sample may limit the extrapolation of the results, and multicenter validation is needed in different populations.

To sum up, this study shows that for patients with BPH with high prostatitis-like symptom scores, the application of Relin Granules on the basis of conventional western medicine treatment can more effectively relieve their pain symptoms, improve the quality of life and overall LUTS, and has good safety. The curative effect may be related to the regulatory system and the local inflammatory state of the prostate, rather than mainly through enhancing urodynamics. These findings support an individualized and complementary treatment strategy for BPH “inflammatory phenotype”, and provide a new evidence-based option for clinical management of such intractable patients.

Disclosure of conflict of interest

None.

Address correspondence to: Xiaokai Hu, Teaching and Research Section of Traditional Chinese Medicine, Qilu Medical University, No. 2018 Jiangmeng Road, Zhoucun District, Zibo 255300, Shandong, China. E-mail: huxiaokai2026@126.com

References

- [1] Togo Y, Yoshioka S, Kaizuka Y and Nagasawa S. Effectiveness of transurethral enucleation with bipolar for benign prostatic hyperplasia patients with chronic prostatitis/chronic pelvic pain syndrome - single center retrospective study. *J Infect Chemother* 2025; 31: 102647.
- [2] Aydogdu O, Erdemoglu O, Bozkurt HI, Degirmenci T and Winder M. Correlation between chronic prostate inflammation and overactive bladder symptoms following transurethral resection of the prostate due to benign prostate hyperplasia. *Can J Urol* 2025; 32: 529-538.
- [3] Teng Z, Jin C, Wang S, Han Z, Zhang Y and Wang Y. Predicting surgical efficacy and diagnosing histological inflammation: the clinical significance of prostate exosome proteins in benign prostatic hyperplasia. *Transl Androl Urol* 2024; 13: 930-939.
- [4] Tao G and Wang X. The real-world study of Qian Lie Shu Tong Jiao Nang combined with finasteride tablets in the treatment of benign prostatic hyperplasia. *Pak J Pharm Sci* 2024; 37: 1591-1597.
- [5] Ma CG, Liu YN and Wang HD. NLRP3 inflammasome in expressed prostatic secretions as a potential biomarker of chronic prostatitis/chronic pelvic pain syndrome. *Adv Clin Exp Med* 2025; 34: 1459-1466.
- [6] Sciacqua LV, Vanzulli A, Di Meo R, Pellegrino G, Lavorato R, Vitale G and Carrafiello G. Minimally Invasive Treatment in Benign Prostatic Hyperplasia (BPH). *Technol Cancer Res Treat* 2023; 22: 15330338231155000.
- [7] Infante Hernández S, Gómez Rivas J and Moreno Sierra J. Benign prostatic hyperplasia. *Med Clin (Barc)* 2024; 163: 407-414.
- [8] Yang F, Yang C, Wang X, Chen D, Wang Z, Wang J, Liang C, Hua L, Ping H, Lu J, Wang Z, Li W and Xing N. Efficacy and Safety of Xialiqli for the treatment of benign prostatic hyperplasia in a randomized trial. *Eur Urol Open Sci* 2025; 82: 73-80.
- [9] Haile ES, Sotimehin AE and Gill BC. Medical management of benign prostatic hyperplasia. *Cleve Clin J Med* 2024; 91: 163-170.
- [10] Mahbubi Sani M, Pradnyan Klopang Y and Surahmad F. Benign prostatic hyperplasia genetic variants in Asians. *Clin Chim Acta* 2025; 565: 119986.
- [11] Suzuki Y, Kaneko H, Okada A, Fujiu K, Jo T, Takeda N, Tanaka A, Node K, Morita H,

- Yasunaga H and Komuro I. Benign prostatic hyperplasia and incident cardiovascular disease. *Circ J* 2024; 88: 408-416.
- [12] Murad L, Bouhadana D, Hamouda A, Arezki A, Layne E, Ganjavi C, Cacciamani GE, Glaser AP, Helfand BT and Zorn KC. Artificial intelligence in benign prostatic hyperplasia. *Urol Clin North Am* 2025; 52: 509-522.
- [13] Shanmugasundaram D, Dwan C, Wimmer BC and Srivastava S. Fucoidan Ameliorates Testosterone-Induced Benign Prostatic Hyperplasia (BPH) in rats. *Res Rep Urol* 2024; 16: 283-297.
- [14] Mdivnishvili M, Khuskivadze N and Khuskivadze A. Giant benign prostatic hyperplasia: a case report. *Cureus* 2024; 16: e61295.
- [15] Zhou XZ, Huang P, Wu YK, Yu JB and Sun J. Autophagy in benign prostatic hyperplasia: insights and therapeutic potential. *BMC Urol* 2024; 24: 198.
- [16] Shi J and Phanumartwiwath A. Airborne chloride exposure and benign prostatic hyperplasia risk. *BMC Res Notes* 2025; 18: 446.
- [17] Koudonas A, Anastasiadis A, Tsiakaras S, Lanas G, Savvides E, Mykoniatis I, Memmos D, Baniotis P, Vakalopoulos I, de la Rosette J and Dimitriadis G. Overview of current pharmacotherapeutic options in benign prostatic hyperplasia. *Expert Opin Pharmacother* 2023; 24: 1609-1622.
- [18] Hata J, Harigane Y, Matsuoka K, Akaiha H, Yaginuma K, Meguro S, Hoshi S, Sato Y, Ogawa S, Uemura M and Kojima Y. Mechanism of androgen-independent stromal proliferation in benign prostatic hyperplasia. *Int J Mol Sci* 2023; 24: 11634.
- [19] Ouyang C, Zhou L, Liu J, Wang L and Lu Y. Benign prostatic hyperplasia increases long-term chronic kidney disease risk. *Mayo Clin Proc* 2025; 100: 790-800.
- [20] Ramanujan S, Orji P, Chiu A, Kumar SS, Jevnikar W, Cox B, Montague D, Almassi N, Lee B, Bena J, Morrison S, Chehroudi AC, Bajic P and De S. Benign prostatic hyperplasia knowledge deficits among male urology patients. *Urology* 2025; 199: 141-146.
- [21] Hennenberg M, Hu S, Tamalunas A and Stief CG. Genetic predisposition to benign prostatic hyperplasia: where do we stand? *Eur Urol Open Sci* 2024; 70: 154-157.
- [22] Cheema AS, Long BG, Moore KE and McVary KT. UroLift, Rezūm, and iTind for benign prostatic hyperplasia. *Urol Clin North Am* 2025; 52: 547-558.
- [23] Yin F, He QD, Chen J, Gui TJ, Cai RJ, Wang Y, Xue QX, Li LY, Tian XK, Wang T and Zhe XW. Benign prostatic hyperplasia associated with white matter hyperintensities in men. *Clin Neurol Neurosurg* 2023; 229: 107738.
- [24] Pollack AS, Kunder CA, Brazer N, Shen Z, Varma S, West RB, Cunha GR, Baskin LS, Brooks JD and Pollack JR. Spatial transcriptomics identifies candidate stromal drivers of benign prostatic hyperplasia. *JCI Insight* 2024; 9: e176479.
- [25] Nikolic VN, Jankovic SM, Vujovic M, Sterovic S, Dinic LA and Milovanovic JR. Population pharmacokinetics of tamsulosine in patients with benign prostatic hyperplasia. *World J Urol* 2024; 42: 427.
- [26] Xu X, Tan H, Zhang W, Liu W, Chen Y, Zhang J, Gu M, Yang Y, Chen Q, Wang Y, Qian K and Xu B. Decoding benign prostatic hyperplasia: insights from multi-fluid metabolomic analysis. *Small Methods* 2025; 9: e2401906.
- [27] Rao X, Xu Z, Zhang J, Zhou J, Huang J, Toh Z, Zheng R and Zhou Z. The causal relationship between sarcopenic obesity factors and benign prostate hyperplasia. *Front Endocrinol (Lausanne)* 2023; 14: 1290639.
- [28] Wei P, Lin D, Luo C, Zhang M, Deng B, Cui K and Chen Z. High glucose promotes benign prostatic hyperplasia by downregulating PDK4 expression. *Sci Rep* 2023; 13: 17910.
- [29] Lu J, Gao W, Fei C, Liao W, Hou G, Lin Y, Rao W, Yang Q and Sui X. Associated factors for benign prostatic hyperplasia in patients with bladder calculi. *Urologia* 2025; 92: 406-414.
- [30] Zekraoui O, Bhojani N, Zorn KC, Elterman D and Chughtai B. Management and treatment of benign prostatic hyperplasia symptoms: current insights. *Res Rep Urol* 2025; 17: 401-420.