

ORIGINAL RESEARCH

Guiyi Tonglong Formula for moderate benign prostatic hyperplasia patients with kidney deficiency and blood stasis syndrome: a protocol for a multicenter, double-blind, double-dummy, randomized controlled trial

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Abstract

Background: Benign prostatic hyperplasia (BPH) is common in middle-aged and older men and frequently causes lower urinary tract symptoms that impair quality of life. Guiyi Tonglong Formula, a standardized traditional Chinese medicine prescription derived from Guizhi Fuling Wan, has shown preliminary efficacy and safety in patients with BPH characterized by kidney deficiency with blood stasis, but robust multicenter evidence is lacking. **Methods:** This multicenter, double-blind, double-dummy, randomized, parallel-controlled superiority clinical trial will recruit 138 men aged 50–75 years with moderate BPH and kidney deficiency with blood stasis syndrome from five centers in China. Participants will be randomized 1:1 to receive Guiyi Tonglong Formula Granules plus a placebo matching tamsulosin hydrochloride extended-release capsules or tamsulosin hydrochloride extended-release capsules plus a placebo matching Guiyi Tonglong Formula Granules. Treatment will last 12 weeks, followed by a 4-week follow-up. The primary endpoint is the change in International Prostate Symptom Score (IPSS) from baseline to Week 12. Secondary endpoints include quality of life scores, maximum urinary flow rate, post-void residual urine volume, prostate volume, Traditional Chinese medicine (TCM) symptom scores, and IPSS subscale scores. Safety will be assessed through physical examinations, vital signs, laboratory tests, electrocardiograms, and adverse-event monitoring. The primary analysis will use a mixed-effects model for repeated measures in the full analysis set. **Results:** The trial is ongoing, and no outcome data are available at this stage. **Conclusions:** This study aims to systematically evaluate the efficacy and safety of Guiyi Tonglong Formula in treating moderate BPH (kidney deficiency with blood stasis syndrome). The results are expected to provide a new reference for TCM treatment options in the management of BPH. **Clinical Trial Registration:** ITMCTR2025001403.

Keywords

Guiyi Tonglong Formula; Benign prostatic hyperplasia; Traditional Chinese medicine

1. Introduction

Benign prostatic hyperplasia (BPH) is a common condition among middle-aged and elderly men, primarily characterized by lower urinary tract symptoms (LUTS) such as urinary frequency and progressive urinary hesitancy [1, 2]. The incidence of BPH rises steeply with age, affecting over 50% of men aged 60 years and exceeding 80% by age 80 years [3, 4]. As a progressive disease, BPH may lead to complications such as urinary retention, recurrent hematuria, recurrent urinary tract infections, bladder stones, and renal insufficiency. The disease not only significantly reduces patients' quality of life (QOL), but also harms patients' physical and mental health, resulting

in substantial social and economic burdens [5, 6].

Current first-line treatments for BPH include alpha-adrenergic receptor blockers (e.g., tamsulosin, doxazosin) and 5 α -reductase inhibitors (e.g., finasteride, dutasteride) [7]. Research demonstrates that combination of these two types of drugs can improve patients' overall symptoms [8–10]. However, surgical intervention is indicated when symptoms worsen, when medication fails to provide significant relief, or when symptoms significantly affect daily life, post-void residual urine (PVR) exceeds 60 mL, or when complications arise [11]. Although pharmacological and surgical treatments can relieve symptoms, responses vary, and treatment may

be associated with adverse effects, including orthostatic hypotension and ejaculatory dysfunction with medication, and urinary tract infection (UTI), bleeding, or postoperative urinary incontinence with surgery [11–13]. Therefore, identifying safer and more effective treatment options seems crucial for improving the QOL of patients with BPH.

Traditional Chinese medicine (TCM) has demonstrated efficacy in treating BPH, with advantages such as marked improvement in urinary symptoms and associated complaints, enhancement of QOL, delay of disease progression, and reduction of complication risk [14–18]. Consequently, TCM has garnered increasing attention and research in recent years. Among these, the Guiyi Tonglong Formula—a prescription of the Andrology Department of Xiyuan Hospital, China Academy of Chinese Medical Sciences—is indicated for treating BPH of kidney deficiency with blood stasis pattern. Derived from Zhang Zhongjing’s Guizhi Fuling Pill, it functions to warm and tonify kidney yang while promoting blood circulation and resolving stasis. Preliminary small-scale clinical studies have already indicated that Guiyi Tonglong Formula is effective and safe for treating BPH, demonstrating superiority over the tamsulosin hydrochloride sustained-release capsule control group in reducing International Prostate Symptom Score (IPSS) scores, improving TCM symptom scores, and enhancing QOL ($p < 0.05$) [19].

Furthermore, in preliminary experiments, the research team successfully established an estrogen/androgen-induced BPH rat model. Hematoxylin and eosin (H&E) staining of the prostate tissue in the control group revealed low numbers of columnar epithelial cells arranged in a single-layered, secretory tubular pattern, filled with a thin layer of eosinophilic material. In contrast, the model group showed marked proliferation of epithelial cells, with excessive glandular development and cells arranged in multiple layers in a disorganized manner. Following intervention with the Guiyi Tonglong Formula, however, cell proliferation and glandular development were markedly inhibited, and the pathological damage to the prostate tissue was significantly improved in the BPH rat model. Concurrently, BPH rats treated with the Guiyi Tonglong Formula were found to have lower levels of malondialdehyde (MDA)—a major lipid peroxidation product—and reactive oxygen species (ROS)—key oxidative stress markers—compared with the model group, while superoxide dismutase (SOD) levels were higher than in the model group. These findings indicate that the formula alleviates the processes of lipid peroxidation and oxidative stress in the prostate tissue of BPH rats, providing a partial mechanistic explanation for the Guiyi Tonglong Formula from an antioxidant perspective.

However, existing clinical studies are limited to single-center exploratory research, lacking sufficient high-quality evidence to confirm their clinical efficacy and safety. To address this gap, we designed an investigator-initiated, multicenter, double-blind, double-dummy, randomized, parallel-group, controlled trial to evaluate the efficacy and safety of Guiyi Tonglong Formula in patients with moderate BPH of kidney deficiency with blood stasis syndrome.

2. Methods

2.1 Study design

This trial employs a multicenter, double-blind, double-dummy, randomized, parallel-group superiority study design. A total of 138 patients with moderate BPH (kidney deficiency with blood stasis syndrome) meeting the inclusion and exclusion criteria will be recruited from August 2025 to December 2026. Recruitment will be conducted across five centers nationwide: the Department of Andrology at Xiyuan Hospital of the China Academy of Chinese Medical Sciences; the Department of Andrology at the First Affiliated Hospital of Tianjin University of Traditional Chinese Medicine; the Department of Andrology at the Affiliated Hospital of Chengdu University of Traditional Chinese Medicine; the Department of Andrology at the Affiliated Hospital of Shandong University of Traditional Chinese Medicine; and the Department of Andrology at the Affiliated Hospital of Shanxi University of Chinese Medicine. Eligible patients will be randomly assigned to either the experimental group or the control group using a stratified randomization method by center. The experimental group will receive Guiyi Tonglong Formula Granules combined with a placebo matching Tamsulosin Hydrochloride Extended-Release Capsules, while the control group will receive a placebo matching Guiyi Tonglong Formula Granules combined with Tamsulosin Hydrochloride Extended-Release Capsules. Both groups will undergo a 12-week intervention period followed by a 4-week follow-up. The primary outcome measure is the IPSS scores. Secondary outcome measures comprise QOL scores, maximum urinary flow rate (Q_{max}), PVR, prostate volume, TCM symptom scores, and IPSS subscale scores. Safety indicators will include complete blood count, urinalysis, liver/kidney function tests, and electrocardiogram (ECG). Baseline patient information to be recorded will include age, ethnicity, body mass index, smoking and drinking status, disease duration, and relevant medical history. The study flowchart is shown in Fig. 1.

2.2 Sample size

This trial is designed as a superiority study with IPSS score being the primary endpoint. Based on previous literature, a 4.2-point reduction in IPSS by Guiyi Tonglong Formula Granules is considered the clinically meaningful threshold (*i.e.*, the margin of superiority δ). A reduction in IPSS score with Guiyi Tonglong Formula that exceeds that of Tamsulosin by more than 4.2 points would be considered clinically meaningful. Accordingly, with $\delta = 4.2$, $\alpha = 0.025$ (one-sided), $\beta = 0.2$ (80% power), and a 1:1 allocation ratio (k) between the experimental and control groups, the required sample size for each group was calculated as 55 subjects. Considering the extended trial duration and a projected 20% loss to follow-up rate, the total study sample size was determined to be 138 subjects, with 69 participants in each group.

2.3 Eligibility criteria

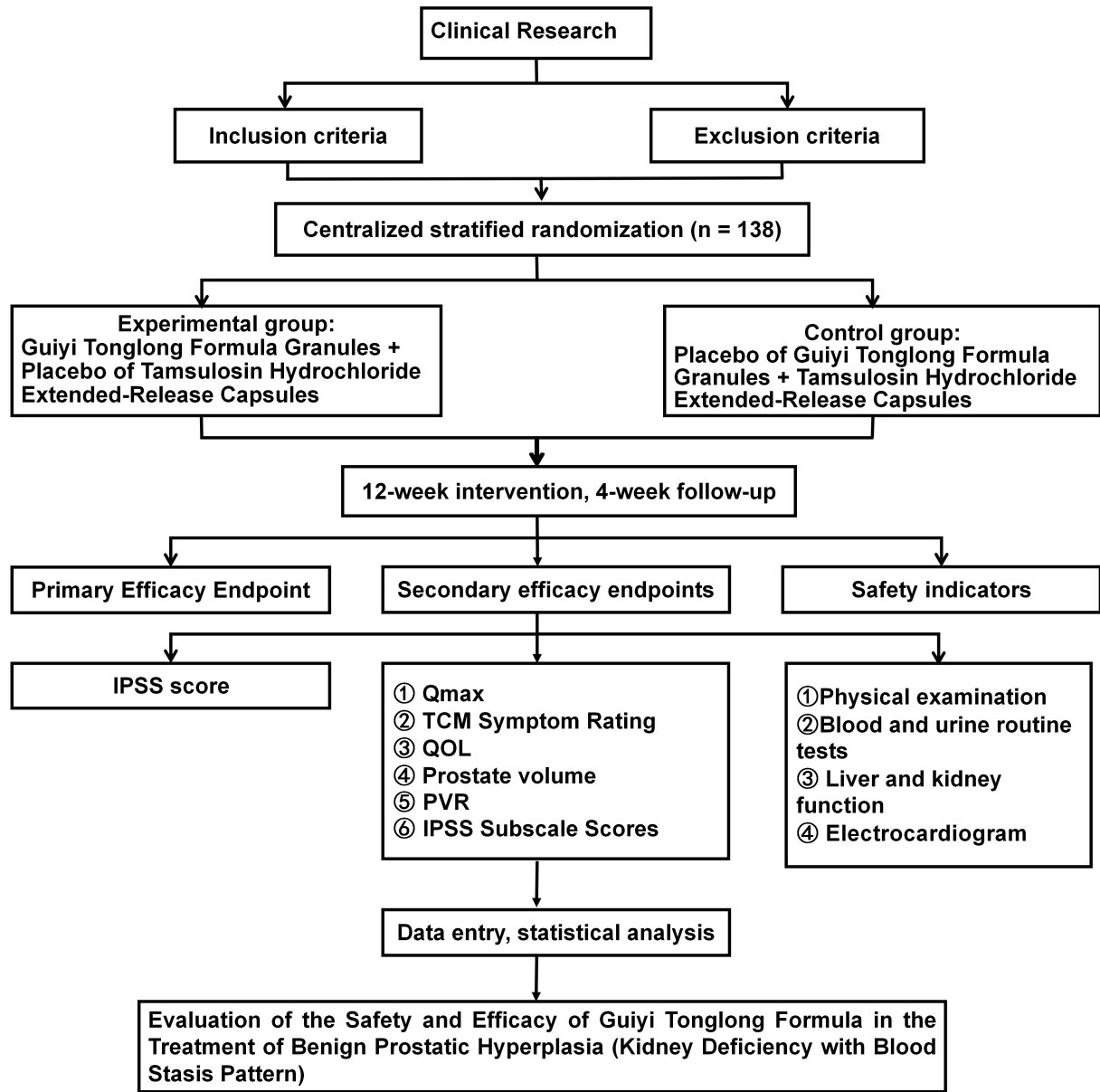


FIGURE 1. Study flow diagram: recruitment, grouping, intervention, follow-up, assessment, and outcomes. IPSS: International Prostate Symptom Score; Qmax: maximum urinary flow rate; TCM: Traditional Chinese Medicine; QOL: Quality of Life Score; PVR: post-void residual.

2.3.1 Inclusion criteria

Subjects must meet all of the following inclusion criteria to be eligible for enrollment: (1) men, aged 50 to 75 years; (2) duration of symptoms ≥ 3 months; (3) diagnosis of BPH according to the Western medical diagnostic criteria; (4) moderate IPSS (8 points $\leq$ IPSS $\leq$ 19 points) and QOL score ≥ 3 points; (5) TCM pattern identification criteria consistent with kidney deficiency and blood stasis in BPH; (6) No prior treatment received or a discontinuation of medication for at least 2 weeks if previously treated; and (7) provision of informed consent.

2.3.2 Quality control for TCM syndrome diagnosis

To ensure diagnostic consistency and rigor, each patient will be independently diagnosed by two TCM practitioners holding the title of Associate Chief Physician or higher, in accor-

dance with the standards set out in the Guidelines for Multidisciplinary Diagnosis and Treatment of Benign Prostatic Hyperplasia Using a Combination of Traditional Chinese and Western Medicine (2022 edition) [4] and the Guidelines for Clinical Research on New Traditional Chinese Medicines. The diagnostic criteria for kidney deficiency with blood stasis syndrome are as follows:

Principal symptoms: Weakness and soreness in the lower back and knees; difficulty urinating or frequent nocturia.

Secondary symptoms: Mental fatigue and general weakness; weak urine stream; aversion to cold and cold extremities.

Tongue and pulse findings: Dull tongue colour with petechiae and ecchymoses; thin white coating; deep and thready pulse.

A diagnosis of kidney deficiency with blood stasis syndrome will be established if two of the above principal symptoms and

any one of the secondary symptoms are present, in conjunction with the tongue and pulse findings.

2.3.3 Exclusion criteria

Participants with any of the following conditions will be excluded from this trial: (1) Prostate cancer, or suspected prostate tumors with prostate-specific antigen (PSA) >10 ng/mL. For patients with PSA >4 ng/mL and <10 ng/mL digital rectal examination and measurement of the f-PSA/t-PSA ratio will be required to exclude prostate cancer; (2) Neurogenic bladder, bladder neck fibrosis, bladder stones, bladder cancer, UTI, or a history of transurethral surgical procedures; (3) Indications for surgical treatment (including renal insufficiency due to obstruction, refractory urinary retention, recurrent cystitis, bladder stones, persistent hematuria); (4) History of severe chronic or acute hepatitis; (5) Concomitant severe hepatic or renal dysfunction, defined as AST (aspartate aminotransferase) and/or ALT (alanine aminotransferase) ≥ 1.5 times the upper limit of normal, or serum creatinine and/or blood urea nitrogen $\geq$ normal range; (6) Uncontrolled diabetes mellitus, fasting blood glucose ≥ 1.5 times the upper limit of normal, or with diabetic complications (diabetic nephropathy, peripheral neuropathy); (7) History of severe central nervous system injury within 6 months (cerebrovascular diseases such as cerebral hemorrhage or ischemia, inflammatory brain diseases such as encephalitis or meningitis, traumatic brain injury, or spinal cord injury), or any peripheral nervous system disorder; (8) History of psychiatric disorders; (9) History of any high-risk arrhythmia or arrhythmia confirmed by ECG, or ECG results deemed clinically significant by the investigator during the screening visit; (10) History of malignant tumors within the past 3 years; (11) Known allergy to the study drug or similar drugs; (12) Orthostatic hypotension, or concomitant use of other medications that may cause orthostatic hypotension, such as alpha-blockers; and (13) Deemed ineligible by the investigator for any other reasons.

2.4 Intervention

Participants in the experimental group will receive Guiyi Tonglong Formula Granules + placebo of Tamsulosin Hydrochloride Extended-Release Capsules, while those in the control group will receive a placebo of Guiyi Tonglong Formula Granules + Tamsulosin Hydrochloride Extended-Release Capsules. Guiyi Tonglong Formula Granules and their placebo will be provided by Tasly Pharmaceutical Group Co., Ltd. (Tianjin, China), supplied in sachets containing 10 g each. Recommended dosage is 1 sachet per dose, taken twice daily with warm water after breakfast and dinner. Tamsulosin Hydrochloride Extended-Release Capsules and their placebo will be provided by Hangzhou Kang'enbei Pharmaceutical Co., Ltd. (Hangzhou, Zhejiang, China), with each capsule containing 0.2 mg of the active ingredient. Participants will take one capsule once daily before bedtime. Throughout the study period, participants will be strictly prohibited from adding other medications or interventions (such as acupuncture) to ensure trial integrity and accuracy of results.

2.5 Control drug design and rationale

Tamsulosin hydrochloride is recommended as a first-line treatment for BPH by the European Association of Urology (EAU), the American Urological Association (AUA), and the Chinese Guidelines for the Diagnosis and Treatment of Urological Diseases. It is also the most commonly used highly selective $\alpha 1$ -receptor antagonist in the clinical management of BPH. By selectively blocking $\alpha 1a$ -adrenergic receptors, it induces relaxation of the prostatic smooth muscle, thereby alleviating urinary difficulties and other LUTS, while exhibiting fewer side effects than other α -receptor antagonists. Consequently, tamsulosin hydrochloride extended-release capsules will be selected as the control drug for this trial.

2.6 Outcome measures

2.6.1 Efficacy measures

The primary efficacy endpoint is the IPSS, a validated and guideline-recommended standard instrument for assessing symptom severity in patients with BPH [20]. It comprises seven questions, each scored on a scale of 0–5, with a total score ranging from 0 to 35. IPSS will be assessed at screening, Visits 1–5, and at Follow-up 1 and Follow-up 2. Secondary efficacy endpoints include Qmax, TCM symptom scores, QOL scores, prostate volume, PVR urine volume, and IPSS subscale scores. The QOL score, which assesses the degree to which patients are troubled by urinary symptoms, is rated on a scale of 0–6, with higher scores indicating greater severity (see Table 1).

2.6.2 Safety endpoints

Safety assessment will encompass patients' general condition, laboratory parameters, and adverse event (AE) occurrence. General condition, including physical examination findings and vital signs, will be monitored at screening period. Laboratory tests will include complete blood count, urinalysis, liver function tests (including ALT and AST), renal function tests (including blood urea nitrogen (BUN) and creatinine (Cr)), and ECG. These parameters will be assessed at baseline and again at Week 12 post-treatment. Adverse events will be monitored and recorded throughout the entire study period.

2.6.3 Grading of adverse events

Adverse events will be classified into three grades according to severity:

Mild: Symptoms are tolerable to the subject, do not affect treatment, require no special management, and have no impact on the subject's recovery.

Moderate: Symptoms are intolerable to the subject, require discontinuation of the drug or special management, and have a direct impact on the subject's recovery.

Severe: Symptoms are life-threatening to the subject, may lead to death or disability, and require immediate discontinuation of the drug or emergency management.

The detailed schedule of enrollment, interventions, and assessments is presented in Table 2.

TABLE 1. Quality of life (QOL) scale.

	Very happy	Satisfied	Mostly satisfied	Fairly satisfied	Not very satisfied	Upset	Very unhappy
If your current urinary symptoms were to persist throughout the rest of your life, how would you feel about that?	0	1	2	3	4	5	6

Higher scores indicate poorer quality of life.

TABLE 2. Visit process schedule.

Item \ Phase	Trial Period						Follow-up Period	
	Screening Period	Visit 1 (Telephone)	Visit 2	Visit 3	Visit 4	Visit 5	Follow-up 1 (Phone)	Follow-up 2 (Phone)
Time	-14 d to 0 d	7 d ± 3 d	14 d ± 3 d	28 d ± 3 d	56 d ± 3 d	84 d ± 3 d	98 d ± 3 d	112 d ± 3 d
Collect basic information								
Sign informed consent form	√							
Demographic characteristics	√							
General Clinical Data	√							
Physical Examination	√							
Vital Signs	√							
Validity Observation								
IPSS	√	√	√	√	√	√	√	√
TCM Symptom Score	√	√	√	√	√	√	√	√
QOL	√	√	√	√	√	√	√	√
Urinary flow rate test	√		√	√		√		
Residual Urine Volume Test	√		√	√		√		
Prostate Ultrasound	√					√		
Safety Monitoring								
Blood and Urine Routine Tests, Liver and Kidney Function Tests	√					√		
Electrocardiogram	√					√		
Adverse events		√	√	√	√	√	√	√
Other								
Medication distribution	√		√	√	√	√		
Combination Therapy	√	√	√	√	√	√		
Distribute patient diary cards	√		√	√	√	√		
Medication Disposal			√	√	√	√		
Recycling Patient Record Cards			√	√	√	√		
Experiment Summary								√

“√” indicates yes. IPSS: International Prostate Symptom Score; QOL: Quality of Life Score; TCM: Traditional Chinese Medicine.

2.7 Randomization and blinding

To minimize potential bias, this study will employ blinding for physicians, enrolled patients, and statisticians. Blinding will be carried out by the Good Clinical Practice (GCP) department of Xiyuan Hospital, China Academy of Chinese Medical Sciences. Randomization codes will be generated using SAS software, employing a center-stratified randomization method with a 1:1 ratio between the experimental and control groups. The selected block length and random seed parameters will be sealed within the blinding envelope along with other confidential data. Based on these random numbers, personnel unrelated to the trial will code the medicinal products, which will then be used sequentially by each clinical research center in accordance with the allocated drug codes and the order of patient enrolment. Two copies of the blinding protocol will be sealed and stored in the office of the National Drug Clinical Trial Base at Xiyuan Hospital of the China Academy of Chinese Medical Sciences. The randomization numbers, drug batch numbers and drug verification codes will be kept by designated personnel following the completion of the blinding process.

To ensure successful blinding, the placebos for both Guiyi Tonglong Formula and Tamsulosin Hydrochloride Extended-Release Capsules will be indistinguishable from their active drugs in terms of shape, size, color, weight, taste, labeling, and packaging.

2.8 Data monitoring and quality control

To ensure precision and consistency throughout the trial, all investigators will receive standardized training before study initiation to maintain strict adherence to the study protocol across all centers. Two trained research assistants will be responsible for data collection. All investigators and statisticians will remain blinded to treatment allocation until statistical calculations are completed. To ensure coordination and smooth monitoring of all trial phases, including subject recruitment, intervention implementation, and follow-up procedures, the principal investigator will provide ongoing oversight and management. Finally, each participating center will be responsible to implement rigorous data quality control processes to ensure data quality and accuracy.

2.9 Statistical analysis

Analysis of the primary efficacy endpoint: The primary efficacy analysis will be conducted using the full analysis set (FAS), with the per-protocol set (PPS) used as supportive analysis. The primary efficacy endpoint of this study will be the change in IPSS score from baseline to after 12 weeks of treatment. Analysis will be performed using a mixed-effects model for repeated measures (MMRM), with the dependent variable defined as the change from baseline in the observed values at each follow-up time point. Fixed effects will include experimental group, center, follow-up time point, and an interaction term between experimental group and follow-up time point, with baseline IPSS values as covariates. Restricted maximum likelihood estimation will be used to calculate the least-squares mean differences between groups and the two-

sided 95% confidence intervals (CIs).

Handling of missing data: For the primary efficacy analysis using MMRM, all available data will be analyzed under the missing-at-random (MAR) assumption. To assess the robustness of our findings, we will conduct sensitivity analyses using multiple imputation (MI). The proportion and pattern of missing data will be summarized descriptively.

Secondary endpoint analysis: Continuous secondary outcomes will be analyzed using analysis of covariance (ANCOVA), with baseline values as covariates. Categorical variables will be analyzed using the Chi-square or Fisher's exact test.

Safety analysis: Safety data will be summarized using descriptive statistics. The incidence of adverse events (AEs) will be compared between groups using Fisher's exact test.

3. Discussion

BPH is a common condition among middle-aged and elderly men, significantly impairing patients' QOL and posing a heavy public health burden as the population ages [21–23]. Although Western medication can effectively alleviate LUTS, their long-term use may be associated with adverse effects such as postural hypotension and sexual dysfunction [12, 13].

The Guiyi Tonglong Formula is a standardized formula used by the Department of Andrology at Xiyuan Hospital of the China Academy of Chinese Medical Sciences for the treatment of BPH (characterized by kidney deficiency with blood stasis). Cinnamon bark is warm in nature and can enter the kidney meridian, warming and tonifying kidney yang. Its pungent and dispersing properties also promote the circulation of qi and blood. Motherwort promotes blood circulation and diuresis. When used in combination, these two herbs serve as the principal ingredients, working together to tonify the kidneys and promote blood circulation. Previous network pharmacology and molecular docking studies have suggested potential molecular targets and signaling pathways for Guiyi Tonglong Formula and its principal herb pair, cinnamon and motherwort, in BPH [24, 25]. Auxiliary herbs such as Suoyang warms the kidneys and aids yang; when used in conjunction with Cinnamon Bark, it enhances the warming and tonifying effect on kidney yang. Turmeric rapidly breaks up blood stasis, unblocks the channels, and descends qi most swiftly; its action is further strengthened when combined with Motherwort, which enhances the ability to invigorate blood circulation. Poria, with its sweet and bland nature, drains dampness and promotes diuresis to eliminate phlegm and facilitate fluid metabolism; when combined with herbs that invigorate blood and resolve stasis, it contributes to the inhibition of BPH.

Another auxiliary herb Astragalus, sweet and warm in property, serves as a key herb for tonifying qi—when qi flows, blood circulates freely and fluid metabolism is regulated. Prepared Rehmannia, also sweet and warm, enters the Liver and Kidney meridians to nourish the yin of these two organs. Its combination with Cinnamon Bark embodies the principle of “seeking yang within yin”, while its concurrent use with the blood-activating herbs (Motherwort and Turmeric) and the diuretic Poria ensures that stasis is resolved and fluid metabolism is restored, while preserving yin essence. Chenpi

harmonizes the various herbs, ensuring that the formula as a whole is tonifying without being cloying, and serves as the guiding herb. When used in combination, these herbs collectively achieve the effects of warming and tonifying kidney yang, as well as promoting blood circulation and resolving blood stasis. Preliminary clinical studies have indicated no significant adverse reactions before or after treatment with the Guiyi Tonglong Formula, with no clear contraindications to date.

A major strength of this study is its multicenter, double-blind, double-dummy, randomized, parallel-controlled superiority design, together with the use of tamsulosin as an active comparator and the inclusion of both patient-reported and objective urological outcomes. It will clarify the role of the formula in improving key indicators such as IPSS scores, maximum urinary flow rate, and residual urine volume, and further reveal the modern scientific rationale of the therapeutic approach “warming and tonifying kidney yang, promoting blood circulation and resolving stasis” in BPH treatment. Moreover, the study will provide a new treatment option for patients with BPH, particularly for patients who cannot tolerate the side effects of Western medicines, who prefer TCM treatment, or who require adjunctive therapy due to inadequate response to Western medicines. The formula consists of eight common Chinese herbal ingredients, with raw materials that are widely available and costs that remain manageable. Additionally, the granule formulation offers convenient administration, making it feasible to promote in China and Southeast Asia. Global promotion will require further validation through multicenter, cross-ethnic clinical trials, as well as health economic evaluations within different healthcare systems.

This study has several limitations. First, the study only includes patients with moderate BPH characterized by kidney deficiency with blood stasis syndrome who are recruited from five centers in China. This may limit the generalizability of the findings to patients with mild or severe LUTS, other TCM syndromes, or populations in other regions. Second, exploratory biomarkers related to oxidative stress, inflammation, and age-related endocrine changes are not assessed, which may limit the mechanistic interpretation of the findings. Future studies involving broader patient populations and relevant biomarker assessments are warranted.

4. Conclusions

This multicenter, double-blind, double-dummy, randomized, parallel-controlled superiority trial is designed to compare the efficacy and safety of Guiyi Tonglong Formula with tamsulosin in patients with moderate BPH characterized by kidney deficiency with blood stasis syndrome. The findings are expected to provide high-quality clinical evidence for Guiyi Tonglong Formula and clarify its potential role as an integrative treatment option for BPH.

AVAILABILITY OF DATA AND MATERIALS

Not applicable as no datasets were generated at this stage, however, the data will be available on reasonable request after the study completion.

AUTHOR CONTRIBUTIONS

HL—drafted the trial protocol. FW and BDG—critically supervised and corrected the manuscript. CFZ, QG, GSL, ZGL, HW and MZ—participated in patient referral and recruitment. All the authors designed the trial and critically reviewed the manuscript. All authors have read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This trial is approved by the Ethics Review Committee of Xiyuan Hospital, China Academy of Chinese Medical Sciences (2023XLA140-2) and other recruiting centers, and will be conducted in accordance with the Declaration of Helsinki. Each participant will receive detailed information about the trial and sign a written informed consent form. The registration number on the International Traditional Medicine Clinical Trials Registry Platform is ITMCTR2025001403.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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