Research Article

Exploring the Efficacy of the Traditional Chinese Medicine Compound Formulas Qianlong Shutong Formula in the Treatment of Benign Prostatic Hyperplasia

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Abstract

Objective: This study aimed to assess the efficacy of the compound formula Qianlong Shutong Formula (QLSTF) in the treatment of benign prostatic hyperplasia (BPH) and its impact on hepatic and renal function. This assessment was conducted through randomized controlled trials and animal experimentation.

Methods: A total of 160 BPH patients aged between 50 and 70 years were randomly allocated into two groups: The tamsulosin hydrochloride sustained-release capsules group (n=80) and the QLSTF + tamsulosin hydrochloride sustained-release capsules group (n=80). Both groups received a 12-week treatment regimen. In the animal experiments, 12 Sprague Dawley rats were categorized into three groups: The control group (n=4), the model group (n=4), and the QLSTF group (n=4). The latter group received herbal treatment for a duration of 28 days.

Results: The current results showed, substantial improvements were observed in the clinical symptoms and signs of BPH within both drug groups. Additionally, no adverse effects on hepatic or renal function were detected. The QLSTF group exhibited a total effective rate of 90.41%, while the control group recorded 77.33%. During the course of treatment, three patients experienced dizziness, and two patients reported nausea and reduced appetite. However, these adverse reactions subsided after a rest period of 4-6h.

Conclusion: Our findings underscore the advantages and safety of orally administered QLSTF. In the treatment of BPH, the combined treatment approach using QLSTF demonstrated a higher clinical efficacy rate when compared to the use of tamsulosin hydrochloride sustained-release capsules alone.
Keywords: clinical research, animal experimentation, herbal, prostatic hyperplasia, traditional Chinese medicine


1 INTRODUCTION

Benign prostatic hyperplasia (BPH) predominantly affects middle-aged and elderly men in clinical practice[1]. According to statistical data, the prevalence of BPH escalates with advancing age, reaching 80% among individuals aged 80 and above. This incidence continues to rise annually[2]. BPH represents a prevalent ailment within the male reproductive system, characterized by the pathological hyperplasia of prostate epithelial and stromal tissues. This condition leads to prostate enlargement, subsequently obstructing and compressing the urethra, thereby engendering a spectrum of urination difficulties[3]. The primary clinical manifestations revolve around an array of lower urinary tract symptoms[4].

The pathogenesis of BPH is intricate, encompassing multiple signaling pathways and inflammatory processes. It is intricately linked to hormonal imbalances within the body[5]. Current treatment approaches for BPH encompass both Western medicine and surgical interventions. Clinical practices predominantly involve the utilization of α-receptor blockers, 5α-reductase inhibitors, and anti-androgen medications. These interventions demonstrate efficacy in reducing prostate volume and ameliorating urinary symptoms[6]. Nonetheless, prolonged administration is prone to eliciting drug resistance and adverse reactions, thereby compromising patients’ quality of life and imposing a strain on healthcare resources[7]. Regrettably, many patients continue to exhibit disease progression despite sustained pharmacological treatment, ultimately necessitating surgical interventions[8]. Surgical procedures, however, entail associated complications and risks, including retrograde ejaculation[9].

Traditional Chinese medicine (TCM) has exhibited promising results in treating BPH, displaying the potential to improve parameters such as prostate volume, quality of life, quality of life (QOL) scores, and maximum urinary flow rate (Q_{max}) scores[10,11]. The Qianlong Shutong Formula (QLSTF) emerges as a TCM compound derived from the clinical expertise of our research group. Preliminary observations suggest its favorable efficacy in selecting BPH patients; however, a definitive verdict on its specific therapeutic efficacy remains outstanding. To this end, we intend to employ a combination of randomized controlled trials and animal experimentation to rigorously examine the therapeutic potential of QLSTF. (Refer to Figure 1 for an illustration of the proposed methodology).

2 MATERIALS AND METHODS

2.1 Animal Experimentation

2.1.1 Drugs and Reagents

The QLSTF was meticulously prepared with a concentration of 1g/mL by the hospital preparation room. Testosterone propionate injection, procured from the Ningbo Second Hormone Factory (batch number: 200801), was utilized. Procaine penicillin injection (Shanghai Gongyi Pharmaceutical Co., Ltd., 3 million units /10mL) and isoflurane (Shenzhen Ruiwode Life Technology Co., Ltd., R510-22-10) were also employed.

2.1.2 Animal Subjects

Twelve healthy adult male Sprague Dawley (SD) rats, specific pathogen free grade, aged 8 weeks, with a weight range of 300-320g, were procured from Hunan Slake Jingda Experimental Animal Co., Ltd. The rats were housed in an environment maintained at a temperature of 23-25℃ and a humidity level of 50%±10%. Illumination was provided for 12h a day, and the rats had ad libitum access to food and water. The experimental phase commenced after a 7-day acclimatization period to the new housing environment.

2.1.3 Equipment

Utilized equipment included a rotary evaporator (Swiss BUCHI, R-220PRO), fluorescence inverted biomicroscope (Japan, NIKON, TS-2), electric blast dryer (Shanghai Shenguang Instrument Co., Ltd., 101AB-1), paraffin slicer (Germany, Leica, LEICA-RM2165), and embedding machine (Shandong Boke Regenerative Medicine Co., Ltd., BK-TE).

2.1.4 Induction of BPH Model

Following a 7-day adaptation period, four SD rats were randomly assigned to the blank group, while eight rats were equally divided into the model group and QLSTF group (four rats each). Anesthesia was induced using 3% isoflurane, followed by castration under 2% isoflurane maintenance (oxygen flow rate 600mL/min). After disinfecting the scrotal skin of anesthetized rats, we utilized equipment to create a BPH model. Upon exposing the testicles, we ligated the vas deferens and blood vessels connecting the testicles, excised the...
connecting part of the testicles, and sutured the testicular skin layer by layer. We then disinfected the local skin and placed the rats on a warm and dry resuscitation board for recovery. Subsequently, procaine penicillin (11000-22000u/kg) was intramuscularly administered once daily. Following a 7-day interval, the establishment of a BPH model involved administering testosterone propionate (5mg/kg) dissolved in corn oil, at a frequency of once daily over 28 days for the model and QLSTF groups. The blank group received subcutaneous corn oil injections for an equal duration. This study received approval from the Medical and Experimental Animal Ethics Professional Committee of Guangxi University of Traditional Chinese Medicine (DW20230620-127).

2.1.5 Grouping and Administration
Upon establishing the BPH model, the crude drug dosage for the rats was set at 14.54g/kg/day for 28 days based on body surface area and human-rat dose conversion[12]. The blank and model groups received daily oral administrations of distilled water in equimolar volumes for 28 days. Throughout the experiment, rat body weights were measured consecutively over 3 days, with dosage adjustments made according to weight fluctuations.

2.1.6 Histopathological Analysis via Hematoxylin and Eosin (HE) Staining
24h post-final administration, rats were anesthetized
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using 3% isoflurane (oxygen flow rate 600mL/min). All rats maintained spontaneous breathing and received continuous oxygen inhalation. Following complete abdominal cavity exposure, liver, kidney, and prostate tissues were fixed in 4% paraformaldehyde, embedded in paraffin, and sectioned into 5μm thick slices. HE staining was performed for morphological evaluation utilizing a light microscope (Olympus BX-53) at 200X magnification. ImageJ software facilitated image processing to quantify prostate cell counts under 200X magnification.

2.1.7 Statistical Analysis
All data was presented as mean±SD. Statistical analysis was performed using SPSS 26.0 software package (IBM, Armonk, NY, United States). A homogeneity of variance test preceded data analysis via one-way ANOVA or Welch’s test, followed by post hoc analysis. Significance was indicated by P<0.05.

2.2 Randomized Controlled Trial

2.2.1 Case Source
From July 2021 to March 2023, a total of 160 patients diagnosed with BPH were enrolled at the Department of Urology, Ruikang Hospital Affiliated to Guangxi University of Traditional Chinese Medicine; Department of Andrology, National Medical Hall. Employing the random number table method, these patients were evenly divided into a treatment group and a control group, with 80 cases in each group. All subjects provided informed consent before participating in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Ruikang Hospital Affiliated to Guangxi University of Traditional Chinese Medicine (NO. KY2021-105).

2.2.2 Diagnostic Criteria
Participants were men aged over 50 with lower urinary tract symptoms, palpably enlarged prostate during digital rectal examination (DRE), elevated prostate volume indicated by B-scan ultrasonography, evidence of residual urine in the bladder on B-scan ultrasonography, and Q\text{max} greater than 150mL with Q\text{max} less than 15mL/s. Individuals meeting at least three of these criteria were diagnosed with BPH.

2.2.3 Inclusion and Exclusion Criteria
Inclusion criteria were based on diagnostic standards for BPH, including male patients aged 50-80 years with no history of BPH treatment in the past month, no prior surgical interventions, and the exclusion of prostate cancer possibility. Participants were required to provide voluntary consent.

Exclusion criteria encompassed prostate specific antigen (PSA) >10ng/mL, indications for surgical intervention (including cases of absolute or relative indications such as benign prostatic obstruction-induced renal insufficiency, intractable urinary retention, recurrent cystitis, medical therapy failure, bladder calculi, and persistent prostatic bleeding-induced hematuria), prior BPH-related surgical treatment, symptom exacerbation necessitating surgical intervention during the study, diagnosis alteration within the study timeframe, concurrent morbidities interfering with treatment, recent administration of BPH-related medications within the preceding six months, and discontinuation due to drug-related side effects. For patients with PSA>4ng/mL and <10ng/mL, DRE and measurement of the free / total PSA ratio were performed to rule out prostatic cancer.

2.2.4 Criteria for Case Elimination, Attrition, and Withdrawal
Patients unable to adhere to treatment, regular follow-up, or exhibit poor compliance were eliminated. Those experiencing severe complications or adverse reactions during the study, non-compliance with the prescribed regimen, unauthorized use of other BPH treatments, or voluntary withdrawal from the study were also excluded.

2.2.5 Drug Selection
The Traditional Chinese Medicine Information Database (TCM-ID: https://bidd.group/TCMID/index.html) was utilized to standardize drug names. The QLSTF comprised of raw Chinese medicinal materials: Qian Jin Ba (root of Philippine Flemingia, Radix Moghaniae philippinensis) 15g, E Zhu (Zedoray rhizome, Curcuma aeruginosa) 6g, Du Zhong (Eucommia, Eucommia ulmoides) 15g, Niu Xi (Twotooth Achyranthes, Achyranthes bidentata) 9g, Dang Shen (Dang Shen, Codonopsis pilosula) 12g, Huang Qi (Membranous milkvetch, Astragalus membranaceus) 15g, Rou Gui (Cassia barktree, Cinnamomum cassia) 6g, Xiao Mao (common Cruculigo, Curculigo orchioides) 10g, Xian Ling Pi (all-grass of longspur epimedium, Herba Epimedi) 10g, Huang Bai (Amur corktree, Phellodendron amurense) 12g, Fu Ling (Indian bread, Wolfiporia cocos) 10g, Mu Dan Pi (Subshrubby peony bark, Paeonia moutan) 10g, Chi Shao (Red peony root, Paeonia officinalis) 10g, Tao Ren (Peach kernel, Prunus persica) were coarsely powdered and subjected to decoction. The resultant decoction liquid was concentrated to 100mL.

Chinese medicine placebo comprised: Lactose 12g, edible caramel pigment 1.3g, edible sunset yellow pigment 0.005g, edible lemon yellow pigment 0.003g, edible bitter agent 0.2g, sodium benzoate 0.1g, purified water 100mL.

Western medicine utilized: Tamsulosin hydrochloride sustained-release capsules, 0.2mg×10×1 box, Sinopharm Approval No. H20000681, Anstel Pharmaceutical (China) Co., Ltd.

2.2.6 Treatment Regimen
The control group received tamsulosin hydrochloride

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sustained-release capsules, 0.2mg/time, once daily before bedtime, along with the Chinese medicine placebo, one dose in the morning and one in the evening.

The QLSTF group received tamsulosin hydrochloride sustained-release capsules, 0.2mg/time, once daily before bedtime, in conjunction with QLSTF, one dose in the morning and one in the evening. The study encompassed a 12-week treatment course, during which participants were consistently treated for a full course.

2.2.7 Observation Indicators

(1) International Prostate Symptom Score (IPSS): The responses to seven questions about urine symptoms (intermittency, nocturia, frequency, urgency, straining, incomplete emptying, and weak stream) plus one question about quality of life are used to calculate the IPSS. For each enquiry on urinary symptoms, the patient can choose one of six possibilities, with the options signifying the intensity of the specific ailment. The responses are graded on a scale of 0 to 5. As a result, the overall score can range between 0 (i.e., asymptomatic) and 35 (i.e., very symptomatic)[9].

(2) QOL: The QOL score serves as a measure to assess the extent of quality of life deterioration among BPH patients due to symptomatic manifestations of the disease. Scores range from 0 to 6 points, with higher scores correlating to a more compromised quality of life [10].

(3) Qmax and Bladder Residual Urine Volume (RUV): Patients were instructed to empty their bladders, following which a pressure tube was introduced into the bladder through the urethra after proper disinfection. Subsequently, the pressure tube was connected to a computer terminal for assessment. A robust urodynamic examination instrument (Ndly11, Guangzhou Pudong Medical Co., Ltd.) was utilized for the evaluation. The measurements of the Qmax and RUV were performed and meticulously documented. Notably, smaller Qmax values and larger RUV values within the same group indicated more severe symptoms.

(4) Hepatic and Renal Function Assessment: Approximately 5mL of fasting venous blood was obtained from both study groups. Following anticoagulation, the blood was placed in a centrifugal device and spun at 3000 revolutions per minute for 10min to extract plasma. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and creatinine (Cr) levels were quantified using an automated biochemical analyzer (Hitachi, Japan, 7600-020).

2.2.8 Observation and Management of Adverse Events

Throughout the treatment duration, regular follow-up assessments were conducted every two weeks for both patient groups. These assessments aimed to gauge the therapeutic impact post-medication administration and monitor the emergence of adverse reactions. In cases where adverse reactions were identified, appropriate symptomatic interventions were administered, while relevant indicators were subject to dynamic monitoring. If necessary, the patient’s drug regimen could be prematurely ceased, accompanied by comprehensive documentation and analysis.

2.2.9 Efficacy Evaluation Criteria

The efficacy of the treatments was evaluated against the following criteria:

(1) Remarkable effect: A reduction of over 70% in the IPSS.
(2) Effective: A decrease of more than 30% in the IPSS.
(3) Ineffective: A decrease of less than 30% in the IPSS or no improvement in clinical symptoms.

The total effective rate was calculated using the formula: (Remarkable effect + Effective cases) / Total cases × 100%.

2.3 Statistical Analysis

The SPSS software, version 26.0 (IBM Corp., Armonk, NY), was employed for comprehensive data analysis. Descriptive statistics including mean, standard deviation, median (with 75th and 25th percentile values), frequency, and percentages were utilized to succinctly depict the variables. To compare quantitative variables between groups, independent t-tests and Mann-Whitney tests were employed based on the outcomes of the Kolmogorov-Smirnov normality test. Paired t-tests and Wilcoxon tests were employed for pairwise comparisons. For repeated measurement data, a generalized estimation equation was adopted. Statistical significance was denoted by P<0.05.

3 RESULTS

3.1 Animal Experimental Results

3.1.1 Prostate Pathology

Prostate pathology evaluations in SD rats revealed successful modeling in the model group, characterized by glandular hyperplasia when compared with the blank group. Notably, the QLSTF group exhibited a significant amelioration in prostate pathology compared to the model group (Figure 2).

Figure 2A: The glands in the prostate tissue of rats were basically normal, and no pathological changes such as hyperplasia were observed. The prostate glands of rats were uniform in size and neatly arranged. There was a small amount of secretion in the glandular cavity. The glandular epithelial cells were single-layer columnar, neatly arranged, and the basement membrane was intact. The nucleus was round or oval, located at the base. There was no hyperplasia of smooth muscle cells and fibrous connective tissue in the stroma, and no obvious inflammatory cell infiltration was observed.

Figure 2B: The prostates of rats were of different sizes, and a large amount of prostatic fluid was stained in the glandular cavity. The glandular epithelium showed stratified high columnar hyperplasia, and some areas of the acinar
showed papillary hyperplasia. Secretory granules were seen in the cytoplasm of multiple glandular epithelium. Fibrous connective tissue hyperplasia appeared in the intercellular substance, and interstitial vasodilation and congestion were obvious.

**Figure 2C:** After QLSTF treatment, the glandular cavity of BPH rats was significantly exposed, papillary hyperplasia was significantly improved, and interstitial vascular hyperplasia was significantly reduced.

### 3.1.2 Liver and Kidney Pathology

Examinations of liver and kidney pathology in the QLSTF group exhibited no conspicuous pathological alterations (**Figure 3**).

**Figure 3A:** Normal renal cortex, glomerulus, small balloon lumen and its surrounding renal tubules are clearly visible. The cortical-medullary boundary of kidney tissue was obvious. Distribution of glomeruli in renal cortex was uniform. Number of cells and matrix in renal glomeruli were uniform. Renal tubular epithelial cells were round and full, and the brush borders were neatly arranged. There was no obvious abnormality in renal medulla. There was no obvious inflammatory change in the kidney.

**Figure 3B:** Hepatic lobules were clearly demarcated and arranged regularly. Hepatocytes were round, full and arranged regularly. The nucleus was clear, no obvious pyknosis, no obvious apoptotic bodies. Hepatic plate is arranged regularly and neatly. There was no obvious expansion or extrusion of hepatic sinus. There was no obvious abnormality in portal area between adjacent hepatic lobules, and no obvious inflammatory changes were observed.
3.1.3 Prostate Cell Count Results
Prostate cell counts were quantified using ImageJ software (National Institutes of Health, version 1.49). Cell enumeration was conducted utilizing the “Find Maxima module” under conditions of 200X field of view, Prominence >40, and exclusion of edge maxima. Statistically significant differences emerged between the blank group and the model group (P<0.05). Likewise, notable statistical significance was observed between the model group and the QLSTF group (P<0.05) (Table 1).

3.2 Randomized Controlled Trial Results
3.2.1. Baseline Comparison
Prior to treatment, no significant disparities were observed in terms of age, disease duration, and BMI between the two groups (P>0.05) (Table 2).

3.2.2 Participant Removal and Inclusion
Throughout the observation phase, 12 cases were excluded (see Supplementary Tables). Ultimately, the observation group encompassed 73 effective cases, while the control group included 75.

3.2.3 IPSS and QOL
No substantial distinctions in IPSS and QOL were evident before treatment (P>0.05). Post-treatment, both IPSS and QOL scores exhibited a decline compared to pre-treatment values (P<0.05), with the QLSTF group displaying a more pronounced decrease compared to the control group (P<0.05) (Table 3).

3.2.4 Urodynamic Indicators
Before treatment, Qmax and RUV showcased no noteworthy divergence between the two groups (P>0.05). Following treatment, RUV values in both groups were lower than pre-treatment levels, while Qmax values were higher (P<0.05). Notably, the QLSTF group demonstrated superior outcomes compared to the control group (P<0.05) (Table 4).

3.2.5 Changes in Outcome Indicators
With the exception of Qmax, a declining trend was observed in the remaining parameters. The increase in Qmax and reduction in IPSS, QOL, and RUV were markedly more significant in the QLSTF group compared to the control group (P<0.05) (Table 5, Figure 4).

3.2.6 Comparative Efficacy
Following treatment, the total effective rate in the QLSTF group reached 90.41%, surpassing the control group’s rate of 77.33%. This discrepancy between the groups was statistically significant (P<0.05) (Table 6).

3.2.7 Hepatic and Renal Function
Even after one month of treatment, both groups maintained hepatic and renal function within the normal range (Table 7).

3.2.8 Adverse Reactions
In the control group, three individuals reported dizziness, while occasional instances of nausea and vomiting were noted in the QLSTF group, failing to meet the exclusion criteria. Adverse reaction cases were duly addressed, yielding no noticeable discomfort post-treatment. Notably, no hepatic or renal function impairment surfaced during the medication period for both groups (see Supplementary Tables).

4 DISCUSSION
The etiology of BPH is intricately tied to factors such as sex hormones, growth factors, inflammatory responses, and aberrant apoptosis, leading to the proliferation of prostate epithelial and stromal cells[14]. BPH is defined as an increased prostate volume, largely due to the cellular proliferation occurring in the transition zone, namely the portion of the prostatic tissue that surrounds the urethra. BPH is an age-dependent disease which can obstruct the prostatic urethra. Its prevalence varies between 5% and 10% in men aged 40, but reaches 80% in men aged 70-80[15]. Despite advancements in medical science, the BPH patient population continues to expand. While α-receptor blockers and 5α-reductase inhibitors have demonstrated clinical efficacy in managing BPH, both conventional Western medicine and surgical interventions entail substantial side effects including sexual dysfunction, dizziness, and retrograde ejaculation[16]. The exploration of more effective and safer therapeutic alternatives remains a pressing concern in clinical practice. TCM presents a promising avenue for enhancing the quality of life, prostate volumes, and Qmax in BPH patients[17].

The findings from both the animal experiments and the randomized controlled trial provide strong evidence supporting the efficacy of the QLSTF in treating BPH. The constituents of the QLSTF were scrutinized using the Chinese medicine systems pharmacology database and analysis platform. We followed the criteria where bioactive ingredients were selected based on oral bioavailability ≥30% and drug-like properties ≥0.18) [18]. This analysis revealed that QLSTF primarily encompasses 249 compounds, including coptisine, cyclopamine, ergosterol peroxide, and obacunone, which collectively inhibit abnormal prostate proliferation[19,20]. Moreover, berberine and spinasterol contribute to BPH improvements[21,22]. Chelerythrine has shown to induce apoptosis in pathological prostate cells[23]. The synergistic effects of these components potentially underpin QLSTF’s efficacy against BPH.

Results from the randomized controlled trial demonstrated that the combined therapy of QLSTF and tamsulosin hydrochloride sustained-release capsules yielded significant reductions in IPSS and QOL scores.
Table 1. Prostate Cell Count

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean±SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blank group</td>
<td>1081.25±155.45</td>
<td>0.005</td>
</tr>
<tr>
<td>Model group</td>
<td>1446.75±160.33</td>
<td>0.630</td>
</tr>
<tr>
<td>Blank group</td>
<td>1081.25±155.45</td>
<td>0.002</td>
</tr>
<tr>
<td>QLSTF group</td>
<td>1031.75±95.83</td>
<td></td>
</tr>
<tr>
<td>Model group</td>
<td>1446.75±160.33</td>
<td></td>
</tr>
<tr>
<td>QLSTF group</td>
<td>1031.75±95.83</td>
<td></td>
</tr>
<tr>
<td>All groups</td>
<td>F=10.44</td>
<td>0.005</td>
</tr>
</tbody>
</table>


Table 2. General Information

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Age (Years)</th>
<th>Course of Disease (Month)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>QLSTF group</td>
<td>73</td>
<td>68 (71, 63)</td>
<td>91.00 (65.50, 106.00)</td>
<td>23.90 (22.00, 26.50)</td>
</tr>
<tr>
<td>Control group</td>
<td>75</td>
<td>67 (70, 61)</td>
<td>98.00 (83.00, 109.00)</td>
<td>23.88 (21.26, 25.95)</td>
</tr>
<tr>
<td>Z</td>
<td>-1.213</td>
<td>-1.755</td>
<td>-0.646</td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>0.225</td>
<td>0.079</td>
<td>0.518</td>
<td></td>
</tr>
</tbody>
</table>


Table 3. Comparison of IPSS and QOL before and after Treatment in the Two Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>IPSS</th>
<th>QOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>QLSTF group</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>21 (25,18)</td>
<td>5 (8,4)</td>
<td>5 (6,4)</td>
</tr>
<tr>
<td>Three Month</td>
<td>5 (8,4)</td>
<td>5 (6,4)</td>
<td>1 (1,2)</td>
</tr>
<tr>
<td>Z</td>
<td>0.018</td>
<td>3.487</td>
<td>-1.689</td>
</tr>
<tr>
<td>P</td>
<td>0.894</td>
<td>0.000</td>
<td>0.091</td>
</tr>
<tr>
<td>Control group</td>
<td>75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>22 (26,18)</td>
<td>7 (14,5)</td>
<td>4 (5,4)</td>
</tr>
<tr>
<td>Three Month</td>
<td>7 (14,5)</td>
<td>4 (5,4)</td>
<td>2 (3,2)</td>
</tr>
<tr>
<td>Z</td>
<td>-0.197</td>
<td>3.675</td>
<td>-0.744</td>
</tr>
<tr>
<td>P</td>
<td>0.844</td>
<td>0.000</td>
<td>0.457</td>
</tr>
</tbody>
</table>


Table 4. Qmax and RUV of Two Groups before and after Treatment

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Qmax (mL/s)</th>
<th>RUV (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QLSTF group</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7 (10, 5)</td>
<td>14 (15, 12)</td>
<td>54 (66, 47)</td>
</tr>
<tr>
<td>Three Month</td>
<td>14 (15, 12)</td>
<td>54 (66, 47)</td>
<td>13 (21, 10)</td>
</tr>
<tr>
<td>Z</td>
<td>-0.197</td>
<td>-3.675</td>
<td>-0.744</td>
</tr>
<tr>
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<td>0.000</td>
<td>0.457</td>
</tr>
<tr>
<td>Control group</td>
<td>75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7 (10, 5)</td>
<td>12 (14, 10)</td>
<td>57 (67, 47)</td>
</tr>
<tr>
<td>Three Month</td>
<td>12 (14, 10)</td>
<td>57 (67, 47)</td>
<td>18 (36, 13)</td>
</tr>
<tr>
<td>Z</td>
<td>-0.197</td>
<td>-3.675</td>
<td>-0.744</td>
</tr>
<tr>
<td>P</td>
<td>0.844</td>
<td>0.000</td>
<td>0.457</td>
</tr>
</tbody>
</table>


Table 5. Changes in Outcome Indicators

<table>
<thead>
<tr>
<th>Group</th>
<th>QLSTF Group</th>
<th>Control Group</th>
<th>Z</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPSS</td>
<td>21 (25, 18)</td>
<td>12 (14, 10)</td>
<td>5 (8, 4)</td>
<td>22 (26, 18)</td>
</tr>
<tr>
<td>Qmax (mL/s)</td>
<td>7 (10, 5)</td>
<td>11 (13, 9)</td>
<td>14 (15, 12)</td>
<td>7 (10, 5)</td>
</tr>
<tr>
<td>RUV (mL)</td>
<td>54 (66, 47)</td>
<td>31 (36, 27)</td>
<td>18 (23, 16)</td>
<td>13 (21, 10)</td>
</tr>
<tr>
<td>QOL</td>
<td>5 (6, 4)</td>
<td>3 (4, 3)</td>
<td>2 (2, 1)</td>
<td>1 (1, 2)</td>
</tr>
</tbody>
</table>

Notes: QLSTF: Qianlong Shutong Formula.

along with decreased RUV and increased Qmax (P<0.05). These findings underscore the superiority of the combined approach in ameliorating prostate symptoms, enhancing quality of life, and mitigating lower urinary tract symptoms. Notably, no significant adverse reactions were observed. Complementing this, animal experimentation revealed that the QLSTF group exhibited a significant amelioration in prostate pathology compared to the model group, indicating its potential in mitigating prostatic hyperplasia. Importantly, examinations of liver and kidney pathology in the QLSTF group exhibited no conspicuous pathological alterations, suggesting that QLSTF can be safely administered without
Figure 4. Changes in outcome indicators. A: Changes in RUV; B: Changes in QOL; C: Changes in Q\textsubscript{max}; D: Changes in IPSS. Red circles and lines represent the QLSTF group. Black squares and lines represent the control group.

Table 6. Comparison of Curative Effect

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Remarkable Effect, n (%)</th>
<th>Effectiveness, n (%)</th>
<th>Ineffectiveness, n (%)</th>
<th>Total Effective Rate, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QLSTF group</td>
<td>73</td>
<td>45 (61.64%)</td>
<td>21 (28.77%)</td>
<td>7 (9.59%)</td>
<td>66 (90.41%)</td>
</tr>
<tr>
<td>Control group</td>
<td>75</td>
<td>25 (33.33%)</td>
<td>33 (44%)</td>
<td>17 (22.67%)</td>
<td>58 (77.33%)</td>
</tr>
</tbody>
</table>

\[ Z = -3.503881 \]
\[ P = 0.0000 \]


Table 7. Hepatic Function and Renal Function

<table>
<thead>
<tr>
<th>Group</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>Cr (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>QLSTF group</td>
<td>Total</td>
<td>19.40</td>
<td>16.50</td>
</tr>
<tr>
<td></td>
<td>Maximum</td>
<td>10.50</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>38</td>
<td>33.40</td>
</tr>
<tr>
<td>Control group</td>
<td>Total</td>
<td>21.00</td>
<td>17.00</td>
</tr>
<tr>
<td></td>
<td>Maximum</td>
<td>10</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>39</td>
<td>27.04</td>
</tr>
</tbody>
</table>

\[ Z = -0.824678 \]
\[ P = 0.409554 \]
\[ Z = -0.506286 \]
\[ P = 0.840376 \]


causing harm to these vital organs.

5 CONCLUSION

In summation, this study underscores that the combined treatment of QLSTF and tamsulosin hydrochloride sustained-release capsules holds substantial promise in managing BPH by positively modulating clinical symptoms, quality of life, and urinary dynamics. Furthermore, the study’s findings
could also open up new avenues of research into the use of TCM for the treatment of other urological conditions. The safety profile of this combined regimen is encouraging, warranting further consideration for wider adoption. The precise mechanisms of QLSTF’s action necessitate further investigation. By leveraging high-quality clinical research in tandem with experimental exploration, the goal of providing more scientifically grounded treatment avenues for BPH can be achieved.

In terms of future research directions, it would be beneficial to conduct a more detailed investigation into the individual components of the QLSTF and their specific mechanisms of action. This could potentially lead to the development of more targeted and effective treatments for BPH.

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Ethical Approval Statement
Ethical approval to report this research was obtained from Guangxi University of Chinese Medicine Institutional Welfare and Ethical Committee (Approval Number: DW20230620-127). The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Ruikang Hospital Affiliated to Guangxi University of Traditional Chinese Medicine (KY2021-105).

Data Availability
The data presented in this study are available in Supplementary Tables.

Conflicts of Interest
The authors declared no conflict of interest.

Author Contribution
Zhang Z conceived and designed the study. Lin Z, Shang C, and Zhu M conducted the data analysis. Zhang Z and Huang S wrote the paper. Hu F and Yang Q were responsible for animal feeding. Zhu M and Huang S reviewed and edited the manuscript. All authors approved the final version of the article. Zhang Z, Huang S, and Shang C contributed equally to this work and are co-first authors.

Abbreviation List
ALT, Alanine aminotransferase
AST, Aspartate aminotransferase
BPH, Benign prostatic hyperplasia
Cr, Creatinine
DRE, Digital rectal examination
HE, Hematoxylin and eosin
IPSS, International Prostate Symptom Score
PSA, Prostate specific antigen
QLSTF, Qianlong Shutong Formula
Qmax, Maximum urinary flow rate
QOL, Quality of life scores
RUV, Residual urine volume
SD, Sprague Dawley
TCM, Traditional Chinese medicine

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