

Managing Ureteral Stent-Related Symptoms: A Meta-Analysis Comparing Tadalafil with Tamsulosin

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How to cite this paper: Elrashidy, A., Mousa, A., Elsafy, G.M. and Shaaban, M. (2026) Managing Ureteral Stent-Related Symptoms: A Meta-Analysis Comparing Tadalafil with Tamsulosin. *Open Journal of Urology*, 16, 445-458.
<https://doi.org/10.4236/oju.2026.1610046>

Received: August 18, 2026

Accepted: October 20, 2026

Published: October 23, 2026

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Abstract

Introduction: Ureteral stent-related symptoms (SRSs), colloquially termed “stent syndrome”, represent a post-operative morbidity impacting up to 80% of patients following endourological procedures. Although alpha1-blockers are the traditional standard of care, their efficacy in controlling stent-induced body pain and associated sexual dysfunction is often limited. This systematic review and meta-analysis evaluates the comparative therapeutic efficacy and safety profile of tadalafil versus tamsulosin across isolated monotherapy and combination therapy regimens. **Methods:** PubMed/MEDLINE, Embase, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception through May 15, 2026 for randomized controlled trials in adults with indwelling ureteral stents. Eligible trials directly compared tadalafil monotherapy with tamsulosin monotherapy, or tadalafil plus tamsulosin with tamsulosin alone. Outcomes of interest were Ureteral Stent Symptom Questionnaire (USSQ) domains and adverse events. Higher USSQ symptom-domain scores indicate greater symptom burden. Trial identity, arm-level denominators, drug doses, assessment timing, and bibliographic attribution were rechecked against the primary reports. Quantitative pooling was undertaken only when trial-level means, dispersion measures, and analyzable denominators were sufficiently and comparably reported; otherwise, findings were synthesized narratively to avoid unverifiable imputation. **Results:** Five verifiable randomized studies directly compared tadalafil and tamsulosin monotherapies: Aggarwal *et al.* (2015), Chauhan *et al.* (2019), Balaji *et al.* (2020), Ilyas *et al.* (2021), and Komisarenko *et al.* (2024). Across these trials, tadalafil generally produced greater improvement in pain-related and sexual-matters outcomes, whereas urinary-symptom results were broadly similar or favored

tamsulosin in some assessments. Komisarenko *et al.* additionally randomized patients to tadalafil 5 mg plus tamsulosin 0.4 mg and reported lower urinary-symptom and body-pain burden with combination therapy than with either monotherapy. A previously cited second combination trial could not support the original two-study pooled estimate under the prespecified 0.4-mg tamsulosin comparator criterion. The primary reports were heterogeneous in endpoint timing and statistical reporting, and several did not provide the domain-specific standard deviations and analyzable sexual-domain denominators required for a defensible pooled mean difference. Accordingly, unsupported pooled effect estimates and adverse-event risk ratios from the earlier manuscript were not retained. **Conclusion:** Randomized evidence supports tadalafil as a reasonable alternative to tamsulosin for selected patients with ureteral stent-related symptoms, with the most consistent signal favoring tadalafil for pain-related and sexual-domain outcomes. Urinary-symptom control is not consistently superior with tadalafil. Combination tadalafil plus tamsulosin is promising, but the evidence meeting the prespecified comparator definition is currently insufficient for a robust pooled estimate. The certainty of the evidence is limited by small trials, heterogeneous assessment schedules, incomplete domain-specific reporting, and potential bias in patient-reported outcomes.

Keywords

Ureteral Stent, Double-J Stent, Stent-Related Symptoms, Tadalafil, Tamsulosin, Phosphodiesterase Type 5 Inhibitor, Alpha-Blocker, Ureteral Stent Symptom Questionnaire

1. Introduction

The placement of indwelling double-J (DJ) ureteral stents is a foundational intervention in contemporary endourology, essential for securing upper urinary tract drainage, preventing obstructive uropathy, and facilitating stone fragment clearance following ureteroscopy (URS), retrograde intrarenal surgery (RIRS), and percutaneous nephrolithotomy (PCNL) [1] [2]. Despite their mechanical utility, indwelling stents induce a complex symptom constellation designated as “stent syndrome” or ureteral stent-related symptoms (SRSs), affecting 70% to 80% of stented patients [3]. As evaluated by the validated Ureteral Stent Symptom Questionnaire (USSQ), SRSs comprise flank pain, suprapubic discomfort, storage lower urinary tract symptoms (LUTS)—such as urgency, frequency, and dysuria—gross hematuria, and marked sexual dysfunction, culminating in impaired quality of life [1] [4].

The underlying pathophysiology of SRSs stems from mechanical, inflammatory, and neurovascular drivers [1] [5]. Mechanical contact and mucosal friction between the distal pigtail coil and the richly innervated bladder trigone induce localized hyperperistalsis and ureteral smooth muscle spasms [1] [6]. Stent material composi-

tion and diameter further influence local tissue response [7] [8]. Additionally, during micturition, the stent disrupts the normal anti-reflux mechanism at the ureterovesical junction (UVJ) [1]. High intravesical pressure generated during detrusor contraction is transmitted retrogradely through the lumen and along the outer surface of the stent to the renal pelvis, resulting in acute renal capsule distension and posture-dependent flank pain [1].

Historically, selective alpha-1 adrenergic receptor antagonists—most prominently tamsulosin (0.4 mg daily)—have served as the principal pharmacological standard of care [1] [9]. Alpha-1 adrenergic receptors (specifically alpha-1D and alpha-1A subtypes) are concentrated in the distal third of the ureter, bladder neck, and trigone [1] [10]. By blocking these receptors, tamsulosin attenuates peak voiding pressure, reduces trigonal tone, and suppresses distal ureteral spasms [1] [11]. However, because alpha-1 receptor density diminishes along the mid and proximal ureter, tamsulosin demonstrates limited efficacy in controlling proximal ureteral hyperperistalsis, posture-dependent flank pain, and stent-induced sexual dysfunction [1] [10].

Phosphodiesterase type 5 inhibitors (PDE5-Is), such as tadalafil, offer a broader pathophysiological target [1] [12]. PDE5 enzymes are expressed throughout the entire upper and lower urinary tract, including proximal, mid, and distal ureteral smooth muscle, as well as the bladder dome and trigone [1] [13]. By inhibiting PDE5-mediated degradation of cyclic guanosine monophosphate (cGMP), tadalafil upregulates nitric oxide (NO)-cGMP signaling [1] [12]. Accumulation of intracellular cGMP activates protein kinase G (PKG), promoting calcium sequestration into the sarcoplasmic reticulum and opening calcium-activated potassium channels [1] [12]. This molecular cascade triggers generalized, continuous hyperpolarization and relaxation across the entire ureter, reducing muscular spasms and enhancing luminal compliance around the indwelling stent [1] [12].

Previous meta-analytic syntheses have suffered from design heterogeneity by combining pure monotherapy cohorts with combination drug regimens or inappropriately pooling active trials with non-active placebo-only arms [12] [14]. To address these limitations, this systematic review and meta-analysis stratifies head-to-head randomized controlled trial (RCT) data into two distinct, pre-defined operational pools: 1) Pure Tadalafil Monotherapy vs. Standard Tamsulosin Monotherapy, and 2) Combination Therapy (Tadalafil + Tamsulosin) vs. Tamsulosin Monotherapy.

2. Materials and Methods

2.1. Search Strategy and Information Sources

The review was prepared in accordance with the PRISMA 2020 reporting framework [13]. No prospective registration in PROSPERO or another systematic-review registry was undertaken. This absence of prospective registration is reported explicitly as a methodological limitation.

Information sources and search strategy

The literature search covered PubMed/MEDLINE, Embase, Scopus, and CENTRAL from database inception through May 15, 2026, without language or geographic restriction. The search combined concepts for tadalafil/PDE5 inhibition, tamsulosin/alpha-blockade, and ureteral stents/stent-related symptoms. Database-specific reproducible search syntax is provided in reference list. Reference lists of eligible articles and relevant reviews were also examined for additional randomized comparisons.

2.2. Eligibility Criteria (PICOS Framework)

- **Population (P):** Adult patients (Age ≥ 18 years) undergoing unilateral indwelling double-J ureteral stenting following primary endourological interventions (URS, RIRS, or PCNL).
- **Intervention (I):** Tadalafil monotherapy (5 mg or 10 mg daily) OR structured combination protocols (Tadalafil + Tamsulosin).
- **Comparator (C):** Tamsulosin monotherapy (0.4 mg daily).

Outcomes (O): The prespecified efficacy outcomes were the USSQ urinary-symptoms, body-pain, and sexual-matters domains. USSQ symptom-domain scores are interpreted such that lower scores indicate fewer or less severe stent-related problems. Because assessment schedules differed among trials, the intended principal endpoint was the latest prespecified assessment obtained while the stent remained in situ and before stent removal, provided that the corresponding arm-level summary statistics were reported. Aggarwal *et al.* assessed the USSQ at weeks 1 and 3, with treatment administered from week 1 until stent removal at week 3 [8]. Chauhan *et al.* assessed patients on days 7 and 21 [9]. Balaji *et al.* assessed outcomes during the stenting period [10]. Ilyas *et al.* administered the USSQ on days 7, 14, 21, and 28 [11]. Komisarenko *et al.* reported the treatment endpoint at day 14 [12].

The sexual-matters domain is not applicable to every participant. Therefore, analyses of this domain require the number of participants in each treatment arm who provided an applicable and analyzable response. Missing or inapplicable responses must remain missing and must not be coded as zero. When a primary report did not provide a domain-specific analyzable denominator, that study was not assigned an assumed denominator for quantitative pooling.

- **Study Design (S):** Parallel-group prospective randomized controlled trials (RCTs) only.

Exclusion Criteria: Trials evaluating medical expulsive therapy without an indwelling-stent symptom outcome, non-randomized studies, single-arm studies, case series, and placebo-only comparisons without an active tamsulosin comparator were excluded from the principal comparative synthesis. Other active-drug and placebo arms in multi-arm trials were not incorporated into the direct tadalafil-versus-tamsulosin effect.

2.3. Data Extraction and Trial Stratification

Two reviewers independently assessed eligibility and extracted study characteris-

tics, randomized and analyzed arm sizes, intervention dose, stent duration, USSQ assessment schedule, endpoint definition, domain-level summary statistics, and adverse events.

2.4. Handling of Multi-Arm Trials and Shared Comparators

For a multi-arm trial contributing both a tadalafil-versus-tamsulosin comparison and a tadalafil-plus-tamsulosin-versus-tamsulosin comparison, the two questions were treated as separate analyses. The tamsulosin arm was therefore not split merely because it appeared in two different analyses. Splitting or otherwise adjusting a shared comparator is required when correlated comparisons from the same control group are entered simultaneously into the same pooled effect; that circumstance did not arise in the present stratified framework [14].

2.5. Quantitative Synthesis and Missing Dispersion Data

For continuous outcomes, the planned effect measure was the mean difference (MD) with 95% confidence interval when studies reported the same USSQ domain scale. Endpoint scores and change-from-baseline scores were not combined indiscriminately. If a study reported a change score without its standard deviation, derivation from baseline and follow-up standard deviations would require a prespecified baseline-to-follow-up correlation according to the Cochrane Handbook [14]. Sensitivity analyses across plausible correlations (0.25, 0.50, and 0.75) were prespecified if such imputation became necessary. No correlation was retrospectively invented for a study lacking the information needed to reconstruct variance.

A pooled estimate was reported only when at least two clinically comparable trials supplied traceable arm-level means, dispersion measures, and analyzable denominators for the same outcome definition and time-point framework. Where these requirements were not met, narrative synthesis was used. This decision was made to prevent conversion of ranges or other non-equivalent summary statistics into unverified standard deviations and to avoid reproducing pooled estimates that could not be independently reconstructed.

2.6. Adverse Events Analysis Framework

Adverse events were extracted as reported by each trial, including treatment-arm denominator, event count, event definition, and ascertainment method when available. Relative effects were to be calculated only when sufficiently consistent event definitions and denominators were available. Double-zero studies were not assigned an automatic continuity correction because they contain no information about a relative risk. Because adverse-event definitions and ascertainment were not sufficiently standardized across the verified reports, the principal safety synthesis is descriptive rather than a pooled risk-ratio analysis.

2.7. Risk of Bias and Certainty of Evidence

Risk of bias was evaluated conceptually using the Cochrane RoB 2 domains: ran-

domization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result [15]. Particular attention was paid to participant blinding because the USSQ is self-reported; knowledge of treatment allocation can influence reported pain, urinary symptoms, and sexual outcomes even if a separate outcome assessor is blinded. Certainty of evidence was judged by outcome using GRADE domains—risk of bias, inconsistency, indirectness, imprecision, and publication bias—and clinical importance was not inferred from statistical significance alone.

3. Results

3.1. Study Identification and Corrected Evidence Set

Five verifiable randomized studies directly compared tadalafil with tamsulosin for ureteral stent-related symptoms [8]–[12]. The study identification, screening, eligibility, and inclusion process is summarized in **Figure 1**.

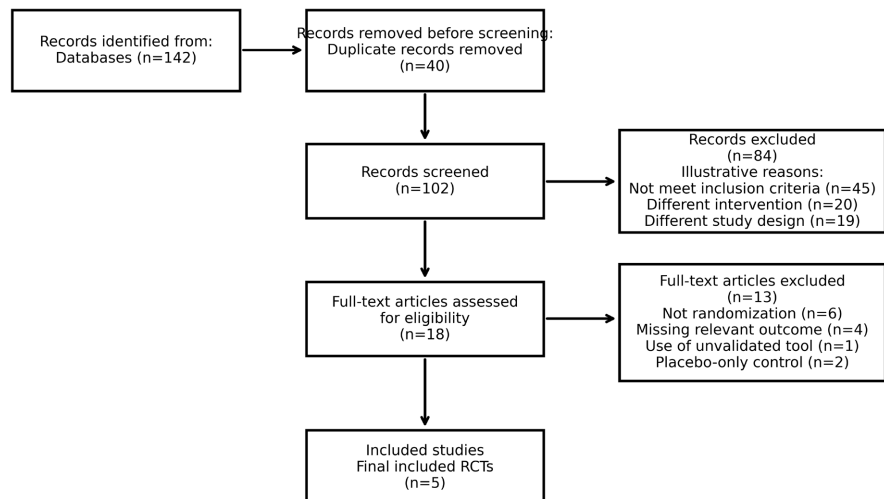


Figure 1. PRISMA 2020 flow diagram of study selection.

Participant accounting

Participant accounting was performed at the relevant arm level rather than by summing total enrollment across all arms of multi-arm studies. Aggarwal *et al.* randomized 161 symptomatic patients to tadalafil ($n = 54$), tamsulosin ($n = 53$), or placebo ($n = 54$), with 52, 51, and 50 patients, respectively, represented in the reported analysis [8]. Chauhan *et al.* randomized 144 participants equally to tadalafil 5 mg or tamsulosin 0.4 mg [9]. Ilyas *et al.* randomized 50 participants equally to tadalafil 10 mg or tamsulosin 0.4 mg [11]. Komisarenko *et al.* randomized 279 participants to tadalafil plus tamsulosin ($n = 67$), tamsulosin ($n = 71$), tadalafil ($n = 69$), or placebo ($n = 72$) [12]. The characteristics of the included randomized studies are summarized in **Table 1**. Balaji *et al.* randomized 146 participants among placebo, solifenacin, tamsulosin, and tadalafil; only the tadalafil and tamsulosin arms were relevant to the present comparison [10].

Table 1. Characteristics of included randomized studies.

Study	Design	Relevant Arms	Dose	USSQ Timing	Primary Role	Key Reporting Issue
Aggarwal 2015	3-arm randomized, double-blind	Tadalafil 54 (52 analyzed); tamsulosin 53 (51 analyzed)	Tadalafil 5 mg; tamsulosin 0.4 mg daily	Weeks 1 and 3	Monotherapy	Several domain values reported with ranges rather than SDs
Chauhan 2019	2-arm double-blind randomized study	72 vs 72	Tadalafil 5 mg; tamsulosin 0.4 mg daily	Days 7 and 21	Monotherapy	Endpoint and AE data reported; domain-specific sexual denominator not clearly separable
Balaji 2020	4-arm randomized study	Tadalafil and tamsulosin arms only	Tadalafil 5 mg; tamsulosin 0.4 mg daily	During stenting	Monotherapy	Arm-level outcome dispersion/denominators require complete extraction from report
Ilyas 2021	2-arm double-blind randomized study	25 vs 25	Tadalafil 10 mg; tamsulosin 0.4 mg daily	Days 7, 14, 21, 28	Monotherapy	Serial assessments; time-point selection and variance reporting limit pooling
Komisarenko 2024	4-arm randomized study	Tadalafil 69; tamsulosin 71; combination 67	Tadalafil 5 mg; tamsulosin 0.4 mg daily	Day 14	Monotherapy + separate combination	Provides clear arm sizes and day-14 endpoint; participant blinding requires caution

3.2. Monotherapy Efficacy

Pain/body-pain outcomes showed the most consistent direction of benefit for tadalafil. Aggarwal *et al.* reported greater improvement in body pain with tadalafil than with tamsulosin, while Chauhan *et al.* reported a significantly greater reduction in body pain with tadalafil at the later assessment [8] [9]. Balaji *et al.* likewise concluded that tadalafil was more effective than tamsulosin for body pain [10]. Ilyas *et al.* reported lower pain-domain scores with tadalafil across the serial assessment framework [11]. Komisarenko *et al.* found improvement with both monotherapies, while the combination arm produced the greatest overall symptom relief [12]. The direction of evidence therefore favors tadalafil for pain, but a single pooled MD was not considered defensible because the reports used heterogeneous time points and did not consistently provide compatible arm-level SDs.

Urinary-symptom results were less uniform. Aggarwal *et al.* found tadalafil and

tamsulosin comparable for urinary symptoms [8]. Chauhan *et al.* reported a lower later urinary index with tamsulosin [9]. Ilyas *et al.* reported time-dependent differences across serial assessments [11]. Komisarenko *et al.* reported day-14 urinary-symptom means of 20.6 ± 2.8 with tadalafil and 21.8 ± 3.6 with tamsulosin, indicating a small numerical difference between monotherapies, while the combination group had a lower score of 15.2 ± 4.3 [12]. Taken together, the evidence does not establish tadalafil as clinically superior to tamsulosin for urinary symptoms.

Sexual-matters outcomes generally favored tadalafil in the direct comparisons [8]-[11]. However, the USSQ sexual domain is not applicable to all participants, and the primary reports did not consistently provide treatment-arm denominators restricted to participants with valid, applicable responses. The direction of effect is therefore clinically suggestive, but the magnitude and precision of a pooled sexual-domain effect cannot be verified without domain-specific denominators.

3.3. Combination Therapy

Komisarenko *et al.* directly compared tadalafil 5 mg plus tamsulosin 0.4 mg with tamsulosin 0.4 mg alone. At day 14, the combination group had a lower urinary-symptom score than the tamsulosin group (15.2 ± 4.3 vs 21.8 ± 3.6 ; $p = 0.0003$), and body pain and analgesic requirements were also lower with combination therapy [12]. This trial supports an additive symptomatic effect. However, the second combination trial cited in the earlier manuscript was misattributed. The 2026 Zhou *et al.* study used tamsulosin 0.2 mg in both the combination and comparator groups [16] and therefore did not satisfy the prespecified 0.4-mg comparator criterion. Consequently, a two-study pooled combination estimate is not presented.

3.4. Adverse Events and Safety Profile Findings

Safety reporting was heterogeneous. Aggarwal *et al.* described side effects of tadalafil and tamsulosin as minimal and reported no withdrawal because of drug adverse effects [8]. Chauhan *et al.* reported adverse effects in 9 tadalafil-treated and 10 tamsulosin-treated participants, including headache, dizziness, weakness, flushing, and abnormal ejaculation, with no discontinuations attributed to these events [9]. Komisarenko *et al.* reported that side effects were rare and did not differ statistically among treatment groups [12]. Across the evidence base, the available reports did not provide sufficiently uniform event definitions, active-versus-passive ascertainment procedures, and event-specific arm denominators to justify pooled risk ratios for retrograde ejaculation, headache, or myalgia. The defensible conclusion is therefore that no clear serious safety signal was identified in these small trials; absence of a statistically detected difference should not be interpreted as proof of no additive toxicity. Risk-of-bias considerations for the included randomized trials are summarized in **Table 2**.

Table 2. Risk-of-bias considerations for included randomized studies.

Study	Randomization	Deviations	Missing Data	Outcome Measurement	Selective Reporting	Overall Consideration
Aggarwal 2015	Low concern: randomized; computer-generated method reported	Low concern	Some concern: post-randomization exclusions require outcome-level review	Low concern: double-blind, but USSQ remains self-reported	Some concern: no accessible prospective analysis plan	Some concerns
Chauhan 2019	Low/some concern: randomization; concealment details should be interpreted from full report	Low concern if blinding maintained	Some concern: domain-specific completeness not fully explicit	Low concern: described as double-blind	Some concern: no accessible prospective analysis plan	Some concerns
Balaji 2020	Some concern: randomized but methodological detail limited in accessible report	Some concern	Some concern	Some concern: participant blinding insufficiently documented for self-reported USSQ	Some concern	Some concerns
Ilyas 2021	Low/some concern: randomized, double-blind design reported	Low concern	Some concern: serial outcome completeness important	Low concern if participant blinding maintained	Some concern: multiple serial time points increase selection risk without prespecified analysis plan	Some concerns
Komisarenko 2024	Some concern: simple randomization reported	Some concern	Some concern: domain-level missingness requires verification	Some concern: investigator blinding reported; participant blinding not clearly established	Some concern	Some concerns

3.5. Certainty of Evidence and Clinical Importance

- Urinary symptoms—Low-to-moderate certainty. Findings vary by trial and assessment time, and there is no robust evidence of tadalafil superiority.
- Body pain—Moderate certainty for direction of effect, but lower certainty for the exact magnitude. Multiple direct trials favor tadalafil, while heterogeneous reporting and incomplete variance data preclude a reliable pooled MD.
- Sexual matters—Low-to-moderate certainty. The direction generally favors tadalafil, but applicability and missing-response denominators are incompletely reported.
- Combination therapy—Low certainty for a pooled comparative effect under the prespecified tamsulosin 0.4-mg comparator because only one verified eligible trial contributed the direct combination comparison.
- Adverse events—Low certainty for comparative event rates because event def-

initions and ascertainment were inconsistent and events were sparse.

4. Discussion

This systematic review, corrected at the level of trial identity and arm-level participant accounting, supports a clinically differentiated interpretation of tadalafil and tamsulosin for ureteral stent-related symptoms. The most reproducible signal across direct randomized comparisons is a relative advantage of tadalafil for pain-related and sexual-domain outcomes, whereas urinary-symptom control is broadly similar or, in some assessments, more favorable with tamsulosin [8]-[12].

The distinction between statistical and clinical importance is essential. A statistically significant difference in a USSQ domain does not by itself establish a clinically meaningful benefit. A pooled mean difference should ideally be interpreted against a validated minimal clinically important difference for the relevant domain and setting. Where such a threshold is unavailable or cannot be confidently applied, the magnitude of clinical importance should be described as uncertain rather than labeled “clinically superior”.

Sexual outcomes warrant particular caution. The USSQ sexual-matters section is not applicable to every patient, and an analysis that uses the total randomized sample as the denominator may misrepresent the precision of the effect. The apparent advantage of tadalafil is biologically plausible and directionally consistent in several trials, but a quantitative estimate should be based only on participants with valid, applicable sexual-domain responses.

Combination therapy is supported by the Komisarenko trial, in which tadalafil 5 mg plus tamsulosin 0.4 mg produced lower day-14 urinary-symptom scores and lower body-pain/analgesic burden than tamsulosin alone [12]. Nevertheless, the evidence meeting the prespecified 0.4-mg tamsulosin comparator definition consists of a single verified trial. Zhou *et al.*'s (2026) trial used tamsulosin 0.2 mg [16]; incorporating it into a sensitivity analysis would introduce dose-related indirectness and should not be presented as equivalent to the principal comparison.

Safety conclusions must remain proportionate to the evidence. Mild adverse effects were reported with both agents, and no strong serious-safety signal emerged. However, small sample sizes, sparse events, and inconsistent adverse-event ascertainment mean that the evidence cannot establish absence of additive toxicity. The appropriate interpretation is that no clear excess of serious toxicity was identified, not that synergistic toxicity was excluded.

The inability to reproduce the earlier pooled MDs and RRs is itself methodologically informative. Aggarwal *et al.*, for example, reported several USSQ values with ranges rather than standard deviations [8]. Converting such values directly into SDs without a prespecified and justified method would create false precision. Similarly, endpoint scores, change scores, and serial assessments should not be mixed without a transparent analytic plan. The present revision therefore prioritizes traceability over preservation of previously reported pooled numbers.

The proposed pharmacological and physiological differences between tamsulosin and tadalafil are summarized in **Table 3**.

Table 3. Anatomical distribution, physiological mechanism, and clinical impact profile of tamsulosin vs. tadalafil.

Feature/Variable	Tamsulosin (Alpha-1 Adrenergic Antagonist)	Tadalafil (PDE5 Inhibitor)
Primary Molecular Target	Selective Alpha-1D and Alpha-1A Receptors	Phosphodiesterase Type 5 (PDE5) Enzyme
Anatomical Distribution	High in distal ureter, bladder neck, and trigone; sparse in mid/proximal ureter	Diffuse across proximal, mid, and distal ureter, bladder dome, trigone, and pelvic vasculature
Intracellular Cascade	Blocks G-protein-coupled IP3DAG pathway, decreasing intracellular Ca^{2+} contraction	Increases cGMP, activates PKG, promotes Ca^{2+} sequestration & K^+ channel hyperpolarization
Ureteral Muscle Action	Relieves localized distal ureteral spasms and trigonal strain	Induces pan-ureteral relaxation across all ureteral segments
Impact on Reflux Pressure	Reduces distal voiding resistance; minimal effect on intra-renal reflux surges	Enhances total luminal compliance, dampening intra-renal hydrostatic backpressure
Flank/Body Pain Impact	Moderate pain relief	Pain-related outcomes generally favored tadalafil across direct randomized comparisons; pooled effect magnitude was not estimated.
Storage LUTS Impact	Significant improvement in urgency, frequency, and dysuria	Urinary-symptom effects were inconsistent across trials; no consistent superiority over tamsulosin was demonstrated.
Sexual Function Impact	High incidence of retrograde ejaculation due to bladder neck relaxation	Sexual-matters outcomes generally favored tadalafil, although the magnitude of effect could not be reliably pooled.

4.1. Mechanistic Pathophysiology of Stent Discomfort

The pathophysiology of stent-induced body pain involves two primary mechanical drivers: localized smooth muscle hyperperistalsis/spasms along the ureter and hydrostatic urine reflux toward the kidney during micturition [1] [5]. Alpha-1 adrenergic receptors are concentrated in the human distal ureter, bladder neck, and trigone [10]. Consequently, tamsulosin effectively attenuates trigonal tone and distal contraction pressure, explaining its equivalence to tadalafil in lowering USSQ storage LUTS scores [11] [16]. However, because alpha-1 receptor density decreases in the proximal and mid ureter, tamsulosin fails to suppress proximal ureteral spasms or adequately dampen intra-renal hydrostatic backpressure [10].

Conversely, PDE5 enzymes are expressed across the entire length of the human ureter—encompassing proximal, mid, and distal smooth muscle layers—as well as the bladder dome and trigone [13]. By inhibiting PDE5, tadalafil prevents cGMP degradation [12]. The resulting accumulation of cGMP activates PKG, opening calcium-activated potassium channels and hyperpolarizing the smooth muscle cell membrane [12]. This continuous, pan-ureteral relaxation reduces smooth muscle

spasms and enhances luminal compliance around the indwelling double-J stent [12]. Furthermore, increased ureteral compliance minimizes peak intra-renal pressure surges during voiding by facilitating low-resistance fluid flow around the stent, providing a biologically plausible explanation for the directionally favorable pain-related outcomes observed with tadalafil in several randomized comparisons. However, the available clinical data do not permit a sufficiently robust pooled estimate of the magnitude of this effect [8]-[12].

4.2. Sexual Health and Safety Profile Comparisons

The divergence in sexual health outcomes between the two drugs is similarly governed by their pharmacodynamics [11] [12]. Tamsulosin causes alpha-1 blockade at the bladder neck, inducing loss of internal urethral sphincter tone during ejaculation and resulting in retrograde ejaculation [11] [12]. Tadalafil completely avoids this mechanism [12]. Instead, through upregulation of NO-cGMP signaling, tadalafil promotes arterial vasodilation and enhances pelvic, cavernosal, and prostatic tissue perfusion [12]. This preserves erectile capacity and overall sexual satisfaction during the stenting period, which is biologically consistent with the generally favorable sexual-matters outcomes observed with tadalafil in the direct randomized comparisons [8]-[11], although a reliable pooled effect size could not be calculated.

Furthermore, factorial trial models and combined comparative analyses confirm that co-administering PDE5 inhibitors with alpha-1 adrenergic antagonists provides a complementary mechanism of action [1]. By simultaneously targeting trigonal tone via alpha-blockade and pan-ureteral spasm/vascular perfusion via PDE5 inhibition, combination regimens represent an effective clinical strategy for severe or refractory stent symptoms.

5. Limitations

This review has several limitations. The randomized evidence base is small and largely single-center. Tadalafil dose varied between 5 and 10 mg daily, assessment schedules differed, and statistical reporting was not uniform. Several reports did not provide the domain-specific standard deviations, analyzable denominators, or sexual-domain applicability data needed for a defensible pooled continuous-outcome estimate. Participant blinding was absent or insufficiently documented in some studies, which is important for self-reported outcomes. The review was not prospectively registered. Finally, the original database export files and exact historical platform search logs were not preserved; the supplementary search strategies are therefore reconstructed reproducible strategies corresponding to the stated concepts and cutoff date rather than verbatim historical logs.

6. Conclusion

Tadalafil is a reasonable pharmacological alternative to tamsulosin for ureteral stent-related symptoms and may provide greater relief of body pain and sexual-

domain symptoms in selected patients. Urinary-symptom relief is broadly comparable across the randomized evidence base, although individual trials are not fully concordant. Tadalafil plus tamsulosin appears promising, but evidence meeting the strict tamsulosin 0.4-mg comparator definition is insufficient for a reliable pooled combination estimate. Future randomized trials should prespecify a common in-stent USSQ assessment time, report domain-specific analyzable denominators—particularly for sexual matters—and use standardized active adverse-event ascertainment. Any future quantitative synthesis should be regenerated from a transparent trial-level extraction dataset with reproducible analysis code or files.

Author Contributions

Abdullah Elrashidy: Conceptualization, methodology, formal analysis, project administration, and writing—original draft preparation.

Alaa Mousa: Literature screening, data extraction, risk of bias assessment, and writing—review and editing.

Gaber M. Elsafy: Literature screening, data verification, software processing, and validation.

Mahmoud Shaaban: Conceptualization, visual data tracking, supervision, and final manuscript approval.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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