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Dear Colleagues,

We are pleased to have published the first issue of The New Journal of Urology for 2026 (Volume 21, Issue 1). This issue includes five (5) original articles and one (1) case report. We believe that these contributions, ranging from functional urology to uro-oncology and reconstructive surgery, will be read with great interest and serve as a reference for future clinical and academic studies.

In this issue, original research papers evaluate the impact of Valsalva leak point pressure on TOT surgery success, provide real-world insights into the stepwise treatment of Interstitial Cystitis/Bladder Pain Syndrome, and identify predictors of success in buccal mucosal graft urethroplasty. Additionally, we feature studies investigating testosterone levels in Peyronie's disease and the effects of neoadjuvant chemotherapy on perioperative outcomes following radical cystectomy. The issue is completed by an intriguing case report on late bladder necrosis presenting as intestinal obstruction.

The New Journal of Urology has been indexed in the TÜBİTAK ULAKBİM TR Index since the first issue of 2011. Our journal is also indexed in DOAJ, Google Scholar, Turkish Medline, Turkish Citation Index, SOBIAD, Scilit, Ideal Online Database, J-GATE, and EBSCO. Furthermore, we continue our collaboration with the ORCID and CrossRef DOI systems.

The editorial team is deeply grateful to all the authors for choosing our platform and to the reviewers who have dedicated their time to maintaining the high scientific standards of this issue.

We invite you to submit your valuable research to The New Journal of Urology, participate in the peer-review process, and cite the articles published in our journal to support the dissemination of urological knowledge.

Respectfully yours

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Evaluating the Impact of Valsalva Leak Point Pressure and Urge Incontinence on the Success of Transobturator Tape Surgery for Stress Urinary Incontinence

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Abstract

Objective: This study aimed to investigate factors influencing the surgical outcomes of patients undergoing transobturator tape (TOT) surgery for stress urinary incontinence (SUI), focusing on the predictive value of Valsalva Leak Point Pressure (VLPP) and the presence of urge incontinence.

Material and Methods: A retrospective study was conducted involving 117 patients from 561 who underwent TOT surgery between May 2017 and March 2024. We excluded patients with prior pelvic surgeries or neurogenic bladder, and included SUI with urethral hypermobility as an inclusion criterion. We performed urodynamic testing, including VLPP measurement, preoperatively. Postoperative outcomes were evaluated using stress tests, the International Consultation on Incontinence Questionnaire- Short Form (ICIQ-SF), and assessments of urge incontinence and cystocele presence.

Results: Postoperative stress tests revealed 14.5% failure and 85.5% success rates. We observed significant differences in urinary incontinence (UI) amount based on VLPP values ($p = 0.001$), where lower VLPP was associated with higher postoperative UI rates. Urge incontinence had a significant impact on postoperative UI ($p = 0.023$), but it did not correlate with preoperative UI frequency. Postoperatively, ICIQ-SF scores and impact on daily life showed significant improvement ($p < 0.001$). ROC analysis indicated that the impact on daily life was a significant predictor of surgical success ($p = 0.035$).

Conclusion: TOT surgery may significantly improve urinary incontinence symptoms and have a positive impact on daily life. However, a VLPP of less than 90 cmH₂O is associated with higher rates of postoperative UI, suggesting a potential intrinsic sphincter deficiency (ISD). Post-surgical urge incontinence presents a significant challenge for individuals, likely due to detrusor muscle overactivity following the surgery. We need further research to refine predictive measures and improve surgical techniques.

Keywords: stress urinary incontinence, transobturator tape, urge incontinence, valsalva leak point pressure

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INTRODUCTION

In many societies, approximately 10–25% of the population seeks treatment for urinary incontinence at urology and gynecology clinics. The prevalence of stress urinary incontinence (SUI) in the general population has been reported to range from 5% to 69% (1). SUI has been reported in 4.7% of nulliparous women, 6.9% of those who delivered via cesarean section, and 12.2% of those with a history of vaginal delivery (2). Due to its high prevalence and economic burden, researchers continue to search for effective treatment methods.

Surgical intervention is typically considered when conservative measures fail. Among surgical options, midurethral sling procedures—especially minimally invasive ones—are widely used, resulting in increased surgical intervention rates for urinary incontinence (UI) in women. Although these sling surgeries are highly effective, they have a failure rate of approximately 20%, and the success rate for repeat surgeries is significantly lower (3). Therefore, the role of urodynamic testing in predicting surgical outcomes and guiding preoperative counseling has become increasingly important.

Some authors argue that the first surgical procedure for a patient with incontinence should ideally be the last. They emphasize the importance of a differential diagnosis based not only on clinical history but also on urodynamic studies to determine the appropriate intervention (4). However, guidelines from the National Institute for Health and Care Excellence (NICE) and the U.S. Agency for Health Care Policy and Research (AHCPR) recommend against routine urodynamic testing prior to conservative treatment. These organizations state that for patients with a clear clinical diagnosis of SUI, history-taking and simple urogynecological tests are often sufficient, eliminating the need for additional urodynamic evaluation (5, 6).

The evaluation of patients with SUI should begin with simple and non-invasive assessments. More complex and costly procedures such as urodynamics should be reserved for selected cases—particularly those with neurological conditions or when the type of incontinence remains unclear based on history and clinical findings.

The International Continence Society (ICS) defines the Valsalva Leak Point Pressure (VLPP) as the intravesical pressure at which urine leakage occurs due to increased abdominal pressure during the Valsalva maneuver. VLPP is considered a quantitative measure of SUI severity (7). Intrinsic sphincter deficiency (ISD), which is generally associated with low VLPP values, is linked to more severe urinary leakage. Preoperative urodynamic studies have demonstrated that patients with low VLPP values are at increased risk of surgical failure (8, 9).

Several factors influence urethral pressure measurements, including age—particularly advanced age—postural changes, and both voluntary and involuntary contractions of the pelvic floor muscles (10). Moreover, VLPP measurements may be unreliable in patients with detrusor overactivity or low bladder compliance. The catheter diameter also affects VLPP readings, with larger catheters yielding higher pressure values (11).

In this study, we aimed to investigate the factors that positively or negatively affect surgical outcomes in patients who underwent the Transobturator Tape (TOT) procedure for the treatment of SUI.

MATERIALS AND METHODS

The study was approved by our hospital's Clinical Research Ethics Committee under approval number 2024/01/11/011 on 2024-01-24. This retrospective study included 117 patients—selected from a total of 561—who had complete urodynamic data and underwent TOT surgery for SUI at our urology and gynecology clinics between May 2017 and March 2024. Written informed consent was obtained from all participants.

Inclusion criteria were defined as SUI associated with urethral hypermobility, in accordance with the guidelines of the ICS. Exclusion criteria included patients without urodynamic testing, those who had previously undergone pelvic surgery or radiotherapy, individuals with prior incontinence surgery, and patients diagnosed with neurogenic bladder or psychiatric disorders.

Demographic and clinical data, including age, height, weight, body mass index (BMI), number of vaginal and cesarean deliveries, and comorbidities, were recorded.

Urodynamic testing was performed using the Locum Plus system (Aymed, Türkiye), following ICS guidelines. Although current guidelines suggest reserving urodynamic evaluation for complex or ambiguous cases, our institution routinely performs preoperative urodynamic testing for all patients undergoing midurethral sling surgery. This policy is based on institutional protocol aimed at improving surgical planning and identifying occult detrusor overactivity or ISD, which could influence postoperative outcomes. As such, all patients in this study underwent urodynamic testing regardless of symptom complexity. VLPP values were stratified into two categories: <90 cm H₂O and >90 cm H₂O. Patients with VLPP <60 cm H₂O who were diagnosed with ISD and treated with periurethral bulking agents were excluded from the study.

All patients underwent a preoperative clinical evaluation, including medical history, physical examination, and urodynamic assessment. The International Consultation on Incontinence Questionnaire–Short Form (ICIQ-SF) was completed preoperatively and postoperatively. Data on urge incontinence and cystocele were also documented. Frequency, volume, and the impact of urge incontinence on daily life were evaluated separately.

Based on the presence or absence of urge incontinence in the preoperative assessment, 93 patients (79.5%) were classified as having pure stress urinary incontinence, and 24 patients (20.5%) were considered to have mixed urinary incontinence. This classification was used in the comparative analysis of surgical outcomes.

All surgical procedures were performed by the same urologist and gynecologist, each with a minimum of five years of experience in urogynecology. A standardized stress test was conducted for all patients both before and after surgery. A positive postoperative stress test result was considered indicative of treatment failure.

The 90 cm H₂O threshold for VLPP was selected based on previous literature, which suggests that this value more accurately identifies patients at risk of intrinsic sphincter deficiency compared to lower cut-off points.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 29.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables were expressed as mean \pm standard deviation (SD), while non-normally distributed variables were presented as median and interquartile range (IQR). Categorical variables were summarized as frequencies and percentages.

The Chi-square test was used to assess associations between categorical demographic and clinical variables (e.g., VLPP category, presence of urge incontinence, and postoperative stress test results). The Independent Samples T-test was used to compare continuous variables between two groups (e.g., VLPP <90 cm H₂O vs >90 cm H₂O). The Paired Samples T-test was applied to compare preoperative and postoperative ICIQ-SF scores and their impact on daily life.

To identify independent predictors of surgical success—defined as a negative result on the postoperative stress test—a binary logistic regression analysis was performed. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs).

Receiver Operating Characteristic (ROC) curve analysis was used to evaluate the predictive accuracy of the preoperative “impact on daily life” score for surgical outcomes. The area under the curve (AUC), optimal cut-off value, sensitivity, and specificity were reported.

A p-value of <0.05 was considered statistically significant.

RESULTS

This current study aimed to evaluate the differences in the frequency, volume, and impact of UI on daily activities between the preoperative and postoperative periods. Additionally, we investigated the role of VLPP values in predicting surgical efficacy and their correlation with urinary incontinence. The analysis focused on assessing the effectiveness of surgery in treating pelvic organ prolapse and UI, the influence of detrusor overactivity on treatment outcomes, and the prognostic value of VLPP.

Tables 1 and 2 summarize the demographic and clinical characteristics of the study participants. Postoperative stress test results revealed that 85.5% of patients had successful outcomes, while 14.5% experienced surgical failure. Comparative analyses based on VLPP values, presence of urge incontinence, and stress test results are presented in Tables 3A–C.

A significant difference was observed in the amount of UI after surgery ($p=0.001$). Specifically, among patients with VLPP <90 cm H₂O, only 16.7% reported no UI, while 83.3% of patients with VLPP >90 cm H₂O were free of UI. Conversely, 94.4% of patients who experienced a small amount of UI belonged to the VLPP <90 cm H₂O group, compared to only 5.6% in the >90 cm H₂O group. These findings suggest that patients with VLPP <90 cm H₂O may have concurrent ISD. Patients with urge incontinence demonstrated less favorable postoperative stress test results, indicating a potential negative association. While no significant relationship was observed between urge incontinence and preoperative UI frequency or volume, urge incontinence was significantly associated with increased UI symptoms in the postoperative period. This may be attributed to de novo detrusor overactivity emerging after surgery. The frequency and volume of postoperative UI were found to be strongly associated with surgical success, highlighting their importance as indicators of treatment efficacy.

Table 1. Mean and Standard Deviation of Demographic Values

Variables	Mean ± SD	Min-Max
Height (cm)	159.08 ± 6.58	149-172
Weight (kg)	76.85 ± 11.38	58-115
BMI (kg/m ²)	30.4 ± 2.6	15.4-51.1
Age (years)	50.03 ± 8.64	30-71
Number of Births	3.20 ± 1.64	1-10
Number of Vaginal Deliveries	2.79 ± 1.76	0-10
Number of Cesarean Deliveries	0.41 ± 0.83	0-4
Preoperative Impact on Daily Life Score	8.36 ± 1.56	3-10
Preoperative ICIQ-SF Score	18.17 ± 2.97	6-21
Postoperative Impact on Daily Life Score	2.25 ± 2.55	0-10
Postoperative ICIQ-SF Score	5.30 ± 5.20	0-20
VLPP	119.95 ± 29.56	58-240

Table 2. Demographic and Clinical Characteristics of Patients

Category	n	Percentage(%)
Comorbidities		
Absent	48	41.0
Present	69	59.0
Pelvic Organ Prolapse Quantification (POP-Q)		
C-0	13	11.1
C-1	5	4.3
C-2	15	12.8
C-3	8	6.8
C-4	32	27.4
C-5	16	13.7
C-6	18	15.4
C-7	6	5.1
C-8	4	3.4
VLPP (cmH₂O)		
VLPP <90 cm H ₂ O	19	16.2
VLPP >90 cm H ₂ O	98	83.8
Stress Test (Postoperative)		
Positive	17	14.5
Negative	100	85.5
Urge Incontinence		
Absent	93	79.5
Present	24	20.5
Cystocele		
Absent	98	83.8
Grade 1	10	8.5
Grade 2	9	7.7

As shown in Table 4, significant improvements were observed in both ICIQ-SF scores and the impact on daily life following surgery ($p < 0.001$), indicating a substantial reduction in both UI symptoms and their daily burden. Furthermore, Table 5 and Figure 1 present the results of ROC curve analysis, which showed that the preoperative impact on daily life score was a statistically significant predictor of surgical success ($p = 0.035$). The model demonstrated acceptable predictive accuracy, suggesting that this variable may be valuable for preoperative evaluation.

Table 3A. Comparison of clinical characteristics according to VLPP groups

Variables	VLPP <90 cmH2O (n,%)	VLPP >90 cmH2O (n,%)	p-value
Comorbidities			0.614
Absent	(9, 18.8%)	(39, 81.3%)	
Present	(10, 14.5%)	(59, 85.5%)	
POP-Q			0.047*
C-0	(1, 7.7%)	(12, 92.3%)	
C-1	(1, 20.0%)	(4, 80.0%)	
C-2	(7, 46.7%)	(8, 53.3%)	
C-3	(0, 0.0%)	(8, 100.0%)	
C-4	(6, 18.8%)	(26, 81.3%)	
C-5	(2, 12.5%)	(14, 87.5%)	
C-6	(1, 5.6%)	(17, 94.4%)	
C-7	(1, 16.7%)	(5, 83.3%)	
C-8	(0,0.0%)	(4,100.0%)	
Cystocele			
Absent	(19, 19.4%)	(79, 80.6%)	
Grade 1	(0, 0.0%)	(10, 100.0%)	
Grade 2	(0, 0.0%)	(9, 100.0%)	
Frequency of Urinary Incontinence (Preoperative)			0.019*
Absent	(2, 50.0%)	(2, 50.0%)	
Once a Week or Less	(0, 0.0%)	(5, 100.0%)	
2-3 Times a Week	(0, 0.0%)	(26, 100.0%)	
Several Times a Day	(17, 20.7%)	(65, 79.3%)	
Amount of Urinary Incontinence (Preoperative)			0.650
Mild	(2, 28.6%)	(5, 71.4%)	
Moderate	(4, 12.5%)	(28, 87.5%)	
Severe	(13, 16.7%)	(65, 83.3%)	
Amount of Urinary Incontinence (Postoperative)			0.001*
None	(7, 16.7%)	(35, 83.3%)	
Little	(3, 5.6%)	(51, 94.4%)	
Moderate	(9, 42.9%)	(12, 57.1%)	
Frequency of Urinary Incontinence (Postoperative)			0.619
None	(7, 16.7%)	(35, 83.3%)	
Once a Week or Less	(4, 11.1%)	(32, 88.9%)	
2-3 Times a Week	(2, 14.3%)	(12, 85.7%)	
Several Times a Day	(3, 33.3%)	(6, 66.7%)	

Chi-Square Analysis

Table 3 B. Comparison of clinical characteristics according to urge incontinence

Variables	Urge Incontinence: Present (n,%)	Urge Incontinence: Absent (n,%)	p-value
Comorbidities			0.390
Absent	(40, 83.3%)	(8, 16.7%)	
Present	(53, 76.8%)	(16, 23.2%)	
POP-Q			0.839
C-0	(10, 76.9%)	(3, 23.1%)	
C-1	(4, 80.0%)	(1, 20.0%)	
C-2	(12, 80.0%)	(3, 20.0%)	
C-3	(5, 62.5%)	(3, 37.5%)	
C-4	(24, 75.0%)	(8, 25.0%)	
C-5	(13, 81.3%)	(3, 18.8%)	
C-6	(17, 94.4%)	(1, 5.6%)	
C-7	(5, 83.3%)	(1, 16.7%)	
C-8	(3, 75.0%)	(1, 25.0%)	
Cystocele			0.121
Absent	(81, 82.7%)	(17, 17.3%)	
Grade 1	(6, 60.0%)	(4, 40.0%)	
Grade 2	(6, 66.7%)	(3, 33.3%)	
Frequency of Urinary Incontinence (Preoperative)			0.249
Absent	(4, 100.0%)	(0, 0.0%)	
Once a Week or Less	(3, 60.0%)	(2, 40.0%)	
2-3 Times a Week	(23, 88.5%)	(3, 11.5%)	
Several Times a Day	(63, 76.8%)	(19, 23.2%)	
Amount of Urinary Incontinence (Preoperative)			0.855
Mild	(5, 71.4%)	(2, 28.6%)	
Moderate	(26, 81.3%)	(6, 18.8%)	
Severe	(62, 79.5%)	(16, 20.5%)	
Amount of Urinary Incontinence (Postoperative)			0.001*
None	(42, 100.0%)	(0, 0.0%)	
Little	(35, 64.8%)	(19, 35.2%)	
Moderate	(16, 76.2%)	(5, 23.8%)	
Frequency of Urinary Incontinence (Postoperative)			0.001*
None	(42, 100.0%)	(0, 0.0%)	
Once a Week or Less	(21, 58.3%)	(15, 41.7%)	
2-3 Times a Week	(9, 64.3%)	(5, 35.7%)	
Several Times a Day	(7, 77.8%)	(2, 22.2%)	

Chi-Square Analysis

Table 3C. Comparison of clinical characteristics according to postoperative stress test results

Variables	Stress Test Negative (n,%)	Stress Test Positive (n,%)	p-value
Comorbidities			0.544
Absent	(8, 16.7%)	(40, 83.3%)	
Present	(9, 13.0%)	(60, 87.0%)	
POP-Q			0.512
C-0	(1, 7.7%)	(12, 92.3%)	
C-1	(0, 0.0%)	(5, 100.0%)	
C-2	(2, 13.3%)	(13, 86.7%)	
C-3	(1, 12.5%)	(7, 87.5%)	
C-4	(3, 9.4%)	(29, 90.6%)	
C-5	(5, 31.3%)	(11, 68.8%)	
C-6	(4, 22.2%)	(14, 77.8%)	
C-7	(1, 16.7%)	(5, 83.3%)	
C-8	(0.0%,)	(100.0%,)	
Cystocele			
Absent	(15, 15.3%)	(83, 84.7%)	0.862
Grade 1	(1, 10.0%)	(9, 90.0%)	
Grade 2	(1, 11.1%)	(8, 88.9%)	
Frequency of Urinary Incontinence (Preoperative)			0.882
Absent	(1, 25.0%)	(3, 75.0%)	
Once a Week or Less	(1, 20.0%)	(4, 80.0%)	
2-3 Times a Week	(3, 11.5%)	(23, 88.5%)	
Several Times a Day	(12, 14.6%)	(70, 85.4%)	
Amount of Urinary Incontinence (Preoperative)			0.531
Mild	(0, 0.0%)	(7, 100.0%)	
Moderate	(5, 15.6%)	(27, 84.4%)	
Severe	(12, 15.4%)	(66, 84.6%)	
Amount of Urinary Incontinence (Postoperative)			0.001*
None	(0, 0.0%)	(42, 100.0%)	
Little	(5, 9.3%)	(49, 90.7%)	
Moderate	(12, 57.1%)	(9, 42.9%)	
Frequency of Urinary Incontinence (Postoperative)			0.001*
None	(0, 0.0%)	(42, 100.0%)	
Once a Week or Less	(1, 2.8%)	(35, 97.2%)	
2-3 Times a Week	(3, 21.4%)	(11, 78.6%)	
Several Times a Day	(3, 33.3%)	(6, 66.7%)	

Chi-Square Analysis

Table 4. Preoperative and Postoperative ICIQ-SF Scores and Mean Impact on Daily Life

Variables	Mean ± SD	N	SD	Test Value	P Value
ICIQ-SF Score (Preoperative)	18.17	117	2.972	26.488	<0.001*
ICIQ-SF Score (Postoperative)	5.30	117	5.205		
Impact of Daily Life (Preoperative)	8.36	117	1.56	24.991	<0.001*
Impact of Daily Life (Postoperative)	2.25	117	2.55		

Paired Sample T Test, *P<0.05

Table 5. The ROC analysis for positive prognostic factors associated with Operation Success

Parameters	Cut-off value	Sensitivity (%)	Specificity (%)	AUC (%95 CI)	P Value
Impact of Daily Life (Postoperative)	9.500	0.770	0.470	0.650 (0.510-0.787)	0.035*

ROC Analysis P<0.05

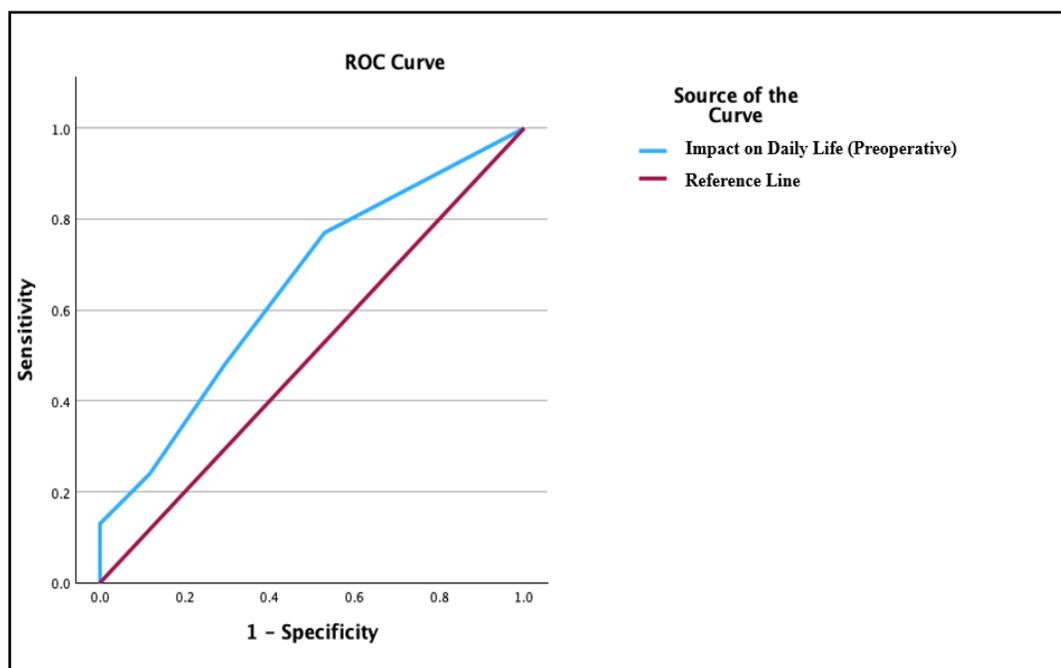


Figure 1. The ROC curve for positive prognostic factors associated with operation success

DISCUSSION

In incontinence surgery, the most critical factor influencing success is not only the surgical technique itself but also its appropriateness for the individual patient. A major limitation of symptom-based diagnosis is its inability to classify the type of SUI accurately. An accurate diagnostic strategy is essential

for achieving favorable surgical outcomes. In a study of 206 patients, Sahin et al. found that symptom-based diagnosis had a sensitivity of 80.2%, specificity of 57.3%, a PPV of 59.8%, and an NPV of 78.5%, suggesting that reliance solely on patient history may reduce treatment success (12).

Urodynamic testing remains the most reliable tool for evaluating urethral function in SUI. In healthy individuals, leakage should not occur with increased abdominal pressure. Leakage at high pressures (>90 cm H₂O) typically indicates urethral hypermobility, whereas leakage at low pressures (<60 cm H₂O) is suggestive of ISD (13, 14). In our study, 94.4% of patients who experienced postoperative UI had VLPP values <90 cm H₂O, suggesting a strong association with ISD.

Some studies report that large cystoceles can artificially elevate VLPP measurements by buffering abdominal pressure or compressing the urethra (15). In our cohort, however, neither POP-Q classification nor cystocele grade 1–2 significantly impacted surgical outcomes. Grade 3 cystocele cases were excluded as they required additional prolapse surgery.

VLPP threshold values have been widely studied to guide surgical decision-making in SUI. Cut-off points such as 60, 70, and 90 cm H₂O are frequently referenced (14, 16, 17), though outcomes vary. In our study, we used 90 cm H₂O as a threshold and explored related influencing factors. Recent literature supports using individualized VLPP thresholds based on patient-specific contexts.

Urethral pressure profile (UPP) measurements are often normal in incontinent patients and tend to remain unchanged even after interventions such as periurethral bulking injections. Due to its simplicity and practicality, VLPP is generally favored over UPP for distinguishing anatomical SUI from ISD. UPP is considered unreliable in evaluating stress incontinence (18, 19). O'Connor reported that patients with VLPP >60 cm H₂O had better outcomes, while those with VLPP ≤60 cm H₂O had reduced success, likely due to ISD (20). However, the limited number of patients with low VLPP in our study precluded detailed statistical analysis on ISD.

Guerette et al. identified VLPP >60 cm H₂O and maximum urethral closure pressure (MUCP) >40 cm H₂O as strong predictors of surgical success (21). These findings underscore the value of preoperative urodynamics for outcome prediction in patients undergoing SUI surgery.

Another important consideration is the occurrence of de novo detrusor overactivity following surgery. In many cases, it is difficult to determine whether the condition existed

preoperatively, complicating postoperative evaluation. The incidence of detrusor overactivity can reach up to 70% in women following unsuccessful incontinence surgery (22). There is consensus that patients with mixed incontinence, neurological conditions, or discordant symptoms and findings should undergo preoperative urodynamic evaluation.

Our findings support this recommendation. Although preoperative urge incontinence was not associated with UI severity or volume, postoperative urge incontinence was significantly linked to persistent UI, possibly due to new-onset detrusor overactivity. The presence of postoperative urge incontinence emerged as a key factor associated with increased UI frequency and volume—both of which were strongly correlated with surgical success. These results suggest that UI symptom burden in the postoperative period may serve as a valuable clinical indicator of treatment outcomes.

The type of incontinence—whether pure stress or mixed—also had a notable influence on surgical outcomes. Patients with mixed urinary incontinence, identified by the presence of urge symptoms preoperatively, demonstrated significantly worse postoperative results. These included higher rates of persistent UI and poorer outcomes on postoperative stress tests. In contrast, patients with pure stress incontinence achieved more favorable results. This pattern supports previous findings indicating that mixed incontinence, particularly when associated with detrusor overactivity, complicates treatment and may increase the likelihood of persistent or de novo symptoms following TOT surgery.

A limitation of our study is that many of the cited references assessed urodynamic parameters retrospectively. These studies were not specifically designed to predict outcomes, limiting the generalizability of their findings prospectively.

CONCLUSION

In evaluating the factors influencing the outcomes of TOT surgery for SUI, we found that patient age, BMI, number and mode of deliveries, POP-Q classification, and grade 1–2 cystoceles had no significant impact on surgical success.

Postoperative analysis of ICIQ-SF scores revealed significant improvements in both symptom severity and the impact of urinary incontinence on daily life, underscoring the clinical efficacy of the TOT procedure.

Patients with VLPP values below 90 cm H₂O exhibited a higher incidence of postoperative urinary incontinence, suggesting a potential association with ISD.

Although preoperative urge incontinence did not significantly influence surgical outcomes, the emergence of de novo urge incontinence postoperatively was strongly associated with persistent UI symptoms. This finding may reflect the development of new-onset detrusor overactivity, highlighting the need for further research and careful postoperative evaluation.

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Informed Consent: Informed consent was obtained from all participants prior to inclusion in the study.

Ethical Approval: The study was approved by the Non-Interventional Clinical Research Ethics Committee of Bağcılar Training and Research Hospital (Approval No: 2024/01/11/011, Date: 2024-01-24). The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Author Contributions: Concept and Design: SY, IOC, AS, TD; Supervision: SG, AC, MMD; Data Collection and/or Analysis: SS, OKA, GC, AC; Analysis and/or Interpretation: SY, IOC, AS, SS; Literature Search: SY, TD, SS, OKA, GC, AC; Writing: SY, IOC; Critical Review: SY, IOC, AS, TD, MMD.

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Stepwise Treatment Strategy for Interstitial Cystitis/Bladder Pain Syndrome: Insights from Real-World Clinical Practice

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Abstract

Objective: To assess the real-world efficacy of a guideline-based stepwise treatment approach in patients with interstitial cystitis/bladder pain syndrome who do not respond to lifestyle modifications.

Material and Methods: This retrospective study included 75 female patients with a confirmed diagnosis of interstitial cystitis/bladder pain syndrome, each with a minimum follow-up period of 12 months. None of the participants responded to initial conservative treatment or subsequently underwent a sequential therapeutic regimen. This regimen was initiated with oral pentosan polysulfate sodium, followed by intravesical sodium chondroitin sulfate and Onabotulinum toxin A injections. Treatment efficacy was assessed on the basis of the patient's global impression of the change scale.

Results: Long-term symptom management with oral pentosan polysulfate sodium was successfully achieved in 38.7% of patients. Among those who transitioned to intravesical sodium chondroitin sulfate, 63.1% reported experiencing "much" or "very much" improvement according to the patient global Impression of change scale. Onabotulinum toxin A significantly improved in 58.8% of the patients. The overall response rate across all treatment levels was 89.3%. Adverse effects are infrequent and generally mild.

Conclusion: A stepwise treatment protocol tailored to individual patient responses has been demonstrated to be both effective and well tolerated in the management of interstitial cystitis/bladder pain syndrome. These findings advocate the incorporation of flexible, patient-centered therapeutic strategies in clinical practice and underscore the need for prospective studies employing validated outcome measures.

Keywords: botulinum toxins, chondroitin sulfates, interstitial cystitis, urinary bladder diseases

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INTRODUCTION

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic condition characterized by pelvic pain, pressure, or discomfort associated with the bladder, typically accompanied by urinary frequency, urgency, and nocturia in the absence of identifiable infection or other overt pathologies. Its prevalence is estimated to range from 6.2% to 11.2%, depending on the diagnostic criteria employed, and it predominantly affects women [1]. The etiology remains multifactorial and incompletely understood, with proposed mechanisms including epithelial barrier dysfunction, mast cell activation, neurogenic inflammation, and central nervous system sensitization [2]. The disease significantly affects patients' quality of life, often leading to psychological distress, impaired sexual function, and social withdrawal [3].

Owing to its heterogeneous nature, IC/BPS requires a personalized and structured treatment approach. Current guidelines advocate for a stepwise treatment algorithm, commencing with conservative interventions and progressing to more invasive options as required [4,5]. Initial therapies include lifestyle modifications, dietary adjustments, and behavioral therapy. Should these prove ineffective, oral medications, such as amitriptyline, hydroxyzine, cimetidine, or pentosan polysulfide sodium (PPS), as well as intravesical instillations, should be considered. On botulinum toxin A injection can be used in cases of treatment resistance. More invasive procedures are required for most refractory cases. This algorithm seeks to balance efficacy and safety, while accommodating individual patient needs.

Although numerous studies have investigated the efficacy of individual treatment modalities for IC/BPS, few have thoroughly examined the real-world application of guideline-recommended stepwise treatment algorithms. Most of the existing data are derived from controlled trial settings or focus on isolated interventions, which may not accurately represent the complexities encountered in clinical practice. Consequently, there is a gap in the literature concerning the longitudinal effectiveness and progression patterns of tiered treatment as implemented in routine urology clinics. Addressing this gap is crucial for validating current recommendations and enhancing patient-centered care strategies.

This study aimed to evaluate real-world outcomes of a tiered treatment strategy in patients with IC/BPS who did not respond to lifestyle modifications. By examining responses across successive treatment steps, we aimed to elucidate the utility and limitations of guideline-driven care pathways in routine clinical practice.

MATERIAL AND METHODS

This retrospective study was conducted in accordance with the principles delineated in the World Medical Association Declaration of Helsinki, "Ethical Principles for Medical Research Involving Human Subjects." The study protocol received approval from the Institutional Ethics Committee (Approval Number: 05.03.2025.83, Date: 2025-03-07). All data were sourced from hospital records and patient confidentiality was maintained throughout the study.

A retrospective review was conducted of patients diagnosed with IC/BPS between January 2022 and June 2025. The inclusion criteria required the presence of symptoms consistent with IC/BPS as defined by the International Continence Society (ICS), characterized by bladder-related pain, pressure, or discomfort accompanied by at least one lower urinary tract symptom, such as urinary frequency or urgency [6].

Only patients with a follow-up period of at least 12 months were included in the study. The exclusion criteria included a positive urine culture, active vaginal infection, urolithiasis, genitourinary neoplasia, pelvic organ prolapse of stage ≥ 3 in any compartment according to the Pelvic Organ Prolapse Quantification System (POP-Q), pregnancy or lactation, a history of pelvic surgery, history of pelvic radiotherapy, those receiving active immunosuppressive therapy and known neurological disorders. Additionally, patients aged < 18 years and those with incomplete data were also excluded.

All patients underwent a thorough evaluation, which included detailed medical history, physical examination, urinalysis, urine culture, and cystoscopy. Patients with Hunner's lesions identified during cystoscopy were excluded from the study due to their distinct pathophysiology and treatment response patterns, which may introduce clinical heterogeneity. The baseline demographic data, body mass index (BMI), and comorbidities were recorded. Patients who did not respond

to initial lifestyle modifications, such as elimination of known bladder irritants (e.g., caffeine, artificial sweeteners, spicy foods) and bladder training, were considered for medical therapy.

Initially, all patients received oral PPS (Elmiron®, Janssen Pharmaceuticals, Titusville, NJ, USA) at a dose of 100 mg three times daily. PPS treatment was considered successful if patients reported at least “much improvement” on the PGI-C scale after a minimum treatment duration of three months and continued therapy due to perceived clinical benefit. Those who experienced inadequate benefits or adverse effects were transitioned to intravesical instillation of 80 mg 0.2% sodium chondroitin sulfate (Gepan® Instill, Pohl-Boskamp, Hohenlockstedt, Germany) administered once weekly for four sessions. Responders to this treatment received an additional four weekly sessions, followed by monthly maintenance instillations for up to one year.

Patients who exhibited either a lack of response or adverse effects following four sessions of intravesical sodium chondroitin sulfate instillation were subsequently offered an intravesical administration of Onabotulinum toxin A (Allergan, Irvine, CA, USA). This intervention involved the intravesical injection of 100 units of the toxin, diluted in normal saline, into the detrusor muscle via a cystoscopic technique. The injections were strategically administered at multiple sites evenly distributed across the bladder wall, employing a trigone-sparing approach. The procedure was performed under local or regional anesthesia, contingent upon patient preference and institutional protocols. Patients who received Onabotulinum toxin A were reassessed after one month, and if therapeutic benefits were observed, repeat injections were not performed routinely but were offered in cases of symptom recurrence following an initial favorable response.

Patients who did not respond to Onabotulinum toxin A were directed towards experimental therapies, including acupuncture, posterior tibial nerve stimulation (PTNS), or intravesical ozone instillation. Patient satisfaction was measured using the Patient Global Impressions of Change (PGI-C) scale, a seven-point Likert scale that assesses changes in clinical status. This scale rates patient satisfaction with surgery, with 1 indicating very much improvement,

4 indicating no change, and 7 indicating very much worse. PGI-C scales reflected patient-perceived symptom changes relative to the most recently initiated treatment modality, rather than baseline at initial diagnosis. A participant flowchart is provided in Figure 1 (Figure 1).

Therapeutic escalation was conducted in a systematic manner, guided by patient-reported outcomes and treatment tolerability. Patients were classified as insufficient responders if they exhibited no change or only minimal improvement on the PGI-C scale following an adequate duration of treatment, or if treatment was discontinued due to adverse effects. In such instances, patients were transitioned to the subsequent treatment modality in accordance with the predefined treatment algorithm.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables are reported as mean ± standard deviation or median (interquartile range (IQR)), contingent upon the distribution ascertained by the Shapiro–Wilk test. Categorical variables are presented as frequencies and percentages.

RESULTS

A cohort of 75 patients diagnosed with IC/BPS and monitored for a minimum of 12 months was included in this study. The median age of the participants was 51 years (IQR: 39–58), and the median BMI was 27.5 kg/m² (IQR: 25.5–30.4). Of these, 41 (54.7%) were postmenopausal. The detailed demographic data and comorbidities are presented in Table 1. The most prevalent comorbidity was psychiatric disorder, affecting 25.3% of the cohort. The median follow-up period was 12 months (IQR: 12–16 months) (Table 1).

All 75 patients initially started oral PPS treatment. Of these, 29 patients (38.7%) persisted with PPS treatment for a minimum duration of one year, whereas 42 patients (56.0%) discontinued treatment due to dissatisfaction. Adverse effects were documented in 12 (16.0%) patients, with gastrointestinal symptoms being the most prevalent. Three patients ceased treatment because of gastrointestinal symptoms and one patient discontinued treatment because of menstrual irregularity. The detailed outcomes and adverse

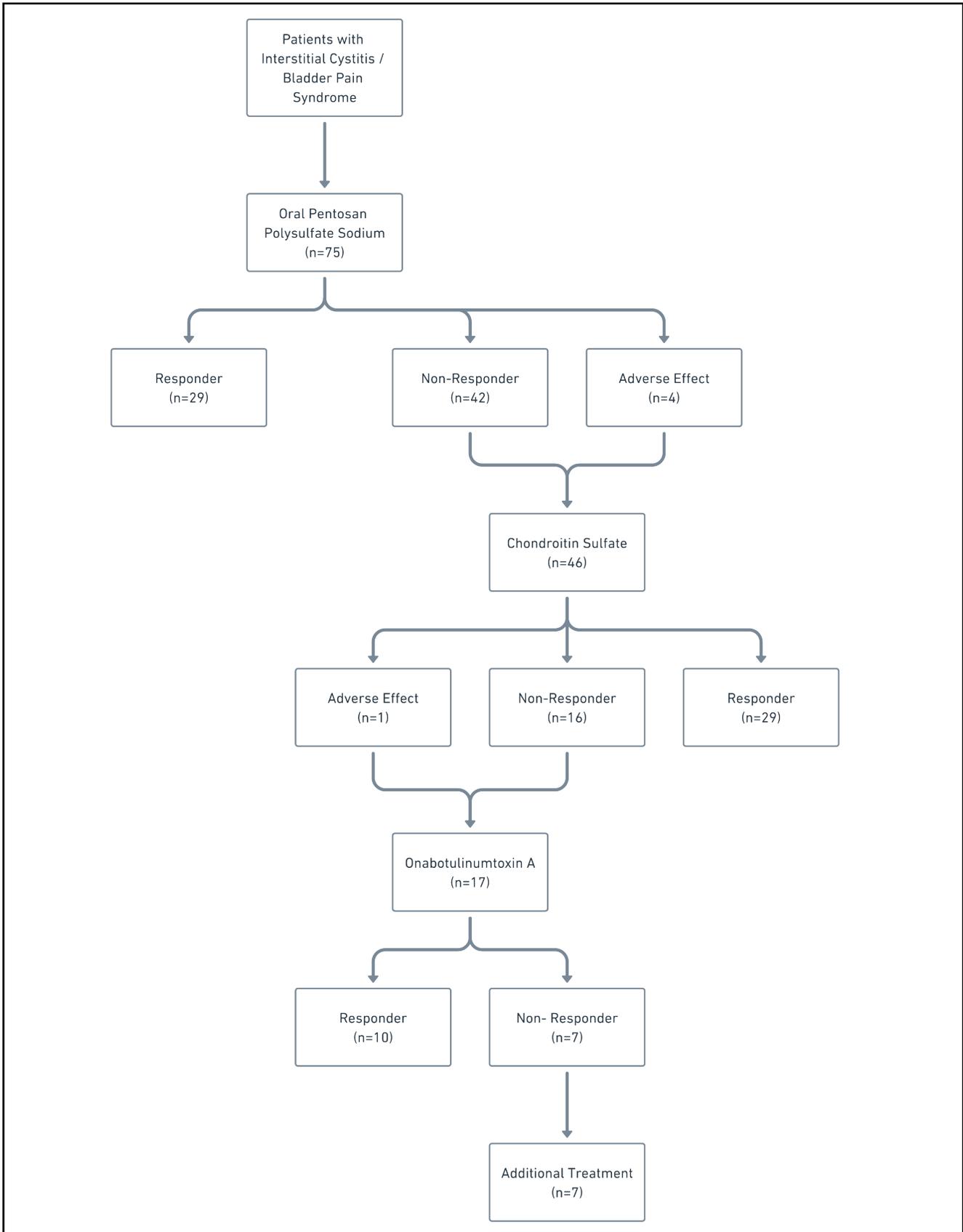


Figure 1. Flowchart of the study

effects associated with the PPS treatment are presented in Table 2 (Table 2). The median duration of PPS usage was six months (IQR: 3-15). Based on the PGI-C scales, 21 patients (28.0%) reported no change, 22 (29.3%) reported minimal improvement, 16 (21.3%) reported much improvement, and 16 (21.3%) reported very much improvement.

Table 1. Demographic data of patients

Number of patient	75
Age (year)*	51 (39-58)
Body mass index (kg/m²)*	27.5 (25.5-30.4)
Menopause	41 (54.7%)
Comorbidities	
Irritable bowel syndrome	7 (9.3%)
Rheumatic disease	6 (8%)
Fibromyalgia syndrome	10 (13.3%)
Allergic diseases	8 (10.7%)
Psychiatric diseases	19 (25.3%)
Diabetes Mellitus	4 (5.3%)
Hypertension	7 (9.3%)
Duration of follow-up (months)*	12 (12-16)

*: median (interquartile range)

A cohort of 46 patients underwent intravesical sodium chondroitin sulfate instillation. Of these, one patient (2.2%) discontinued treatment due to adverse events, while 16 patients (34.8%) ceased participation due to dissatisfaction. The median number of instillations administered was four, with an IQR of 4–10. Based on the PGI-C scales, 11 patients (23.9%) reported no change, six (13.0%) indicated minimal improvement, 16 (34.8%) experienced much improvement, and 13 (28.3%) reported very much improvement. The sole adverse effect documented was urinary tract infection (UTI) in one patient (2.2%) (Table 3).

Seventeen patients who did not respond to prior therapies received intravesical Onabotulinumtoxin A injections. According to the PGI-C scales, four patients (23.5%) exhibited no change, three (17.6%) reported minimal improvement, five (29.4%) experienced much improvement, and five (29.4%) reported very much improvement. Following the procedure, one patient (5.9%) experienced a urinary tract infection (Table 4). No cases of urinary retention were

reported among the patients. Of the seven patients who did not respond to intravesical Onabotulinum toxin A, four received acupuncture, two received PTNS, and one received intravesical ozone therapy.

Table 2. Oral pentosan polysulfate sodium treatment outcomes

Number of patient using PPS	75
Number of patients using PPS for at least 1 year	29 (38.7%)
Number of patients who discontinued PPS due to adverse effects	4 (5.3%)
Number of patients who discontinued PPS due to dissatisfaction	42 (56%)
Duration of PPS use (months)*	6 (3-15)
Patient Global Impression of Change score	
No change	21 (28%)
Minimally improved	22 (29.3%)
Much improved	16 (21.3%)
Very much improved	16 (21.3%)
Adverse effects	
Gastrointestinal symptoms	5 (6.6%)
Allergic reaction	4 (5.3%)
Headache	1 (1.3%)
Visual impairment	1 (1.3%)
Menstrual irregularity	1 (1.3%)

*: median (interquartile range), PPS: Pentosan polysulfate sodium

Table 3. Sodium chondroitin sulfate treatment outcomes

Number of patient	46
Number of patients who discontinued SCS due to adverse effects	1 (2.2%)
Number of patients who discontinued SCS due to dissatisfaction	16 (34.8%)
Number of SCS session*	4 (4-10)
Patient Global Impression of Change score	
No change	11 (23.9%)
Minimally improved	6 (13%)
Much improved	16 (34.8%)
Very much improved	13 (28.3%)
Adverse effects	
Urinary tract infection	1 (2.2%)

*: median (interquartile range), SCS: Sodium chondroitin sulfate

Table 4. Onabotulinum toxin A treatment outcomes

Number of patient	17
Patient Global Impression of Change score	
No change	4 (23.5%)
Minimally improved	3 (17.6%)
Much improved	5 (29.4%)
Very much improved	5 (29.4%)
Adverse effects	
Urinary tract infection	1 (5.9%)

A visual summary of patient-level responses to each treatment modality is presented in Figure 2 (Figure 2). This figure delineates the tiered escalation of therapy and the corresponding PGI-C responses in all 75 patients. Notably, numerous patients who did not benefit from the initial treatment subsequently responded to higher-tier therapies. The cumulative effectiveness of the stepwise approach was evident, with 89.3% of patients achieving at least minimal improvement at some point during the treatment pathway.

The overall improvement rate encompasses any degree of patient-reported enhancement, including minimal improvement, rather than solely clinically significant responses. Notably, several patients who did not derive substantial benefit from initial treatment steps exhibited clinically relevant improvement following the escalation to subsequent therapies. This observation underscores the cumulative and adaptive value of a stepwise treatment strategy in routine clinical practice.

DISCUSSION

This study provides real-world evidence on the effectiveness of a guideline-based, stepwise therapeutic approach for patients with non-Hunner IC/BPS who do not respond to lifestyle modifications. The treatment algorithm progressed from oral PPS to intravesical sodium chondroitin sulfate and, when necessary, to intravesical Onabotulinum toxin A. Our findings demonstrate that while some patients benefit from early-line therapies, a substantial proportion require escalation to subsequent treatment tiers to achieve meaningful symptom relief. A significant strength and innovative aspect of this study is its comprehensive, real-world portrayal of a longitudinal, stepwise treatment strategy for IC/BPS across multiple escalating modalities. While prior research has

predominantly concentrated on isolated interventions or controlled trial environments, few studies have systematically assessed patient-level responses throughout successive treatment stages in routine clinical practice. By examining outcomes within a homogeneous cohort of non-Hunner IC/BPS patients, our study offers pragmatic insights into the performance of guideline-recommended therapies when applied sequentially in daily urology practice.

While an overall improvement rate of 89.3% was observed, this result should be interpreted with caution, as it encompasses patients reporting only minimal improvement on the PGI-C scale. Notably, clinically significant symptom relief—characterized as “much” or “very much” improvement—was more frequently attained following escalation to intravesical therapies or Onabotulinum toxin A. This finding highlights that early treatment failure does not preclude subsequent benefit and supports the clinical rationale for a flexible, stepwise management strategy in IC/BPS.

Phenotypic heterogeneity is a critical factor in interpreting treatment outcomes in IC/BPS. Patients with Hunner’s lesions represent a distinct inflammatory subtype with different pathophysiology and therapeutic responses. These patients often benefit from lesion-directed interventions such as transurethral fulguration or resection [7–9]. To minimize heterogeneity and enhance interpretability, patients with Hunner lesions were intentionally excluded from the present study.

Oral pharmacological therapy is the primary medical intervention for patients with IC/BPS who do not respond to conservative treatment. Commonly used agents include amitriptyline, hydroxyzine, cimetidine, and PPS. PPS is the sole pharmacological agent approved by the Food and Drug Administration (FDA) for IC/BPS. It has been hypothesized to restore the bladder glycosaminoglycan (GAG) layer, thereby mitigating permeability and inflammation [9]. Nevertheless, response rates are generally modest, and concerns regarding long-term safety, including rare instances of retinal toxicity, have been raised [11,12]. In our cohort, only 38.7% of patients continued PPS therapy beyond one year, with most discontinuations attributable to insufficient symptom improvement rather than adverse effects.

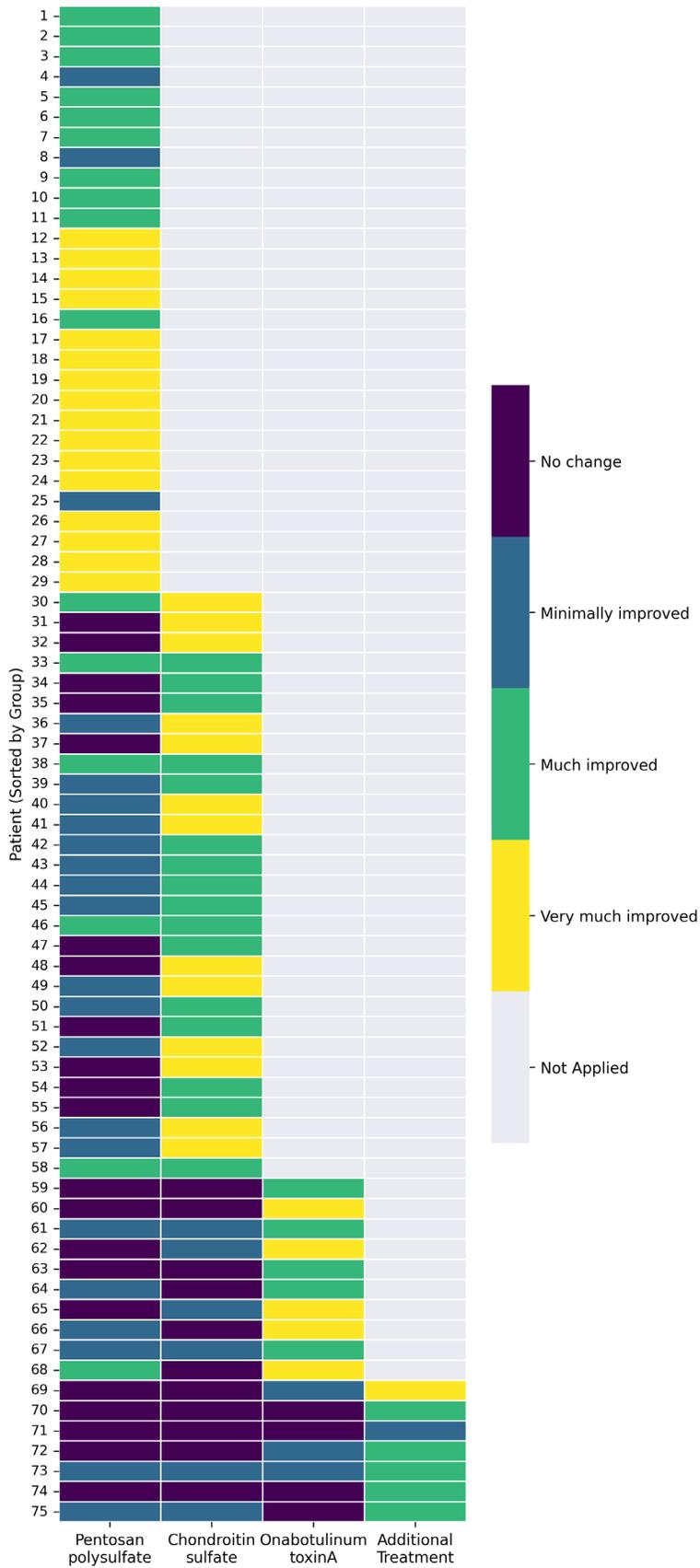


Figure 2. Patient-level responses to stepwise treatment modalities in interstitial cystitis/bladder pain syndrome

Intravesical therapies are pivotal in the management of IC/BPS, especially in patients who do not respond to oral medications. GAG replenishment using agents such as hyaluronic acid or chondroitin sulfate aims to restore urothelial integrity and reduce afferent nerve sensitization. Clinical studies have documented significant symptom relief and enhanced quality of life following repeated instillations [13,14]. In our study, the response was favorable, with 63.1% of patients reporting “much” or “very much” improvement on the PGI-C scale with excellent tolerability and minimal adverse events.

Onabotulinum toxin A represents an established third-line treatment option for refractory IC/BPS. Its therapeutic effects are attributed to inhibition of acetylcholine release and modulation of sensory afferent pathways, resulting in reduced pain and urgency. Reported response rates range from 50% to 70%, although benefits are often temporary and may require repeat injections [15,16]. In our cohort, 58.8% of patients experienced clinically meaningful improvement, with only one documented UTI and no cases of urinary retention.

For patients who remain refractory to conventional therapies, several experimental or adjunctive options have been explored. Less invasive modalities such as acupuncture, posterior tibial nerve stimulation (PTNS), and intravesical ozone therapy have shown preliminary efficacy in small studies [17–19]. These approaches may offer additional benefit in carefully selected patients, although robust evidence remains limited.

More invasive interventions, including sacral neuromodulation, augmentation cystoplasty, or cystectomy with urinary diversion, are reserved for the most refractory cases. Sacral neuromodulation has demonstrated success rates of approximately 50–60% in selected populations but requires permanent implantation and carries procedural risks [20]. Surgical reconstruction or diversion remains a last-resort option due to high morbidity and irreversible consequences, necessitating thorough patient counseling and individualized decision-making [21].

This study provides valuable insight into the application of guideline-based treatment algorithms in clinical practice. However, this study has several limitations. First, the retrospective design inherently introduces the risks of

selection bias and incomplete documentation. Second, the relatively small sample size of later treatment tiers limits the generalizability of the findings. Third, symptom burden and treatment outcomes were primarily assessed using the PGI-C scale, rather than validated disease-specific instruments, which constrain precision. The absence of validated quality-of-life measures limits the precision and comparability of outcome assessment. Finally, the absence of a control group precludes causal inference. Future prospective studies employing validated instruments and standardized treatment pathways are necessary to elucidate the optimal management strategies for IC/BPS.

CONCLUSIONS

This study illustrates that a guideline-based, stepwise treatment algorithm is a viable and effective method for managing patients with non-Hunner IC/BPS in real-world clinical settings. Although long-term symptom control with oral PPS was limited, a significant proportion of patients experienced clinically meaningful improvement following escalation to intravesical chondroitin sulfate or Onabotulinum toxin A. It is important to interpret overall improvement rates with caution, as meaningful symptom relief was frequently observed only after progressing to later treatment tiers. These findings underscore the necessity of individualized, flexible treatment pathways and support the continued use of stepwise management strategies, while highlighting the need for prospective studies employing validated outcome measures.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Informed Consent: Written informed consent was obtained from all participants prior to their inclusion in the study.

Ethical Approval: This prospective, randomized study was conducted in accordance with the principles outlined in the Declaration of Helsinki by the World Medical Association, titled “Ethical Principles for Medical Research Involving Human Subjects.”

The study protocol was approved by the Başakşehir Çam and Sakura City Hospital ethics committee (Approval Number: 05.03.2025.5.5.8333, Date: 2025-03-07).

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Supervision: HLC

Data Collection and/or Analysis: AIM, YCF

Analysis and/or Interpretation: AIM, YCF

Literature Search: MS, KT

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Critical Review: KT, YÇ

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Predictors of Success in Buccal Mucosal Graft Urethroplasty: The Impact of Stricture Length and Smoking on Surgical Outcomes – A Retrospective Observational Study

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Abstract

Objective: Buccal mucosa graft (BMG) urethroplasty is a well-established treatment option for complex anterior urethral strictures. However, factors affecting surgical outcomes remain under investigation. This study aimed to evaluate the impact of stricture length and smoking on surgical success following dorsolateral onlay BMG urethroplasty.

Materials and Methods: This retrospective observational study included 51 patients who underwent single-stage dorsolateral onlay BMG urethroplasty between 2021 and 2025. Patients with short strictures (<1.5 cm), urethral fistula or abscess, prior failed urethroplasty, or oral mucosal pathology were excluded. The primary outcome was surgical success, defined as the absence of obstructive symptoms and the need for further intervention. Statistical analysis included the Mann–Whitney U test, Fisher’s exact test, and logistic regression.

Results: The overall success rate was 74.5%. Patients in the success group had significantly shorter strictures compared to the failure group (median: 2.1 [2.0–2.8] cm vs. 5.0 [2.25–5.25] cm; $p=0.002$), and smoking prevalence was lower (21.1% vs. 69.2%; $p=0.005$). No significant differences were observed in age, comorbidities, stricture location, etiology, or preoperative Qmax. In the multivariate analysis, stricture length (OR: 0.461; 95% CI: 0.252–0.844; $p=0.012$) and smoking (OR: 5.572; 95% CI: 1.130–27.845; $p=0.035$) remained independent predictors of surgical failure.

Conclusions: Stricture length and smoking are independent risk factors for failure following dorsolateral BMG urethroplasty. These factors should be addressed during preoperative counseling.

Keywords: buccal mucosal graft, smoking, stricture length, urethral stricture, urethroplasty

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INTRODUCTION

Urethral stricture disease (USD) is a complex medical condition defined by the narrowing of the urethra, potentially leading to significant urinary complications. The etiology of urethral strictures is multifactorial and includes traumatic, inflammatory, iatrogenic, and idiopathic causes(1). USD typically develops through progressive epithelial injury and spongiofibrosis of the corpus spongiosum, which gradually reduces luminal caliber and contributes to persistent obstruction.

The treatment options for urethral stricture disease vary based on the stricture's characteristics, including its location and length. Initial management often includes urethral dilation, direct vision internal urethrotomy (DVIU), which are minimally invasive procedures aimed at widening the urethra and are commonly used for strictures. Dilation or DVIU may be used for short urethral strictures, but are not recommended when the stricture exceeds 2 cm (2). Moreover, these methods have high recurrence rates, reported between 30% and 90%, and this variation is influenced by factors such as the stricture's location, its length, and whether previous procedures had been performed (3–5). In addition, while these endoscopic approaches may offer short-term improvement, repeated interventions can lead to progressive fibrosis and diminish long-term success.

Urethroplasty is widely regarded as the preferred treatment for long, complicated, or recurrent strictures, providing a reconstructive approach that offers the most durable and effective outcomes in this patient group (6,7). Reported long-term outcomes for various urethroplasty techniques frequently reach the 90% range(8,9).

Reconstructive urethroplasty commonly involves grafts or flaps derived from buccal mucosa or penile skin to restore urethral continuity(10). The success rates of buccal mucosa graft (BMG) urethroplasty vary across studies; however, most series describe generally favorable long-term outcomes. In selected cohorts, BMG urethroplasty performed using different techniques has even been shown to achieve success rates approaching 100% (6,11).

Outcomes of BMG urethroplasty depend on multiple factors, including stricture length and location, surgical technique,

surgeon experience, and patient-related clinical factors (12). This study aimed to explore potential factors influencing the outcomes of BMG urethroplasty in cases of complex urethral strictures.

MATERIAL AND METHODS

Following ethical approval from the Hisar Hospital Intercontinental Local Ethics Committee (Approval No: 25-27, Date: 2025-02-28), a retrospective observational study was conducted using data from 60 patients who underwent single-stage dorsolateral onlay BMG urethroplasty for urethral stricture between January 2021 and January 2025. Short strictures (<1.5 cm) were excluded because such strictures are generally suitable for endoscopic management (13). Moreover, patients with complex strictures associated with fistula or abscess, prior oral surgery, oral mucosal abnormalities, limited mouth opening, or a history of failed urethroplasty were also excluded. Preoperative evaluations included demographic data, uroflowmetry (UFM), urethrography, cystourethroscopy, and assessment of stricture and oral mucosal characteristics. All procedures were performed only after confirmation of sterile urine cultures. All surgeries in this cohort were conducted by the same operating surgeon.

Surgical Technique

All procedures were carried out under general anesthesia via a midline perineal approach. To preserve vascular integrity, the bulbospongiosus muscle was meticulously dissected, and the urethra was mobilized unilaterally from the corpus cavernosum, extending slightly beyond the midline. Stricture length was measured intraoperatively after performing the longitudinal urethrotomy on the lateral aspect of the urethra. Following submucosal injection of lidocaine with adrenaline, the buccal graft was obtained from the inner cheek. Care was taken to protect Stensen's duct by preserving the surrounding mucosa. Donor sites were left open for healing. The graft was harvested approximately 2 cm longer than the measured stricture to compensate for an anticipated 10% contraction over time. The graft width ranged between 15 and 25 mm, aiming to achieve a final urethral lumen of at least 24 Fr. After excision, the graft was defatted until a creamy-white appearance. To prevent postoperative diverticula formation and postvoid dribbling, the graft was fixed to the urethral plate using a dorsolateral onlay approach with interrupted

4-0 absorbable polyglactin (Vicryl) sutures (Ethicon, Johnson & Johnson, USA). In the final step, the urethra was closed over a 16 Fr catheter using 4-0 Vicryl sutures.

Postoperative Follow-up

Patients were discharged on postoperative day 3 with antibiotics and oral antiseptics, and the urethral catheter was removed between postoperative days 21 and 28. Follow-up visits were scheduled at 6 weeks, 3 months, 6 months, and 12 months, and subsequently continued at six-month intervals. Primary screening for stricture recurrence was based on uroflowmetry and the Turkish-validated IPSS, while urethrography or cystourethroscopy was performed only in patients with obstructive symptoms or in those with a screening Qmax <15 mL/s(14). The primary outcome of the study was urethroplasty success, defined as the absence of obstructive symptoms and the absence of any need for additional interventions such as dilatation, cystourethroscopy, or internal urethrotomy.

Statistical Analysis

Descriptive statistics for continuous variables were expressed as mean \pm standard deviation or median (IQR), while categorical variables were summarized using frequencies and percentages. The distribution of data was assessed using the Shapiro-Wilk test. Comparisons between groups were performed with the Mann-Whitney U test for continuous variables and either the Chi-square or Fisher's exact test for categorical variables, when appropriate. Logistic regression was used to identify factors independently associated with surgical failure. Variables with a p-value < 0.2 in the univariate analysis were included in the multivariate logistic regression model. Results were presented as odds ratios (OR) along with 95% confidence intervals (CI), and a p-value < 0.05 was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Out of 60 patients initially selected, five were excluded based on predefined criteria, and data from four patients were not analyzed due to loss to follow-up (Fig. 1). Thus, 51 patients constituted the final study group.

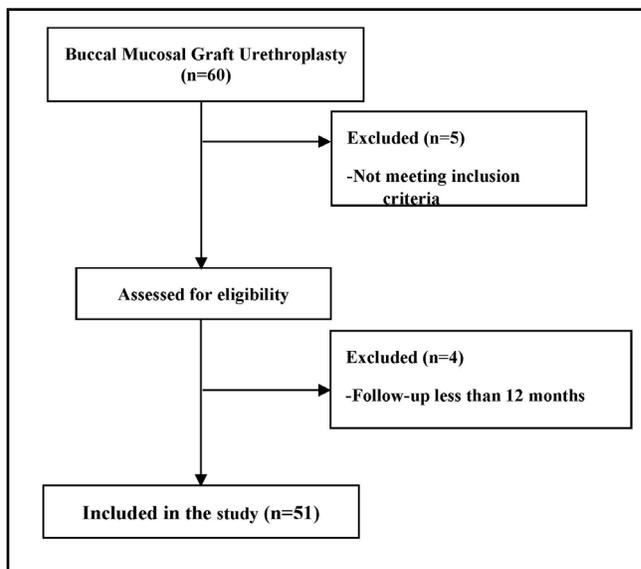


Figure 1. Patient selection and inclusion flowchart

Follow-up averaged 15.8 months (12–18 months). The median age was 50 years (IQR: 45–62 years). Comorbidities were present in 41.1% of patients, including hypertension (25.5%), diabetes mellitus (23.5%), and coronary artery disease (5.9%). Smoking was reported in 33.3% of patients. The median preoperative Qmax was 5.9 mL/s (IQR: 5.0–6.5 mL/s). Stricture location was most commonly in the bulbar urethra (70.6%), followed by bulbar+penile (21.6%) and penile (7.8%) segments. The leading etiological factors were trauma (39.2%), prior endourological interventions (29.4%), hypospadias surgery (9.8%), Fournier's gangrene (7.8%), gunshot injury (3.9%), lichen sclerosus (3.9%), urethral catheterization (3.9%), and previous urethritis (2.0%). The overall success rate of BMG urethroplasty was 74.5%, while failure was observed in 25.5% of patients. No surgical or buccal mucosa site complications were reported.

Patients were divided into two groups according to urethroplasty outcomes: successful (Group 1, n=38) and unsuccessful (Group 2, n=13). Stricture length was significantly shorter in the successful group compared to the unsuccessful group (2.1 [2.0–2.8] cm vs. 5.0 [2.25–5.25] cm, p=0.002). Smoking prevalence was also lower in Group 1 (21.1% vs. 69.2%, p=0.005). No statistically significant differences were found between the groups regarding age, comorbidities, stricture location, or preoperative Qmax (Table 1).

For additional analysis, stricture etiology was reclassified into three categories: iatrogenic, consisting of endourological interventions and urethral catheterization (n=17); traumatic, consisting of external trauma and gunshot injury (n=22); and other etiologies (n=12). Their distributions in the successful and unsuccessful groups were iatrogenic (14 vs. 3), traumatic (17 vs. 5), and other (7 vs. 5). Fisher's exact test demonstrated no significant association between these etiological categories and surgical outcome ($p = 0.28$).

Univariate and multivariate logistic regression analyses were performed to identify factors associated with urethroplasty success. In the univariate analysis, longer stricture length (OR: 0.403; 95% CI: 0.234–0.692; $p=0.001$) and smoking

(8.437; 95% CI: 2.055–34.649; $p=0.003$) were significantly associated with lower odds of surgical success. Diabetes mellitus also showed a borderline association (OR: 2.768; 95% CI: 0.692–11.069; $p=0.150$), while other variables, including age, hypertension, coronary artery disease, and preoperative Qmax, were not significantly associated with outcome.

In the multivariate model, both stricture length (OR: 0.461; 95% CI: 0.252–0.844; $p=0.012$) and smoking status (OR: 5.572; 95% CI: 1.130–27.845; $p=0.035$) remained independent predictors of urethroplasty success. Diabetes mellitus was not independently associated with the outcome (OR: 1.383; 95% CI: 0.204–9.361; $p=0.74$)(Table 2).

Table 1. Comparison of groups in terms of urethroplasty success

Parameters	Group 1 (n:38)	Group 2 (n:13)	p-value
Age, years, median (IQR)	50 (46 – 60.5)	50 (35.5 – 62.5)	0.393 ^a
Preoperative Qmax, mL/sec, median (IQR)	5.85 (4.975 – 6.525)	5.9 (5.05 – 6.35)	0.787 ^a
Stricture length, cm, median (IQR)	2.1 (2.0 – 2.8)	5.0 (2.25 – 5.25)	0.002 ^a
DM, (%)	8 (18.4)	5 (38.5)	0.141 ^b
HT, (%)	9 (23.6)	4 (30.8)	0.716 ^c
CAD, (%)	2 (5.3)	1 (7.7)	>0.99 ^c
Smoking, (%)	8 (21.1)	9 (69.2)	0.005 ^c
Stricture site, (%)			
Bulbar+Penile Urethra	8 (21)	3 (23.1)	
Penile urethra	1 (2.6)	3 (23.1)	
Bulbar urethra	29 (76.3)	7 (53.8)	0.087 ^c
Stricture etiology, (%)			
Endourological intervention	13 (34.2)	2 (15.4)	
Trauma	16 (42.1)	4 (30.8)	
Fournier's gangrene	2 (5.3)	2(15.4)	
Infection	1 (2.6)	0 (0)	
Hypospadias repair	2 (5.3)	3 (23.1)	
Gunshot injury	1 (2.6)	1 (7.7)	
Lichen sclerosus	2 (5.2)	0 (0)	
Urethral catheterization	1 (2.6)	1 (7.7)	0.203 ^c

IQR: Interquartile range, Group 1: Successful urethroplasty group, Group 2: Unsuccessful urethroplasty group, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease

^a Mann-Whitney U test, ^b Chi-square test, ^c Fisher's exact test

Table 2. Univariate and multivariate logistic regression analysis for predictors of urethroplasty success

	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age (years)	1.017	0.971 – 1.066	0.468			
DM	2.768	0.692 – 11.069	0.15	1.383	0.204 – 9.361	0.74
HT	1.432	0.355 – 5.779	0.614			
CAD	1.500	0.125-18.052	0.749			
Stricture length	0.403	0.234 – 0.692	0.001	0.461	0.252 – 0.844	0.012
Smoking	8.437	2.055 – 34.649	0.003	5.572	1.130 – 27.845	0.035
Preoperative Qmax	1.215	0.582 – 2.538	0.605			

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease. P-values were calculated using logistic regression analysis.

DISCUSSION

Urethral strictures are a common problem in urology and can lead to significant morbidity. Various techniques, including urethral dilation, DVIU, and surgical reconstruction, are used in the treatment of urethral strictures, with surgical reconstruction generally providing superior long-term outcomes. Although skin flaps, bladder mucosa, and penile and preputial flaps have been used in urethroplasties, oral mucosal grafts remain the most commonly utilized material (10). Oral mucosal grafts can be harvested more easily than penile flaps and have a lower risk of morbidity. Additionally, they possess a thick epithelium with a thin lamina propria and a dense panlaminal vascular plexus, which facilitates early inosculation. Chapple et al., in their systematic review, reported that the success rates of augmentation urethroplasty varied between 43% and 100%, depending on the surgical technique used(15). The observed success rate of 74.5% in this study is consistent with previously published data and further supports the effectiveness of buccal mucosal graft urethroplasty.

There are various techniques used for BMG urethroplasty. In our cohort, all patients underwent the dorsolateral onlay graft technique due to its low complication rates and high success rate. The dorsolateral onlay technique involves unilateral urethral dissection, preserving the contralateral vascular supply, bulbospongiosus muscle, and its innervation, while a perineal incision minimizes chordee risk and offers a cosmetic advantage(16). Kartal et al., in their study comparing the dorsal onlay graft and dorsolateral onlay graft techniques, reported success rates of 70.3% and 87.1%,

respectively. Furthermore, they noted lower complication rates with the dorsolateral onlay graft technique(11).

Although BMG urethroplasty generally yields high success rates, several factors may contribute to recurrence, including stricture location and length, etiology, whether the procedure is primary or a revision, and the patient’s overall health status(17). Among these, stricture length is the most frequently emphasized factor in the literature. Shalkamy et al. identified stricture length greater than 4.5 cm as a predictor of urethroplasty failure(18). Consistently, Kay et al. reported that strictures longer than 5 cm were associated with a significantly increased risk of recurrence (19). Our findings indicated that patients in the failure group had longer strictures than those in the successful group, in line with previous studies. Moreover, both univariate and multivariate analyses confirmed stricture length as an independent risk factor for recurrence following urethroplasty.

In this study, the recurrence rate was significantly higher among smokers compared to non-smokers. Both univariate and multivariate analyses identified smoking as an independent risk factor for BMG urethroplasty failure. This may be attributed to the adverse vascular effects of smoking, as well as the harmful impact of tobacco smoke on oral mucosal integrity and graft viability. Chronic tobacco exposure contributes to vascular and immune dysfunction in the oral mucosa by increasing prostaglandin synthesis and the number of Langerhans cells(20). A review on smoking in urologic reconstructive surgery suggested that smoking and poor oral hygiene may negatively affect surgical

outcomes. It emphasized the importance of encouraging patients to quit tobacco use preoperatively(21). Furthermore, the urethroplasty failure prediction model developed by Barbagli et al. highlighted smoking, graft usage, and instrumentation-related strictures as significant predictors of long-term treatment failure(22).

In line with our findings, a recent systematic review and meta-analysis by Ma et al. also reported that smoking may increase the risk of stricture recurrence following urethroplasty(23). However, that study included a wide range of surgical techniques, graft types, and etiologies, with substantial methodological heterogeneity. Moreover, subgroup analysis specific to buccal mucosa graft urethroplasty was not performed, despite the potential impact of smoking on oral mucosal graft viability. In contrast, our study focused exclusively on patients undergoing single-stage dorsolateral onlay BMG urethroplasty performed by a single surgeon, providing a more homogeneous surgical cohort and controlled setting for evaluating risk factors.

On the other hand, Baradaran et al., in a multi-institutional study evaluating recurrence following anterior urethroplasty, reported that smoking was not a significant factor associated with urethroplasty failure(24). However, in this study, buccal mucosa graft urethroplasties accounted for less than 10% of the cohort, which may explain the discrepancy between their results and those observed in our study.

This study has several limitations that should be acknowledged. First, the sample size was relatively small, which may limit the statistical power to detect associations, particularly for variables with subtle effects. In addition, the etiological distribution observed in our cohort likely reflects the referral pattern of our tertiary center and may differ from large population-based series. However, all surgeries were performed by a single experienced surgeon using a standardized dorsolateral onlay technique, providing a homogeneous cohort that reduces inter-operator variability and enhances internal validity.

Second, although the follow-up duration was extended to an average of 15.8 months, longer-term data would be necessary to evaluate late recurrences and assess the durability of surgical success. Nevertheless, the majority of recurrences

in urethroplasty tend to occur within the first postoperative year, and the follow-up duration in our study exceeds the minimum threshold used in many previously published series(2).

Third, the retrospective nature of the study may introduce potential selection bias and limit the granularity of some clinical variables such as smoking intensity, duration, and cessation timing. Future prospective studies incorporating detailed tobacco exposure history and objective oral mucosa assessments could provide further insights into the mechanism by which smoking influences graft-related outcomes.

Lastly, although our findings align with previous reports, the exclusive inclusion of patients undergoing BMG urethroplasty may limit the generalizability of the results. Nonetheless, this focused approach enhances the internal consistency of the study.

CONCLUSION

This study points out that buccal mucosa graft urethroplasty using the dorsolateral onlay technique is an effective and reliable surgical approach for the treatment of complex anterior urethral strictures. Stricture length and smoking status were identified as independent predictors of surgical failure. These findings highlight the importance of thorough preoperative assessment, particularly in patients with long-segment strictures and a history of tobacco use. These factors should be considered when counseling patients prior to surgery. Further prospective studies with larger cohorts and longer follow-up are warranted to validate these results and refine patient selection criteria.

Conflict of Interest: The authors declare no conflicts of interest.

Consent for Publication : As this study does not involve identifiable images or personal/clinical details that could compromise participant anonymity, the “Consent for Publication” is not applicable.

Funding: No financial support was received for this study.

Ethics Approval: This study was conducted in accordance

with the Declaration of Helsinki. It received approval from the Ethics Committee of Hisar Hospital Intercontinental (Decision Number: 25-27, Decision date: February 28, 2025). Informed consent to participate was obtained from all participants.

Author Contributions: • Concept and Design: CTG, NCC • Supervision: NCC, BÇ, MBCB • Data Collection and/or Analysis: CTG, BÇ, AE • Analysis and/or Interpretation: CTG, BÇ, • Literature Search: NCC, AE • Writing: CTG, NCC • Critical Review: BÇ, MBCB

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Testosterone Deficiency Does Not Predict Penile Curvature or Plaque Size in Men with Peyronie's Disease

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Abstract

Objective: To investigate the association between serum testosterone levels and the severity of penile curvature and plaque size in men with Peyronie's disease (PD).

Materials and Methods: This retrospective cross-sectional study included 108 men diagnosed with Peyronie's disease who presented to our urology outpatient clinic between January 2022 and July 2025. Patients with prior testosterone replacement therapy, pelvic surgery, intralesional treatment, or systemic conditions affecting testosterone metabolism were excluded. Demographic and clinical data—including disease duration, penile pain, erectile dysfunction (assessed by IIEF-5), and disease phase—were recorded. Penile curvature was assessed via self-photographs during natural or pharmacologically induced erections, and plaque size was measured ultrasonographically. Fasting morning serum samples were analyzed for total testosterone (TT), free testosterone (FT), sex hormone-binding globulin (SHBG), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol, and metabolic parameters.

Results: Mean age was 59.6 ± 7.5 years, and mean disease duration was 22.7 ± 29.4 months. Mean horizontal and vertical curvatures were $12.1 \pm 19^\circ$ and $28.5 \pm 19.8^\circ$, respectively. Mean plaque size was 8.9 ± 7 mm. No significant differences were observed between hypogonadal and eugonadal groups in curvature severity ($p > 0.05$), plaque size ($p = 0.54$), or disease phase. Hypogonadal men had significantly lower SHBG and estradiol levels and higher HbA1c and triglyceride values (all $p < 0.05$). No correlations were found between testosterone levels and curvature degree or plaque dimensions.

Conclusion: Serum testosterone levels are not associated with PD severity. Hypogonadism appears to be a comorbidity rather than a determinant of disease severity, suggesting routine testosterone evaluation may not be necessary in PD management.

Keywords: Peyronie's disease, penile curvature, penile plaque, testosterone levels

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INTRODUCTION

Peyronie's disease (PD) is a connective tissue disorder characterized by the presence of a fibrous inelastic scar involving the tunica albuginea of the penis, which can cause penile curvature, pain, palpable plaque, and erectile dysfunction (1). Reported prevalence varies widely, from well below 1% to over 20%, depending on population and methodology, but most series agree that PD predominantly affects middle-aged and older men, typically between the fifth and sixth decades of life (2-5). Beyond the physical deformity, PD can substantially impair sexual function and intimate relationships, is associated with considerable psychological distress, and negatively affects overall quality of life (5). Although its precise etiology remains uncertain, repeated microvascular trauma during intercourse, followed by abnormal wound healing and excessive collagen deposition, is believed to play a central role (6).

In recent years, attention has turned to possible hormonal influences on the development and severity of PD, particularly testosterone. Androgens affect connective tissue metabolism, endothelial function, and nitric oxide activity, all of which contribute to wound healing and fibrosis regulation (7-9). Some reports have found lower serum testosterone levels among men with PD and suggested an association with greater curvature or plaque burden (7,10), whereas other studies found no significant correlation (9,11,12). The inconsistent evidence leaves unclear whether hypogonadism contributes to PD pathogenesis or merely coexists due to shared risk factors such as age and metabolic comorbidities. This study aimed to determine whether serum testosterone levels are associated with plaque size or the severity of penile curvature in patients with Peyronie's disease.

MATERIALS AND METHODS

Study Design and Population

In this retrospective cross-sectional study, a total of 108 men diagnosed with Peyronie's disease (PD) who presented to our urology outpatient clinic between January 2022 and July 2025 and fulfilled the study inclusion criteria were included. The study was approved by the Scientific Research Ethics Committee of Antalya Training and Research Hospital on 2025-05-08 (Approval number: 2025-172-8/17). Full compliance with the Declaration of Helsinki was ensured, and informed consent was obtained from all patients enrolled

in the study. Additionally, all patient data were anonymized, and no personally identifiable information was disclosed. The diagnosis of PD was based on the presence of palpable penile plaques and/or penile deformity confirmed by ultrasonography, physical examination, and clinical history. Patients with a history of pelvic surgery, ongoing testosterone replacement therapy, recent testosterone replacement therapy within the past year, previous intralesional therapy, or systemic conditions known to interfere with testosterone metabolism (such as pituitary or testicular disorders, chronic corticosteroid use, or androgen therapy) were excluded from the study.

Clinical Evaluation

Demographic and clinical characteristics were recorded for all participants, including age, medical comorbidities (hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease), smoking status, and medication history. Disease-specific parameters such as disease duration, presence of penile pain, erectile dysfunction (ED), penile trauma history, and disease phase (active or chronic) were documented. Erectile function was evaluated using the International Index of Erectile Function-5 questionnaire (IIEF-5). The onset of PD was determined by the first instance of pain at erection or the initial finding of a penile plaque or deformity. The direction and degree of penile curvature were assessed from two-axis self-photographs obtained during either natural erection or artificial erection induced by intracavernosal injection of vasoactive agents. The maximal degree of curvature was measured using a goniometer placed at the point of maximal angulation. Both horizontal (lateral) and vertical (dorsal or ventral) curvature angles were recorded. Penile length was measured on stretch from the pubic bone to the tip of the glans. Plaque size was determined by penile ultrasonography. Disease phase was categorized as active (presence of pain and/or deformity progression within the last 3 months) or stable/chronic (\geq 6-12 months after onset of PD or once the deformity has remained stable and painless for \geq 3 months) (13).

Laboratory Evaluation

Fasting morning venous blood samples were drawn between 07:00 and 11:00 am after overnight fasting. Laboratory assessments included total testosterone (TT), free testosterone (FT), sex hormone-binding globulin (SHBG),

luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol (E2), prolactin, and basic metabolic and lipid parameters (hemoglobin, HbA1c, total cholesterol, LDL, HDL, triglycerides). Complete blood count analyses were performed on a Sysmex XN-1000 hematology analyzer (Sysmex Corp., Kobe, Japan). Biochemical parameter analyses were conducted using an enzymatic colorimetric method on an AU5800 analyzer (Beckman Coulter, Florida, USA). Follicle-stimulating hormone (FSH), luteinizing hormone (LH), and total testosterone were measured using a chemiluminescent immunoassay (CLIA) on a UniCel DxI 800 Access immunoassay system (Beckman Coulter, Florida, USA). Free testosterone was measured by a chemiluminescent immunoassay (CLIA) on the Snibe Maglumi X3 immunoassay system (Snibe Company, Shenzhen, China).

In this study, hypogonadism was defined as total testosterone (TT) < 12 nmol/L (\approx 3.5 ng/mL), according to current EAU guidelines (14,15).

Statistical Analysis

Statistical analyses were performed using a commercially available software (SPSS version 25.0, Chicago, IL). The Shapiro-Wilk test was used to determine whether the distribution of continuous variables was normal. The continuous data were presented as mean \pm standard deviation (SD). The data that were not normally distributed were given as median and interquartile range, and the Mann-Whitney U test was used to compare. In addition to frequency and percentage distributions of the data, the Student t test was used in group comparisons, and the chi-square test was used for variables between categorical data. $P < 0.05$ was considered to be statistically significant.

RESULTS

A total of 108 men diagnosed with Peyronie’s disease were included in the study. The mean age was 59.6 ± 7.5 years, and the mean disease duration was 22.7 ± 29.4 months. The mean IIEF-5 score was 16.1 ± 4.6 . Horizontal and vertical curvature degrees were $12.1 \pm 19^\circ$ and $28.5 \pm 19.8^\circ$, respectively. Mean plaque size, as measured by ultrasonography, was 8.9 ± 7 mm. The mean total testosterone level was 3.88 ± 1.16 ng/mL, and 38.9% ($n=42$) of the patients were classified as hypogonadal based on EAU guidelines (TT < 12 nmol/L or \approx 3.5 ng/mL) (14,15). Demographic, clinical, and laboratory data of the

study population are summarized in Tables 1 and 2. In 91 patients, penile curvature was uniplanar, whereas 14 patients had multiplanar curvature. In 3 patients, no curvature was observed; however, these individuals presented with hourglass or notching deformities only.

Table 1. Disease-specific and hematological, biochemical, hormonal parameters of the study group

Parameters	Mean \pm SD (min-max)
Age (years)	59.62 \pm 7.5 (39-74)
Disease duration (months)	22.66 \pm 29.4 (2-120)
ED duration (months)	14.35 \pm 18.3(0-120)
IIEF-5 score	16.09 \pm 4.6 (6-24)
Horizontal curvature degree (Right/Left)	12.13 \pm 19 (0-60)
Vertical curvature degree (Dorsal/Ventral)	28.52 \pm 19.8 (0-75)
Penile length (cm)	13.105 \pm 0.9 (11-18)
Plaque size on USG (mm)	8.93 \pm 7 (2-30)
Hemoglobin (g/dL)	14.705 \pm 1.42 (10.8-18.7)
HbA1C (%)	6.169 \pm 1.33 (4.5-13.6)
Neutrophil count (/ μ L)	4603.33 \pm 1650.64 (2120-10410)
Lymphocyte count (/ μ L)	2521.30 \pm 833.94 (890-4990)
Platelet count (/ μ L)	253268.52 \pm 65119.1 (125000-432000)
NLR	1.98 \pm .87 (0.62-4.78)
PLR	108.39 \pm 38.15 (35.07-216.44)
FSH (U/L)	7.52 \pm 5.74 (1.96-40.89)
LH (U/L)	5.11 \pm 2.49 (1.60-15.18)
Prolactin (μ g/L)	8.9671 \pm 7.64 (0.23-55.65)
SHBG (nmol/L)	40.237 \pm 15.77 (0.94-82.1)
Estradiol (ng/L)	28.95 \pm 8.06 (15-60)
Total testosterone (ng/mL)	3.88 \pm 1.16 (1.93-7.78)
Free testosterone (pg/mL)	9.31 \pm 4.71 (3.36-25.40)
Total cholesterol (mg/dL)	200.94 \pm 39.73 (117-362)
Triglyceride (mg/dL)	166.19 \pm 99.48 (37-583)
LDL (mg/dL)	124.41 \pm 43.04 (51-400)
HDL (mg/dL)	48.42 \pm 10.02 (35-85)
Albumin (g/L)	43.630 \pm 2.9 (33.7-51.7)

Values are mean \pm SD, Abbreviations: ED, erectile dysfunction; IIEF-5, International Index of Erectile Function; USG, ultrasonography; HbA1c, hemoglobin A1c; NLR, Neutrophil to Lymphocyte ratio; PLR, Platelet to Lymphocyte ratio; FSH, follicle-stimulating hormone; LH, luteinizing hormone; SHBG, sex hormone binding globulin; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

When comparing hypogonadal (n=42) and eugonadal (n=66) patients, there were no significant differences in age, disease duration, erectile function scores, severity of curvature (horizontal: $13.6 \pm 18.9^\circ$ vs $11.2 \pm 19.1^\circ$, $p=0.53$; vertical: $29.4 \pm 19.0^\circ$ vs $27.9 \pm 20.4^\circ$, $p=0.71$), or plaque size (8.4 ± 5.8 mm vs 9.3 ± 7.7 mm, $p=0.54$). Hypogonadal men showed significantly lower SHBG (32.27 ± 12.59 vs 45.30 ± 15.58 nmol/L, $p<0.001$) and estradiol levels (25.81 ± 6.55 vs 30.95 ± 8.33 pg/mL, $p<0.001$), and higher HbA1c (6.1 [1] vs 5.7 [0.7] %, $p=0.001$) and triglyceride values (168 [72] vs 140 [97] mg/dL, $p=0.008$) than eugonadal men. Detailed comparative data are presented in Table 3.

There were no significant differences between hypogonadal and eugonadal groups with respect to the prevalence of hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, smoking status, distribution of active versus chronic disease phase, presence of penile pain, or rate of calcified plaques. Detailed comparisons of these clinical characteristics between the two groups are presented in Table 4.

No significant correlations were found between total or free testosterone levels and either the degree of penile curvature or plaque size (all $p>0.05$).

DISCUSSION

Peyronie's disease is a benign acquired fibrotic condition of the tunica albuginea that leads to penile curvature, pain, palpable plaque, and erectile dysfunction, with prevalence increasing with age (1,2,5). Overall, penile deformity represents the most common initial symptom of Peyronie's disease, occurring in 52–94% of patients. Penile pain is the second most frequent symptom, reported by approximately 20–70% of patients during the early phase of the disease (16). Consistent with the literature, penile deformity was the most common initial

symptom in our study (65.7%), followed by pain (20.4%) and erectile dysfunction (13.9%) as the second and third most frequent presenting symptoms, respectively. Kadioglu et al., in a population-based study, reported dorsal and lateral curvatures as the most common deformities, with dorsal curvature observed in 45.6% and lateral curvature in 29.3% of patients (17). Similarly, Moreno and Morgentaler found that the primary direction of curvature was dorsal in 66.9% of cases, followed by ventral in 12.4% and lateral in 8.3% (7). In line with these findings, the most frequent curvature pattern in our cohort was also dorsal curvature, which was identified in 56.5% of patients. (Table 2).

Table 2. Comorbidities and general characteristics of Peyronie's population sample

Characteristics	n (%)
Hypertension	32 (29.6)
Diabetes	35 (32.4)
Coronary artery disease	17 (15.7)
COPD	7 (6.5)
Antiplatelet use	23 (21.3)
Active smoking	43 (39.8)
PDE-5 inhibitor use	47 (43.5)
Disease phase (Active/Chronic)	28(25.9) / 80(74.1)
Penile pain	25 (23.1)
History of penile trauma	8 (7.4)
Horizontal curvature (Right/Left)	7(6.5) / 28(25.9)
Vertical curvature (Dorsal/Ventral)	61(56.5) / 23(21.3)
Curvature interfering with intercourse	41 (38)
Concomitant LUTS	25 (23.1)
Initial symptom (Pain/Deformity/ED)	22(20.4) / 71(65.7) / 15(13.9)
Notching/ Hourglass deformity	20 (18.5)
Calcified plaque	44 (40.7)
Hypogonadism	42 (38.9)

Abbreviations: COPD, Chronic obstructive pulmonary disease; PDE-5 inh, Phosphodiesterase type 5 inhibitor; LUTS, Lower urinary tract symptoms; ED, Erectile dysfunction.

Table 3. Comparison between hypogonadal and eugonadal patients according to Disease-specific and Hematological, biochemical, hormonal parameters

Parameters	Hypogonadal (n=42)	Eugonadal (n=66)	p
Normally distributed variables (mean ± SD)			
Age (years)	59.86 ± 6.0	59.47 ± 8.3	0.795
IIEF-5 score	16.12 ± 4.7	16.08 ± 4.6	0.962
Horizontal curvature degree (Right/Left)	13.57 ± 18.9	11.21 ± 19.1	0.532
Vertical curvature degree (Dorsal/Ventral)	29.40 ± 19.0	27.95 ± 20.4	0.712
Plaque size on USG (mm)	8.40 ± 5.8	9.26 ± 7.7	0.541
Hemoglobin (g/dL)	14.60 ± 1.7	14.76 ± 1.2	0.572
Neutrophil count (/μL)	4978.33 ± 1652.36	4364.70 ± 1616.86	0.059
Lymphocyte count (/μL)	2529.29 ± 802.78	2516.21 ± 859.21	0.937
NLR	2.14 ± 0.92	1.87 ± 0.82	0.115
PLR	108.16 ± 34.26	108.54 ± 40.69	0.959
SHBG (nmol/L)	32.27 ± 12.59	45.30 ± 15.58	<0.001
Estradiol (ng/L)	25.81 ± 6.55	30.95 ± 8.33	<0.001
Total testosterone (ng/mL)	2.81 ± 0.40	4.56 ± 0.96	<0.001
Free testosterone (pg/mL)	6.82 ± 3.63	10.89 ± 4.66	<0.001
Total cholesterol (mg/dL)	204.62 ± 30.67	198.61 ± 44.62	0.445
Albumin (g/L)	43.73 ± 3.04	43.56 ± 2.83	0.768
Non-normally distributed variables (median [IQR])			
Disease duration (months)	12 [18]	12 [11]	0.207
ED duration (months)	12 [16]	12 [15]	0.801
Penile length (cm)	13 [1]	13 [0.5]	0.054
HbA1C (%)	6.1 [1]	5.7 [0.7]	0.001
Platelet count (/μL)	247500 [88250]	249000 [100500]	0.816
FSH (U/L)	6.52 [4.72]	6.3 [3.9]	0.733
LH (U/L)	4.5 [1.92]	4.5 [3.1]	0.398
Prolactin (μg/L)	7.3 [5.4]	7.8 [6]	0.712
Triglyceride (mg/dL)	168 [72]	140 [97]	0.008
LDL (mg/dL)	128.5 [42]	116 [51]	0.298
HDL (mg/dL)	46 [11]	47 [13]	0.661

Data are presented as mean ± SD for normally distributed variables and as median [IQR] for non-normally distributed variables. Normality was assessed using the Shapiro–Wilk test. Abbreviations: IQR, interquartile range; ED, erectile dysfunction; IIEF-5, International Index of Erectile Function; USG, ultrasonography; HbA1c, hemoglobin A1c; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; FSH, follicle-stimulating hormone; LH, luteinizing hormone; SHBG, sex hormone-binding globulin; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Table 4. Comparison between hypogonadal and eugonadal patients according to comorbidities and general characteristics of PD

Characteristics	Hypogonadal (n=42)	Eugonadal (n=66)	p
Hypertension	14 (33.3%)	18 (27.3%)	0.523
Diabetes	17 (40.5%)	18 (27.3%)	0.206
Coronary artery disease	6 (14.3%)	11 (16.7%)	0.793
COPD	4 (9.5%)	3 (4.5%)	0.427
Antiplatelet use	11 (26.2%)	12 (18.2%)	0.344
Active smoking	16 (38.1%)	27 (40.9%)	0.842
PDE-5 inhibitor use	17 (40.5%)	30 (45.5%)	0.692
Disease phase (Active/Chronic)	7 (16.7%) / 35 (83.3%)	21 (31.8%) / 45 (68.2%)	0.114
Penile pain	7 (16.7%)	18 (27.3%)	0.247
History of penile trauma	2 (4.8%)	6 (9.1%)	0.479
Horizontal curvature (Right/Left)	3 (7.1%) / 12 (28.6%)	4 (6.1%) / 16 (24.2%)	0.842
Vertical curvature (Dorsal/Ventral)	25 (59.5%) / 8 (19)	36 (54.5%) / 15 (22.7%)	0.863
Curvature interfering with intercourse	16 (38.1%)	25 (37.9%)	0.982
Concomitant LUTS	13 (31%)	12 (18.2%)	0.161
Initial symptom (Pain/Deformity/ED)	7 (16.7%) / 31 (73.8%) / 4 (9.5%)	15 (22.7%) / 40 (60.6%) / 11 (16.7%)	0.352
Notching/ Hourglass deformity	9 (21.4%)	11 (16.7%)	0.353
Calcified plaque	18 (42.9%)	26 (39.4%)	0.437

Abbreviations: COPD, Chronic obstructive pulmonary disease; PDE-5 inh, Phosphodiesterase type 5 inhibitor; LUTS, Lower urinary tract symptoms; ED, Erectile dysfunction.

It is widely recognized that PD plaque development may originate from penile trauma or repeated microvascular injury during erection (6,18), leading to an imbalance between profibrotic and antifibrotic pathways. This dysregulation—particularly involving transforming growth factor- β 1 (TGF- β 1)—promotes excessive collagen deposition and subsequent plaque formation (19); however, the pathogenesis of PD is likely multifactorial, involving an interplay among genetic predisposition, mechanical injury, local inflammatory processes, and dysregulated wound healing (13). Clinical studies have identified several comorbid conditions that cluster with PD, including diabetes mellitus, hypertension, dyslipidemia, hypogonadism, smoking, Dupuytren's contracture, and other systemic fibrotic or autoimmune disorders, suggesting that local penile pathology develops on a background of systemic vascular and connective tissue susceptibility (8,20,21).

The relationship between testosterone and PD has attracted particular interest over the past decade. Androgens are known to influence tissue repair and collagen metabolism, with experimental and clinical data linking androgen deficiency to impaired wound healing and increased fibrosis (22,23). These findings support a theoretical basis for the hypothesis that low testosterone may predispose to fibrotic tissue remodeling and PD development. Moreover, testosterone deficiency may contribute indirectly to PD via diminished erectile rigidity, thereby increasing susceptibility to repetitive penile trauma during sexual activity (24). Additionally, androgens have been shown to positively regulate nitric oxide (a potent anti-fibrotic mediator), which further supports the protective role of testosterone against fibrotic processes (25).

However, the clinical evidence regarding the association between testosterone levels and PD has been conflicting. Moreno and Morgentaler reported that 74% of men with

PD had low testosterone (defined by either total or free testosterone), with a significant correlation between low free testosterone and penile curvature severity (54.3° vs. 37.1° , $p = 0.006$) (7). Similarly, Nam et al. found that patients with testosterone deficiency had a significantly greater mean degree of penile curvature than those with normal testosterone levels ($32.0 \pm 16.9^\circ$ vs. $21.8 \pm 15.4^\circ$, $p = 0.033$), and a higher prevalence of moderate to severe curvature (40% vs. 23.7%, $p = 0.015$), proposing mechanisms such as reduced nitric oxide activity and upregulated TGF- β 1 expression in hypogonadal states (26). Cavallini et al. reported that PD patients had lower bioavailable testosterone compared to controls, with larger plaque size in hypogonadal men, while penile curvature did not differ significantly. They also reported improved treatment outcomes with combined testosterone replacement and intralesional verapamil (8).

In contrast, more recent studies have largely failed to confirm these associations, aligning closely with our findings. Kirby et al. found no difference in curvature severity between hypogonadal and eugonadal PD patients (35.4° vs. 34.0° , $p = 0.70$) and comparable testosterone levels between men with PD and age-matched men with isolated erectile dysfunction (328 vs. 332 ng/dL, $p = 0.98$), suggesting that low testosterone may represent a common feature of sexual dysfunction rather than a PD-specific phenomenon (11). Mulhall et al., in a rigorous analysis of 184 men with PD undergoing intracavernosal injection-induced erections, found no association between total or free testosterone levels and the magnitude of penile deformity ($r = -0.01$, $p = 0.95$) (12). Similarly, Candela et al. analyzed 149 men with chronic-phase PD and observed no correlation between testosterone levels and penile curvature across testosterone quartiles ($p = 0.31$), with only disease duration independently predicting deformity severity (9). Can et al. also found no significant association between testosterone and plaque dimensions or curvature degree in 147 PD patients, despite lower mean testosterone levels compared to controls (3.9 ± 1.1 vs. 4.2 ± 1.7 ng/mL, $p = 0.062$) (27). In a recent study, Schneider et al. evaluated the impact of testosterone on collagenase clostridium histolyticum (CCH) treatment outcomes in 36 men with PD and found that neither baseline testosterone levels nor hypogonadal status (<300 ng/dL) predicted treatment response, with no significant difference in curvature improvement between hypogonadal and eugonadal groups ($p = 0.41$) (28). Our study, consistent

with these studies, reinforces the prevailing evidence that serum testosterone levels are not associated with objective measures of PD severity. In our cohort of 108 men, 38.9% were classified as hypogonadal according to EAU guidelines (total testosterone <12 nmol/L or approximately 3.5 ng/mL). Despite this substantial prevalence of low testosterone, we observed no significant differences between hypogonadal and eugonadal groups in horizontal curvature (13.6° vs. 11.2° , $p = 0.53$), vertical curvature (29.4° vs. 27.9° , $p = 0.71$), plaque size (8.4 mm vs. 9.3 mm, $p = 0.54$), or disease phase distribution. Furthermore, correlation analysis revealed no association between total or free testosterone levels and either the degree of penile curvature or plaque dimensions, suggesting that hormonal status does not influence the anatomical manifestations of PD.

In the literature, several studies have investigated comorbidities associated with PD (17,29), including hyperlipidemia as a potential risk factor, though findings remain inconsistent. While Rhoden et al. found no correlation between serum lipid profiles and PD, Can et al. reported significantly elevated LDL levels in PD patients (27,30). In our study, no significant differences were observed between eugonadal and hypogonadal groups regarding hypertension, diabetes, coronary artery disease, or COPD. However, hypogonadal men exhibited significantly lower SHBG and estradiol levels, along with higher HbA1c and triglyceride values. These findings suggest that hypogonadism may be associated with a distinct metabolic profile characterized by impaired glucose regulation and dyslipidemia, potentially contributing to PD pathophysiology through altered tissue repair and increased fibrotic remodeling (29).

Our study has several limitations. First, the retrospective design may have introduced selection bias. Second, the absence of a healthy control group and comparisons exclusively between PD subgroups may limit the generalizability of our findings. Third, plaque measurements by multiple radiologists may have introduced inter-observer variability, potentially affecting the consistency of radiological assessments.

CONCLUSION

In conclusion, our findings suggest that serum testosterone levels are not associated with the severity of penile curvature or plaque dimensions in men with Peyronie's disease.

Hypogonadism appears to represent a comorbid condition rather than a determinant factor in disease severity. These results have important clinical implications, as they suggest that testosterone evaluation and supplementation may not be necessary as part of routine PD management unless indicated for other reasons. Further prospective, controlled studies are warranted to definitively clarify the relationship between testosterone and PD pathophysiology.

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Informed Consent: All patients participating in the study were informed about the study, and their informed consent was obtained.

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- Analysis and/or Interpretation: MŞ, AE, ÇÖ
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Effects of Neoadjuvant Chemotherapy Treatment on Perioperative Outcomes Following Radical Cystectomy

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Abstract

Objective: This study aimed to assess the impact of neoadjuvant chemotherapy (NAC) on perioperative outcomes in patients undergoing radical cystectomy (RC) for urothelial carcinoma. **Materials and Methods:** We retrospectively analyzed the clinical records of 317 patients who underwent RC and ileal loop diversion between February 2019 and May 2025. Patients were categorized into NAC+RC and RC-only groups. Demographic, preoperative, intraoperative, and postoperative variables were evaluated. Propensity score matching (PSM) was conducted to match the groups in a 1:1 ratio using the nearest-neighbor matching algorithm in terms of age, body mass index (BMI), previous surgery history, American Society of Anesthesiologists (ASA) score, preoperative T stage, hemoglobin, white blood cell (WBC), incision length and urinary diversion technique.

Results: Among the 317 patients, 60 (18.9%) received NAC+RC and 257 (81.1%) underwent RC alone. Preoperative T2 stage was more prevalent in the NAC group compared with the RC-only group (85% vs. 68.5%, $p=0.024$). Preoperative hemoglobin (12.6 vs. 11.9 g/dL, $p=0.006$) and white blood cell levels (8886.9 vs. 7416.8/ μ L, $p<0.001$) were significantly higher in the RC-only group. Postoperative complications were more frequent among RC-only patients (47.5% vs. 31.7%, $p=0.027$). After PSM, 57 matched pairs were obtained. The RC-only group demonstrated higher blood transfusion requirements (1 vs. 0 units, $p=0.048$), longer hospitalization (17 vs. 15 days, $p=0.015$), and delayed return to oral intake (3 vs. 3 days, $p=0.028$) compared with the matched NAC+RC group. Although complications were more common in the RC-only group, the difference was not statistically significant (29% vs. 19%, $p=0.058$).

Conclusion: NAC does not adversely affect perioperative morbidity following RC and may enhance specific postoperative recovery parameters. These findings support the safety and clinical value of NAC in appropriately selected patients with muscle-invasive bladder cancer.

Keywords: complication, neoadjuvant chemotherapy, radical cystectomy, treatment

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INTRODUCTION

Bladder cancer (BCa) is the tenth most common cancer among adults and the sixth most frequent cancer among males, as more than 75% of cases occur in men. (1). Similar to most other cancers, BCa is considered treatable when it remains confined to the bladder. Once the disease extends to distant organs, treatment is generally limited to life-prolonging approaches, such as chemotherapy or immunotherapy. The therapeutic approach of non-metastatic BCa is mainly operative and depends on the stage/ local extension of the disease. More precisely, the infiltration of detrusor muscle is applied as the limit between patients eligible for superficial tumor excision (transurethral resection of bladder tumor, TURBT for non-muscle invasive bladder cancer, NMIBC) and patients eligible for radical bladder excision (radical cystectomy [RC] for muscle invasive bladder cancer [MIBC]) (2). Nevertheless, in the recent years, the role of detrusor infiltration as sole criterion for deciding between superficial and radical excision has been reconsidered since a patient subset with NMIBC seems to benefit from undergoing an early cystectomy (aggressive histological subtypes, multiple TURBTs, unresponsiveness to intravesical therapy), while other meticulously selected MIBC patients are managed by multimodal approaches (radiochemotherapy plus radical TURBT) in the context of a bladder- preserving treatment strategy (3).

In parallel to the surgical methods, which comprise the main approach of localized BCa management, systemic therapy, in the form of chemotherapy or other newer pharmaceutical agents, represents a basic component of the management in a continuously increasing number of specific clinical scenarios. Initially, chemotherapy was primarily used in metastatic BCa; however, it has now become an established component of perioperative treatment (before or after RC) or in MIBC patients that opt for bladder-preserving management. The rationale for this expanded indication is to enhance the effectiveness of local treatment by reducing tumor burden and increasing the likelihood of achieving negative surgical margins. Moreover, chemotherapy can eradicate micrometastases that are not detectable by the available diagnostic methods (3).

Regarding the perioperative chemotherapy, there is strong evidence supporting its administration before (neoadjuvant

chemotherapy, NAC) rather than after RC (adjuvant chemotherapy, AC). In addition to the advantages of NAC, the latter can bring upon serious morbidity, insufficient tumor response, and prolongation of time to RC, which may affect the patient's oncological course. Up to the present, there are no criteria to delineate the patients who are eligible for NAC and are bearing the highest possibility for increased clinical benefit-to-cost ratio. Nevertheless, available data suggest that NAC may be more effective in patients with genomically unstable and urothelial-like tumors (4), while the presence of advanced nodal disease seems to be a negative predictor of NAC effectiveness (5). Moreover, female patients seem to perform better in terms of survival after NAC+RC than the respective male patients (6), while the NAC regimen may also be of clinical significance since dose-dense methotrexate/ vinblastine/ adriamycin/ cisplatin (ddMVAC) induces longer survival prolongation than the gemcitabine/ cisplatin (GC) regimen (7). In conclusion, despite the wide indication for NAC administration, there are many issues that should be further investigated to maximize the clinical benefit in the MIBC patient population.

In the current study, we aimed to examine another aspect of NAC administration, which is the perioperative events of the subsequent RC in the respective patient cohort. Our aim was to unveil or to exclude any detrimental effect of NAC on the patients during the RC procedure and their postoperative course, and to confirm the safety of NAC in combination with the RC.

MATERIAL AND METHODS

Data from 386 patients who underwent RC and ileal loop diversion for urothelial carcinoma between February 2019 and May 2025 were retrospectively analyzed. All procedures were performed by urooncologists with at least 10 years of experience in major oncologic surgery and a minimum annual volume of ten radical cystectomies at a high-volume tertiary cancer center, with the choice of surgical technique left to the discretion of the operating surgeon. Each patient underwent an extended pelvic lymph node dissection.

Sixty-nine patients with insufficient data or a diagnosis of non-urothelial bladder cancer were excluded from the study. The data of 317 patients were included in the study. The Institutional Review Board of Ankara Bilkent City Hospital

approved this study (TABED1/1513/2025, Date: 2025-10-22).

Before undergoing RC, every patient received a preoperative TURBT. Subsequently, comprehensive staging with total-body computed tomography (CT) was carried out for staging. Following diagnostic evaluation, patients were referred to a medical oncologist for cisplatin-based NAC. Eligibility for NAC was determined by a multidisciplinary team including urooncologists and medical oncologists according to contemporary guideline recommendations. Patients were considered eligible for cisplatin-based NAC if they had muscle-invasive bladder cancer, adequate renal function (estimated glomerular filtration rate ≥ 60 mL/min/1.73 m²), acceptable functional capacity, and no contraindications such as severe cardiac dysfunction, uncontrolled infection, or significant hearing impairment. Patients who were medically unfit, who did not want to wait more for RC because of NAC (declined chemotherapy), or had contraindications to cisplatin were assigned to the RC alone group (3). Those in the NAC cohort were treated with either the GC regimen or the MVAC regimen (methotrexate, vinblastine, adriamycin, and cisplatin), each administered for four cycles prior to surgery. The interval between the completion of chemotherapy and RC did not exceed six weeks for any patient.

The demographic (age, gender and body mass index [BMI], preoperative (previous surgery history, intravesical treatment history, neoadjuvant chemotherapy history, concomitant malignancy, presence of ascites, presence of hydronephrosis, smoking status, American Society of Anesthesiologists classification [ASA] score, functional capacity, T stage, grade, clinical lymph node positivity, hemoglobin, white blood cell [WBC], serum creatinine, blood nitrogen urea, serum albumin, sodium and potassium levels, comorbidities), intraoperative (operation duration, incision length, urinary diversion technique, length of bowel segment used in urinary diversion, amount of bleeding,) and postoperative (amount of blood transfusion, duration of total parenteral nutrition administration, hospitalization, time to oral nutrition, ureteral catheterization duration, complications, pathological T stage, pathological N stage) characteristics of patients were collected from hospital database. The patients were divided into two groups according to the administration of neoadjuvant chemotherapy. The comparison was made between the two groups in terms of perioperative outcomes.

Postoperative complications were evaluated according to the Clavien–Dindo classification system (8). Preoperative T stage was determined based on the pathological findings of TURBT in conjunction with preoperative imaging. Tumor grade was assessed exclusively according to TURBT pathology (9). Postoperative complications were evaluated within 30 days after surgery according to the Clavien–Dindo classification system (8). Tumor staging was determined based on the current TNM classification of bladder cancer (9).

Statistical Analysis

Data coding and statistical analyses were performed on the computer using the SPSS 22 software package program (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The normality of the variables was assessed using the Shapiro–Wilk test. Variables with a normal distribution were expressed as mean \pm standard deviation, while non-normally distributed variables were expressed as median (interquartile range). For non-categorical variables, the independent samples t-test or Mann–Whitney U test was used. For categorical variables, the Chi-square test or Fisher's exact test was used. To address potential baseline disparities arising from the non-randomized study design, propensity score matching (PSM) was employed. Based on the calculated propensity scores, patients undergoing radical cystectomy (RC) alone were paired with those receiving RC plus NAC in a 1:1 ratio using the nearest-neighbor matching algorithm in terms of age, BMI, previous surgery history, ASA score, preoperative T stage, hemoglobin, WBC, incision length and urinary diversion technique. The balance of matched covariates was evaluated through standardized mean differences (SMDs), with an SMD below 0.10 considered to indicate adequate balance between groups. Cases with a p-value below 0.05 were considered statistically significant.

RESULTS

The mean age of the 317 patients who underwent RC was 65.8 \pm 7.8 years. NAC plus RC was administered to 60 patients (18.9%) (n=51 for GC and n=9 for MVAC) and among patients receiving NAC, the median interval between completion of NAC and RC was 31 (IQR: 22–39) days. RC alone was performed in 257 patients (81.1%). In RC alone group, 151 (58.8%) patients who were considered eligible for NAC but declined treatment or proceeded directly to surgery due to

patient preference or logistical reasons while 106 patients were not eligible for NAC. Among the patients who received NAC plus RC, 51 (85%) were at preoperative stage T2, compared to 176 (68.5%) in the RC alone group (p = 0.024). In the RC alone group, preoperative serum hemoglobin and WBC levels were significantly higher compared to the NAC plus RC group (12.6 vs. 11.9 g/dL, p = 0.006; 8886.9 vs. 7416.8/ μ L, p < 0.001, respectively). The postoperative complication rate was

significantly higher in the RC alone group compared to the NAC plus RC group (47.5% vs. 31.7%, p = 0.027). Detailed demographic, preoperative, intraoperative and postoperative characteristics of patients who underwent RC for urothelial carcinoma and comparative analysis according to the administration of neoadjuvant chemotherapy were shown in Table 1.

Table 1. Demographic, preoperative, intraoperative and postoperative characteristics of patients who underwent radical cystoprostatectomy for urothelial carcinoma and comparative analysis according to the administration of neoadjuvant chemotherapy

	Total (n=317)	NAC plus RC (n=60, 18.9%)	RC alone (n=257, 81.1%)	P
Demographic characteristics				
Age (year) (Mean \pm SD)	65.8 \pm 7.8	64 \pm 8.7	66.2 \pm 7.6	0.115 ^m
Male gender, n (%)	279 (88)	52 (86.7)	227 (88.3)	0.721 ^c
BMI (kg/m ²) (Mean \pm SD)	26.2 \pm 3.8	26.1 \pm 3.4	26.2 \pm 3.9	0.837 ^m
Preoperative characteristics				
Previous surgery history, n (%)	54 (17)	9 (15)	45 (17.5)	0.641 ^c
Intravesical treatment history, n (%)	34 (10.7)	7 (11.7)	27 (10.5)	0.794 ^c
Concomitant malignancy, n (%)	13 (4.1)	3 (5)	10 (3.9)	0.718 ^f
Presence of ascites, n (%)	1 (0.3)	0 (0)	1 (0.4)	0.811 ^f
Presence of hydronephrosis, n (%)	138 (43.5)	21 (35)	117 (45.5)	0.139 ^c
Smoking status, n (%)	285 (89.9)	54 (90)	231 (89.9)	0.978 ^c
ASA score				
1, n (%)	6 (1.9)	3 (5)	3 (1.2)	0.235 ^f
2, n (%)	162 (51.1)	28 (46.7)	134 (52.1)	
3, n (%)	142 (44.8)	28 (46.7)	114 (44.4)	
4, n (%)	7 (2.2)	1 (1.6)	6 (2.3)	
Functional capacity				
Independent, n(%)	310 (97.8)	59 (98.3)	251 (97.7)	0.606 ^f
Partially-dependent, n (%)	7 (2.2)	1 (1.7)	6 (2.3)	
Dependent, n (%)	0 (0)	0 (0)	0 (0)	
Preoperative T stage				
Ta, n (%)	16 (5)	3 (5)	13 (5.1)	0.024 ^c
T1, n (%)	74 (23.4)	6 (10)	68 (26.4)	
T2, n (%)	222 (70)	51 (85)	176 (68.5)	
Preoperative grade				

Grade 1, n (%)	12 (3.8)	4 (6.7)	8 (3.1)	0.251 ^f
Grade 2, n (%)	0 (0)	0 (0)	0 (0)	
Grade 3, n (%)	305 (96.2)	56 (93.3)	249 (96.9)	
Clinical lymph node positivity, n (%)	74 (23.3)	19 (31.7)	55 (21.4)	0.091 ^c
Hemoglobin (g/dl) (Mean ± SD)	12.5±1.9	11.9±1.4	12.6±2	0.006^m
WBC (g/dl) (Mean ± SD)	8608.6±3368.8	7416.8±4408.5	8886.9±3019.7	<0.001^m
Serum Creatinine (mg/dl) (Mean ± SD)	1.1±0.4	1±0.3	1.1±0.4	0.301 ^m
Blood nitrogen urea (mg/dl) (Mean ± SD)	19.6±7	18.1±6.7	19.9±7.1	0.081 ^m
Serum albumin (gr/l) ((Mean ± SD)	41.5±4.8	41.6±4.6	41.4±4.9	0.922 ^m
Sodium (mEq/l) (Mean ± SD)	139.6±2.7	139.7±2.8	139.6±2.7	0.813 ^m
Potassium (mEq/l) (Mean ± SD)	4.4±0.4	4.4±0.4	4.4±0.5	0.938 ^t
Comorbidities				
Coronary artery disease, n (%)	47 (14.8)	12 (20)	35 (13.6)	0.21 ^c
Heart failure, n (%)	15 (4.7)	1 (1.7)	14 (5.4)	0.319 ^f
HT, n (%)	137 (43.2)	27 (45)	110 (42.8)	0.757 ^c
DM, n (%)	75 (23.7)	15 (25)	60 (23.3)	0.786 ^c
Thyroid disease, n (%)	13 (4.1)	0 (0)	13 (5.1)	0.138 ^f
CKD, n(%)	138 (43.5)	24 (40)	114 (44.4)	0.54 ^c
CVD, n(%)	15 (4.7)	2 (3.3)	13 (5.1)	0.745 ^f
COPD, n(%)	37 (11.7)	6 (10)	31 (12.1)	0.654 ^c
Intraoperative characteristics				
Operation duration (minutes) (Mean ± SD)	366.3±85.8	356.7±83.8	368.6±86.3	0.281 ^m
Incision length				
Infraumbilical midline, n (%)	142 (44.8)	25 (41.7)	117 (45.5)	0.588 ^c
Supra and infraumbilical midline, n (%)	175 (55.2)	35 (58.3)	140 (54.5)	
Urinary diversion technique				
Bricker, n (%)	188 (59.3)	34 (56.7)	154 (59.9)	0.644 ^c
Wallace, n (%)	129 (40.7)	26 (43.3)	103 (40.1)	
Length of bowel segment used in urinary diversion (cm) (Mean ± SD)	19.9±4.7	20.4±6.7	19.8±4.2	0.879 ^m
Amount of bleeding (mL) (Median) (IQR)	800 (500-1275)	750 (425-1240)	800 (500-1300)	0.364 ^m
Postoperative characteristics				
Amount of blood transfusion (Unit) (Median) (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0.22 ^m
Duration of TPN administration (days) (Median) (IQR)	0 (0-4)	0 (0-4)	0 (0-5)	0.975 ^m
Hospitalization (days) (Median) (IQR)	15 (12-19.5)	15 (13-17)	15 (12-20)	0.582 ^m
Time to oral nutrition (days) (Median) (IQR)	3 (2-4)	3 (2-3)	3 (2-4)	0.598 ^m
Ureteral catheterization duration (days) (Median) (IQR)	19 (10.5-21)	16 (11-21)	20 (10-21)	0.972 ^m
Complications (Clavien-Dindo classification system), n (%)	141 (44.5)	19 (31.7)	122 (47.5)	0.027^c

Grade 1, n (%)	64 (20.2)	11 (18.3)	53 (20.6)	0.429 ^f
Grade 2, n (%)	3 (0.9)	0 (0)	3 (1.2)	
Grade 3a, n (%)	43 (13.6)	7 (11.7)	36 (14)	
Grade 3b, n (%)	21 (6.6)	1 (1.7)	20 (7.8)	
Grade 4a, n (%)	2 (0.6)	0 (0)	2 (0.8)	
Grade 4b, n (%)	2 (0.6)	0 (0)	2 (0.8)	
Grade 5, n (%)	6 (1.9)	0 (0)	6 (2.3)	
Pathological T stage				
Tis, n (%)	9 (2.8)	3 (5)	6 (2.3)	0.003 ^f
T0, n (%)	33 (10.4)	16 (26.7)	17 (6.6)	
Ta, n (%)	8 (2.5)	1 (1.6)	7 (2.7)	
T1, n (%)	21 (6.6)	3 (5)	18 (7)	
T2a, n (%)	20 (6.3)	3 (5)	17 (6.6)	
T2b, n (%)	50 (15.9)	7 (11.7)	43 (16.7)	
T3a, n (%)	58 (18.3)	7 (11.7)	51 (19.9)	
T3b, n (%)	60 (18.9)	12 (20)	48 (18.7)	
T4a, n (%)	55 (17.4)	7 (11.7)	48 (18.7)	
T4b, n (%)	3 (0.9)	1 (1.6)	2 (0.8)	
Pathological N stage				
N0, n (%)	226 (71.3)	49 (81.7)	177 (68.9)	0.147 ^c
N1, n (%)	36 (11.3)	6 (10)	30 (11.7)	
N2, n (%)	45 (14.2)	5 (8.3)	40 (15.6)	
N3, n (%)	10 (3.2)	0 (0)	10 (3.8)	

NAC: Neoadjuvant Chemotherapy, RC: Radical cystoprostatectomy, BMI: Body Mass Index, IQR: Interquartile Range, ASA: American Society of Anesthesiologists, WBC: White Blood Cell, HT: Hypertension, DM: Diabetes Mellitus, CKD: Chronic Kidney Disease, CVD: Cerebrovascular Disease, COPD: Chronic Obstructive Pulmonary Disease, TPN: Total Parenteral Nutrition, †: Independent Sample T Test, ‡: Mann Whitney U Test, †: Chi-Square Test, ‡: Fisher’s Exact Test

Bold p values indicate statistical significance.

Patients undergoing NAC plus RC were paired with patients undergoing RC alone based on the calculated propensity scores in a 1:1 ratio using the nearest-neighbor matching algorithm in terms of age, BMI, previous surgery history, ASA score, preoperative T stage, hemoglobin, WBC, incision length and urinary diversion technique. It was possible to match 57 patients undergoing NAC plus RC with 57 patients undergoing RC alone. According to the comparative analysis, the median amounts of blood transfusion, hospitalization duration, and time to oral nutrition were significantly higher

in the RC alone group compared to the NAC plus RC group (1 [IQR: 0–2] vs. 0 [0–1] units, $p = 0.048$; 17 [IQR: 14–20.5] vs. 15 [IQR: 13–17] days, $p = 0.015$; 3 [IQR: 3–4] vs. 3 [2–3] days, $p = 0.028$, respectively). The postoperative complication rate was higher in the RC alone group, although this difference was not statistically significant (29% vs. 19%, $p = 0.058$). The two groups were similar in terms of operation duration and intraoperative blood loss ($p = 0.33$ and $p = 0.127$, respectively) (Table 2).

Table 2. Perioperative outcomes of patients who underwent radical cystoprostatectomy for urothelial carcinoma and comparative analysis according to the administration of neoadjuvant chemotherapy after propensity score matching

	NAC plus RC (n=57)	RC alone (n=57)	P
Intraoperative outcomes			
Operation duration (minutes) (Mean ± SD)	359±84	372±73.4	0.33 ^m
Amount of bleeding (mL) (Median) (IQR)	750 (450-1225)	600 (300-1200)	0.127 ^m
Postoperative outcomes			
Amount of blood transfusion (Unit) (Median) (IQR)	0 (0-1)	1 (0-2)	0.048^m
Duration of TPN administration (days) (Median) (IQR)	0 (0-4)	0 (0-4.5)	0.848 ^m
Hospitalization (days) (Median) (IQR)	15 (13-17)	17 (14-20.5)	0.015^m
Time to oral nutrition (days) (Median) (IQR)	3 (2-3)	3 (3-4)	0.028^m
Ureteral catheterization duration (days) (Median) (IQR)	16 (11-21)	14 (10-21)	0.767 ^m
Complications (Clavien-Dindo classification system), n (%)	19 (33.3)	29 (50.9)	0.058 ^c
Grade 1, n (%)	11 (19.3)	17 (29.8)	0.187 ^f
Grade 2, n (%)	0 (0)	1 (1.8)	
Grade 3a, n (%)	7 (12.3)	6 (10.5)	
Grade 3b, n (%)	1 (1.7)	2 (3.5)	
Grade 4a, n (%)	0 (0)	0 (0)	
Grade 4b, n (%)	0 (0)	0 (0)	
Grade 5, n (%)	0 (0)	3 (5.3)	

NAC: Neoadjuvant Chemotherapy, RC: Radical cystoprostatectomy, IQR: Interquartile Range, TPN: Total Parenteral Nutrition, ^m: Mann Whitney U Test, ^k: Chi-Square Test, ^f: Fisher's Exact Test

Bold p values indicate statistical significance.

DISCUSSION

In the current study, we collected the clinical data of 317 patients who underwent RC as local treatment for BCa, and 18.9% of them received a complete preoperative chemotherapy course, as recommended by the respective guidelines. Regarding the clinical characteristics of the patient subgroups (NAC+RC, RC only), they were comparable in almost every parameter except for the preoperative T stage. The latter was more advanced (higher percentage of MIBC patients) in the NAC+RC subgroup. Postoperatively, the NAC+RC subgroup demonstrated significantly lower percentage of complications. As expected, significantly more NAC+RC patients were found with no residual tumor in their cystectomy histological specimen. To exclude the effect of other factors (preoperative performance status, age, sex, BMI, etc.) and to consolidate the initial finding of reduced complication rate among NAC+RC patients, we performed patient matching based on calculated propensity scores. Subsequently, we compared

two similar subgroups in terms of clinical parameters that have a major effect on the postoperative course. The above comparison demonstrated that NAC had no detrimental role in the respective patients after RC. Interestingly, NAC was associated with a significant improvement in specific aspects of the postoperative time period, such as the blood transfusion rate, the length of hospital stay, and the time to adequate gastrointestinal mobilization and return to oral nutrition. The sum of our results demonstrates that NAC administration is a safe measure to enhance the oncological results of RC without risking a prolonged and eventful recovery period.

To compare our results with the respective findings of other researchers, we performed a thorough literature search and found that the available bibliographical data are mostly in line with our conclusions. In 2019, Aldhaam et al. performed an analysis of the data of 298 patients who underwent NAC plus robotic radical cystectomy (RARC), and the respective data

of 858 patients, who received only RARC. The NAC+RARC patients had similar perioperative parameters (operative time, length of stay), yet they had significantly more 90-day readmissions and demonstrated a trend towards more 90-day complications (10). In the same year, Jerlström et al. published the results of the comparison between NAC+RC vs. RC patients after propensity score matching, and found no deterioration of short-term complication and mortality rates for NAC. Interestingly, the latter was associated with a significant reduction of gastrointestinal complications (11). Another report by Riveros et al. demonstrated that, after adjustment for the rest of the affecting factors, NAC is not associated with any difference in 30-day postoperative complications after RC (12). In 2022, Hoeh et al. analyzed the perioperative and postoperative parameters of NAC+RC patients and found that the latter performed better in terms of wound, cardiac, pulmonary and genitourinary complications and demonstrated shorter length of stay and lower in-hospital mortality compared to RC-only patients (13). More recently, the safety of NAC was confirmed by two reports, which demonstrated a lack of association between NAC before RARC and any effect on perioperative complication rates (14, 15).

From the above data can be concluded that patients after NAC+RC perform at least as well as the respective patients who receive only RC, in terms of perioperative events and postoperative morbidity. This conclusion, combined with the perspective of an improved oncological course after NAC, further consolidates the recommendation for NAC administration in MIBC patients who are going to undergo RC. Interestingly, a report by Kitamura et al. explored the life quality deterioration after the NAC procedure compared with the RC-only treatment and found that the respective indices under evaluation (physical well-being, functional well-being, etc.) were indeed lower during the period between NAC and RC, but not after RC (16).

Provided that the current neoadjuvant pharmaceutical regimens were once first-line treatments in the metastatic setting of BCa, it is plausible that the current first-line agents for metastatic patients are evaluated for their effectiveness in patients before RC. According to a review by Suartz et al., immune checkpoint inhibitors (ICI) combined with chemotherapy seem to further improve the rates of

pathological complete response and the prolongation of OS at the cost of a manageable complication profile and an increased financial burden (17). Molecular targeted agents (mostly kinase inhibitors) demonstrate also a significant effect on the prolongation of survival, yet ICI-based regimens seem to drive the further evolution of MIBC neoadjuvant therapy (18). Since the emergence of innovative pharmaceutical agents in cancer is continuous, the recommendations of urological societies regarding the proposed pharmaceutical regimens in the various clinical scenarios of BCa are expected to change accordingly. The scientific effort of the researchers should focus not only on the validation of the effectiveness of these innovative drugs but also on the demarcation of predictive biomarkers, which will render the administration of systemic therapy more selective, beneficial for the BCa patients, and financially sustainable.

The present study has several limitations that should be acknowledged. First, its retrospective and single-center design may introduce selection bias and limit the generalizability of the findings. Second, although propensity score matching was applied to reduce baseline imbalances, residual confounding due to unmeasured variables cannot be completely excluded. In addition, the overall sample size and the relatively small number of patients in certain subgroups may have limited the statistical power of some analyses. Specifically, patients received different neoadjuvant chemotherapy regimens (GC vs. MVAC), which may have distinct toxicity profiles and could theoretically influence perioperative outcomes. However, the number of patients in each subgroup was limited, particularly in the MVAC group (n=9), which precluded a statistically reliable subgroup or sensitivity analysis. Performing such analyses with very small sample sizes would substantially reduce statistical power and increase the risk of type II error and overinterpretation. Therefore, potential regimen-specific effects on perioperative outcomes could not be adequately evaluated in this cohort.

CONCLUSIONS

In the current study, we compared the perioperative events and the postoperative course of patients who underwent NAC+RC with the respective data of RC-only patients to examine the safety of NAC in this specific clinical setting of BCa. Our analysis showed that perioperatively and postoperatively, NAC+RC patients perform at least as well

as the RC-only patients. This finding confirms the safety of NAC in combination with RC and further consolidates the recommendation of NAC administration in MIBC patients in order to improve their oncological course.

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Late Bladder Necrosis due to Inguinal Hernia, Presented as Intestinal Obstruction: A Case Report

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Abstract

Inguinal bladder hernias are a rare condition, representing only 0.5-3% of inguinal hernia. The vast majority of the cases are diagnosed inadvertently intraoperatively. We report the case of a 71-year-old patient with a history of right inguinal hernia who showed symptoms of incarcerated inguinal hernia, but diagnosed with a strangulated bladder hernia intraoperatively. This case presents an interesting development of a bladder hernia that required two surgical procedures with partial resection due to late necrosis.

Keywords: acute abdomen, bladder hernia, bladder necrosis, inguinal hernia

INTRODUCTION

To this day, inguinal hernia repairs are among the most prevalent procedures done by general surgeons all around the world, with an estimated number of 800.000 surgical repairs done annually in the United States alone (1). Among the possible contents found inside a hernial sac, the bladder

in an uncommon organ, with inguinal bladder hernias comprising only 0.5-3% of all inguinal hernias (2), and with an incidence that reaches up to 10% of all inguinal hernias found in patients over 50 years old (3). However, only 77% of those hernias are correctly diagnosed intraoperatively (4), and are commonly associated with iatrogenic bladder injuries

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(5). This report aims to present a rather uncommon surgical diagnosis and development, and also to raise awareness to the possibility of inguinal bladder hernias during the repair of the abdominal wall hernias in general.

CASE REPORT

A 71-year-old male with a history of coronary artery disease –recent acute myocardial infarction and angioplasty– presented to the emergency department with acute abdominal pain, inability to pass stool or flatus, abdominal distension, and urinary retention. On physical examination, the abdomen was distended, and an irreducible right inguinal hernia was noted.

The patient underwent an emergency exploratory inguinoscopy, which revealed the herniation of viable small bowel and urinary bladder. During dissection, an inadvertent cystostomy occurred, exposing necrotic bladder mucosa (Fig. 1), although the serosal and muscular layers remained viable. The bladder was repaired using a two-layer suture technique. Postoperatively, the patient was discharged on the seventh day with a bladder catheter in place, which was maintained for 18 days.

During follow-up patient presented mild dysuria and urinary urgency with total regression of those findings after oral antibiotics and also showed a control Computed Tomography (CT) scan showing only a postoperative status with no complications.

On postoperative day 41, the patient returned to the emergency department with symptoms of fatigue, dysuria, and foul-smelling urine. A CT scan with intravenous, rectal, and oral contrast was performed, raising suspicion for an enterovesical fistula (Fig. 2). The patient was subsequently taken to the operating room for cystoscopy and cystography, which revealed necrosis of the right lateral bladder wall and dome, along with the presence of an extraperitoneal fistula.

Given these findings, the patient underwent a partial cystectomy, which involved resection of the right lateral bladder wall and dome, resulting in a residual bladder capacity of approximately 100 mL. A cystostomy was performed, and the cavity was drained. Postoperatively, the patient showed no signs of hematuria or fecaluria. Both the drainage tube

and cystostomy were removed on postoperative day 19, and the patient was discharged after a 49-day hospital stay due to clinical developments, without the need for a urinary catheter. The patient is now followed up monthly and has not experienced surgical complications such as hematuria or urinary urgency.

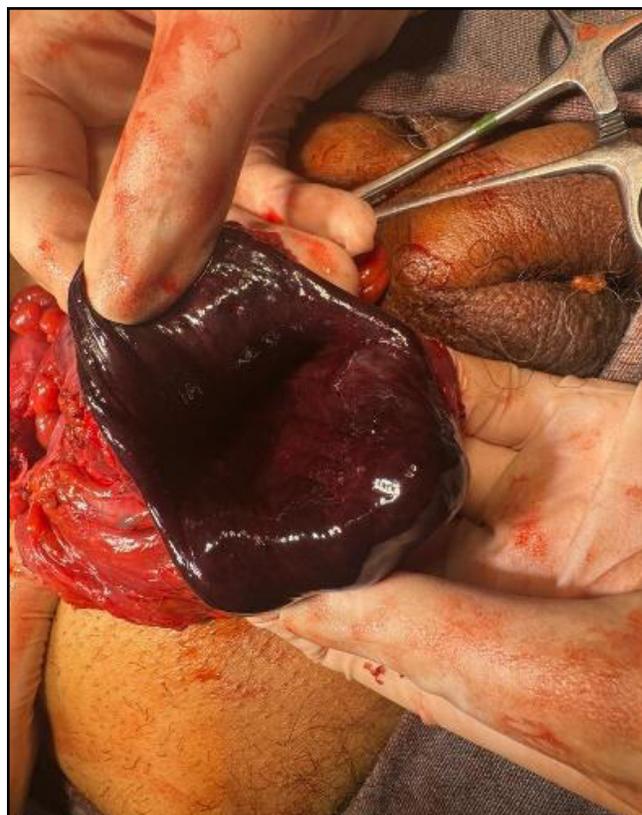


Figure 1. Necrosis of the bladder mucosa



Figure 2. Triple contrast CT scan of patient

DISCUSSION

The incidence of urinary bladder herniation is rare, but several risk factors can be associated with this diagnosis including male gender, obesity, age over 50 years old and bladder outlet obstruction as seen in benign prostatic hyperplasia (5).

The majority of diagnoses are made intraoperatively, with only 7% detected preoperatively (6). However, this trend has been shifting due to the increased frequency of preoperative imaging. Most preoperative diagnoses occur in patients presenting with lower urinary tract symptoms (LUTS), particularly voiding symptoms such as pollakiuria. Additionally, many patients exhibit Mery's sign, characterized by the sensation and visible reduction of an inguinal mass after urination. When these symptoms are present, thorough investigation is essential, with cystography being considered the gold standard diagnostic tool (7). However, CT scans are also commonly used due to their availability and also have high sensitivity (7). Ultrasound and magnetic resonance imaging (MRI) may also be employed, particularly in patients with compromised renal function. In the present case, the patient exhibited acute obstructive abdominal symptoms, prompting urgent surgical intervention without prior imaging.

Potential complications include incomplete bladder emptying, recurrent urinary tract infections, ureterolithiasis, vesicoureteral reflux, rupture, strangulation, or necrosis; such risks make the surgical treatment of bladder inguinal hernias a preferable option (8).

Castro-Rosas *et al.* (9) demonstrated that bladder reduction through the hernial defect, followed by Lichtenstein hernioplasty yields excellent outcomes when there is no inadvertent cystotomy and the bladder shows no signs of compromise. Additionally, there are reports of bladder herniation repairs performed via trans-abdominal preperitoneal (TAPP), following the same principle of bladder reduction, with favorable outcomes. In cases of unintended bladder injury, cystorrhaphy is recommended if the outer layers remain intact. Bladder resection is reserved for instances of necrosis, complex perforations, herniation involving bladder diverticulum, and can be considered in cases where the bladder neck is significantly narrowed (less

than 0.5 cm in its largest diameter) (10). In the case presented, the serosal and muscular layers were viable, leading to the decision to perform cystorrhaphy and Lichtenstein hernioplasty, however, as patient persisted with symptoms and bladder necrosis was found in cystoscopy, a partial resection of the bladder was ultimately performed. Although the outcome was favorable in this scenery, it is important to highlight that a reduced bladder capacity can lead to an impact on patient's life quality and should be assessed during follow-up visits.

Postoperative follow-up for bladder herniation is highly variable in the literature. Some professionals advocate for cystoscopy to assess bladder healing and rule out further complications, while others rely solely on physical examination and symptom monitoring; the latter method was chosen in this case.

There is no consensus regarding the optimal duration of postoperative follow-up, highlighting the need for further studies to establish guidelines for the long-term management of these cases. Despite these variations in approach, no cases of mortality related to bladder herniation have been reported in the literature.

CONCLUSION

Bladder hernias present non-specific symptoms, making the diagnosis frequently intraoperatively, however, cystography or CT can be performed in male patients over 50 years old presenting obstructive or irritative urinary signs.

The treatment for bladder hernias typically involves bladder reduction to the retropubic space and repair of inguinal hernia. A partial cystectomy can be performed when there are signs of necrosis.

Even though bladder hernias are considered a rare diagnosis, it is crucial for surgeons to be aware of the possibility of finding the bladder in the hernial sac, given that hernia repairs are among the most commonly performed surgical procedures worldwide.

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For experimental, clinical, and drug studies mandated to be approved by an ethical committee for publication in The New Journal of Urology, the authors must furnish an ethical committee approval report in line with international agreements (<https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>).

In the case of experimental animal studies, adherence to animal rights guidelines ("Guide for the Care and Use of Laboratory Animals" <https://www.ncbi.nlm.nih.gov/books/NBK54050>) is mandatory, with requisite approval from the animal ethics committee.

The "Materials and Methods" section must specify the ethical committee's approval, including the approval number, and the provision of "informed consent" by patients.

Authors are obligated to disclose conflicts of interest and financial support related to their articles.

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The rules for the title page, references, figures and tables are valid for all types of articles published in this journal.

Authors are required to submit the following:

- Cover Letter
- Copyright Agreement and Acknowledgement of Authorship Form
- Patient Consent Form
- ICMJE Disclosure of Interest
- Title Page
- Main text
- Figures
- Tables

PREPARATION OF THE MANUSCRIPT

Authors should adhere to the ICMJE recommendations for “preparing a manuscript for submission to a medical journal”. <https://www.icmje.org/recommendations/browse/manuscript-preparation/preparing-for-submission.html>

The articles should be written in 12-point, Times New Roman, double-spaced with at least 2.5 cm margin on all edges of each page. The main text should not include any information about the authors’ names or affiliations. This information should only be included on the title page, along with their ORCID IDs, the title, abstract, and keywords.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be explained clearly in parentheses following the definition and custom abbreviations should not be used.

Statistical analysis is usually necessary to support results in original articles. Information on statistical analyses should be provided with a separate subheading under the Materials and Methods section and the statistical software that was used during the process must be specified.

Whenever a product, software, or software program is mentioned in the main text, product information (including state in the USA) must be given in parentheses, including the product name, product manufacturer, city of production, and country of the company.

All references, tables, and figures should be sequentially

numbered and referred to in the main text. All pages of the manuscript should be numbered at the bottom center, except for the title page. Papers should include the necessary number of tables and figures to provide better understanding.

Authors are required to prepare manuscripts in accordance with the relevant guideline listed below:

- Randomized research studies and clinical trials: [CONSORT](#) guidelines (for protocols, please see the [SPIRIT guidance](#))
- Observational original research studies: [STROBE](#) guidelines
- Studies on diagnostic accuracy: [STARD](#) guidelines
- Systematic reviews and meta-analysis: [PRISMA](#) guidelines (for protocols, please see the [PRISMA-P guidelines](#))
- Experimental animal studies: [ARRIVE](#) guidelines and [Guide for the Care and Use of Laboratory Animals](#), 8th edition
- Nonrandomized evaluations of behavioral and public health interventions: [TREND](#) guidelines
- Case report: the [CARE case report guidelines](#)
- Genetic association studies: [STREGA](#)
- Qualitative research: [SRQR guidelines](#)

Manuscript Types

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Original Research Articles should include subheadings below;

- Title
- Abstract
- Keywords
- Introduction
- Material and Methods
- Results
- Discussion
- Conclusions

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- Figures and Tables Legend
- References

Review Articles

Review articles should provide a comprehensive overview of the current state of knowledge on a topic in clinical practice, and should include discussions and evaluations of relevant research. The subheadings of the review articles can be planned by the authors. Review articles are scientific analyses of recent developments on a specific topic as reported in the literature. No new information is described, and no opinions or personal experiences are expressed.

- Title
- Abstract (unstructured)
- Keywords (both Turkish and English)
- Main text
- Conclusion
- Figures and Tables Legend
- References

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New, interesting and rare cases can be reported. They should be unique, describing a great diagnostic or therapeutic challenge and providing a learning point for the readers. Cases with clinical significance or implications will be given priority.

Case Reports should include subheadings below;

- Title
- Abstract (unstructured)
- Keywords (
- Introduction
- Case Presentation
- Discussion and Conclusion
- Figures and Tables Legend
- References

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A “Letter to the Editor” is a type of manuscript that discusses important or overlooked aspects of a previously published article. This type of manuscript may also present articles on subjects within the scope of the journal that are of interest to readers, particularly educational cases. Readers can also use the “Letter to the Editor” format to share their comments on

published manuscripts. The text of a “Letter to the Editor” should be unstructured and should not include an abstract, keywords, tables, figures, images, or other media.

Letters to Editor should include subheadings below;

- Title
- Keywords
- Main text
- Figures and Table Legend
- References

Article Structure

Title page

A separate title page should be submitted with all submissions.

The title page should include:

1. The full title of the manuscript as well as a short title (running head) of ≤50 characters
2. Name(s), affiliations, highest academic degree(s), and ORCID IDs of the author(s),
3. Name, address, telephone (including the mobile phone number), and email address of the corresponding author
4. If the author(s) is a member of the journal’s Editorial Board, this should be specified in the title page
5. If the content of the paper has been presented before, and if the summary has been published, the time and place of the conference should be denoted on this page.
6. If any grants or other financial support has been given by any institutions or firms for the study, information must be provided by the authors
7. Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfill the authorship criteria should be included

Abstract

Original articles should have a structured English (Objective, Methods, Results, Conclusion). Review articles and case reports should have an unstructured abstract. Articles and abstracts should be written in accordance with the word limits specified in the table. References, tables and citations should not be used in an abstract.

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Each submission must be accompanied by a minimum of three to a maximum of six keywords for subject indexing at the end of the abstract. The keywords should be listed in full without abbreviations. The keywords should be selected from the National Library of Medicine, Medical Subject Headings database (<https://www.nlm.nih.gov/mesh/MBrowser.html>).

Limitations for each manuscript type;

Type of Article	Abstract word limit	Word limit	References limit	Table limit	Figure limit
Original Article	250 (Structured)	3000	30	6	5
Review Article	250 (Unstructured)	4000	50	6	5
Case Reports	250 (Unstructured)	2000	10	1	3
Letter to the Editor	No abstract	1000	5	1	1

Figures and Tables

Figures, graphics, and photographs should be submitted as separate files (in JPEG format) through the submission system. The files should not be embedded in a Word file of the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system.

Images should be numbered by Arabic numbers to indicate figure subunits.

Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. The minimum resolution of each submitted figure should be 300 DPI. Figures or illustrations must not permit the identification of patients and written informed consent for publication must be sought for any photograph.

Figure legends should be listed at the end of the main document. Figures should be referred to within the main text, and they should be numbered consecutively in the order in which they are mentioned.

Tables should embed in the main document. Tables should support and enhance the main text rather than repeat data presented in the main text. All tables should be numbered

consecutively in the order they are used to within the main text. Tables legends should be listed at the end of the main document.

Units of Measurement

Units of length, weight and volume should be reported in metric (meter, kilogram, liter) system and in decimal multiples. Temperatures should be expressed in degrees Celsius, and blood pressures in millimeters of mercury. Both local and International Unit Systems (International System of Units, SI) should be used as measurement units. Drug concentrations should alternatively be given in either SI units or mass units written in parentheses.

Abbreviations and Symbols

Use only standard abbreviations, non-standard abbreviations can be very confusing for the reader. The use of abbreviation(s) should be avoided in the title. If there is no standard unit of measurement, provide the long version of the abbreviation in parentheses when it is first used in the text.

Supplementary Materials

Supplementary materials, including audio files, videos, datasets, and additional documents (e.g., appendices, additional figures, tables), are intended to complement the main text of the manuscript. These supplementary materials should be submitted as a separate section after the references list. Concise descriptions of each supplementary material should be included to explain their relevance to the manuscript. Page numbers are not required for supplementary materials.

Identifying products

When mentioning a drug, product, hardware, or software program in a manuscript, it is important to provide detailed information about the product in parentheses. This should include the name of the product, the producer of the product, and the city and country of the company.

Author Contributions

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While citing publications, preference should be given to the latest, most up-to-date publications. Authors should avoid using references that are older than ten years. All the references should be written according to the Vancouver reference style. The references used in the article must be written in parenthesis, at the end of the sentences. References should be numbered in the order they appear in the text and listed in the same order in which they are cited in the text. Be consistent with your referencing style across the document.

References must contain surnames and initials of all authors, article title, name of the journal, the year and the first and last page numbers. If there are more than 6 authors, an abbreviation of “et al.” should be used for the authors out of the first three.

You must add the DOI (Digital object identifier) at end of each reference.

For Examples

Article in journal: Tasci A, Tugcu V, Ozbay B, et al. Stone formation in prostatic urethra after potassium-titanyl-phosphate laser ablation of the prostate for benign prostatic hyperplasia. *J Endourol.*2009;23:1879-1881. <https://doi.org/10.1089/end.2008.0596>

For Books:

Günalp İ. *Modern Üroloji*. Ankara: Yargıçoğlu Matbaası, 1975.

Chapters in books: Anderson JL, Muhlestein JB. Extra corporeal ureteric stenting during laparoscopic pyeloplasty. Philadelphia: W.B. Saunders, 2003; p. 288-307.

For website;

Gaudin S. How moon landing changed technology history [serial online]. 2009 [cited 2014 June 15]. Available from: <http://www.computerworlduk.com/in-depth/it-business/2387/how-moon-landing-changed-technology-history/>

For conference proceeding;

Anderson JC. Current status of chorion villus biopsy. Paper presented at: APSB 1986. Proceedings of the 4th Congress of the Australian Perinatal Society, Mothers and Babies; 1986 Sep 8-10; Queensland, Australian. Berlin: Springer; 1986. p. 182-191.

For Thesis;

Ercan S. Venöz yetmezlikli hastalarda kalf kası egzersizlerinin venöz fonksiyona ve kas gücüne etkisi. Süleyman Demirel Üniversitesi Tıp Fakültesi Spor Hekimliği Anabilim Dalı Uzmanlık Tezi. Isparta: Süleyman Demirel Üniversitesi; 2016.

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