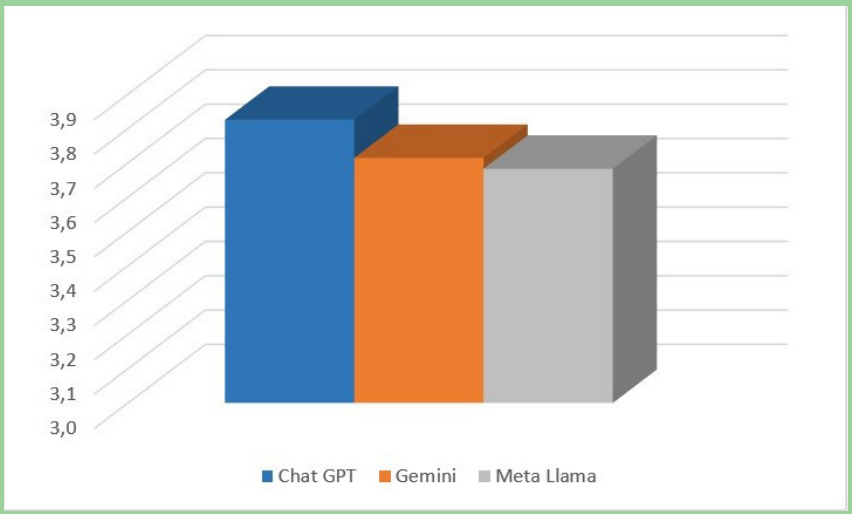
eISSN 3023-6940

THE
NEW JOURNAL
OF UROLOGY



Sungur U, Arikan Y, Turkay AT, Polat H. **The Responses of Artificial Intelligence to Questions About Urological Emergencies: A Comparison of 3 Different Large Language Models. New J Urol. 2025;20(2):89-96.**

eISSN 3023-6940

THE NEW JOURNAL OF UROLOGY

• Volume **20** • Number **2** • June **2025**

THE
NEW JOURNAL
OF UROLOGY

New J Urol
eISSN 3023-6940

Volume 20 / Number 2 / June 2025

Publishing Service
Pera Publishing Services
https://www.perayayincilik.com/

Publishing Coordinator
Seda Karlıdağ

Contact
Istanbul St. Yenimahalle Mah. Kosk Apt.
N:113/A Bakırkoy / Istanbul
0533 726 72 55
www.newjournalurology.com

The New Journal of Urology is an international peer-reviewed journal, published triannually (in February, June, October). Publication languages is English. All responsibility for the submitted and published content rests solely with the author(s).

Indexed by
TÜBİTAK–ULAKBİM TR-Dizin, DOAJ, EBSCO,
SCILIT, Google Schoolar,
SOBIAD, J-GATE, Türk Medline Pleksus,
Türkiye Atıf Dizini, İdeal Online

OPEN ACCESS

EURASIAN
URO-ONCOLOGICAL
ASSOCIATION

Dear Colleagues,

We are pleased to have published the second issue of The New Journal of Urology for 2025. This issue includes six (6) original articles and two (2) case reports. We believe that all the current articles will be read with interest and these articles are expected to contribute to the literature and serve as a reference for future studies.

The New Urology Journal has been indexed in the TUBİTAK ULAKBİM TR Index since the first issue of 2011. Our journal is indexed in DOAJ, Google Scholar, Turkish Medline, Turkish Citation Index, SOBIAD, Scilit, Ideal Online Database, J-GATE, and EBSCO. In addition, the New Journal of Urology is in collaboration with the Orcid and CrossRef DOI systems. The process of our journal being included in the ESCI, PubMed, and EMBASE indexes is ongoing. The editorial team is very grateful to all the authors and reviewers who have contributed to this issue.

We request that you submit your articles to The New Journal of Urology, take timely and rigorous action as a referee, and read the articles published in the journal and cite them where appropriate.

Respectfully yours,

Ali İhsan Taşçı
Editor-in-Chief

Yavuz Onur Danacıoğlu
Editor

EDITORIAL BOARD

CONTENTS

Original Research

Case Report

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1550632

RESEARCH ARTICLE

Efficacy of 200 IU OnabotulinumtoxinA (Botulinum Toxin Type A) in Patients with Idiopathic Overactive Bladder Resistant to Anticholinergic Treatment: A Retrospective Analysis

Ali Egemen Avcı [1], Basri Çakıroğlu [2*], Mehmet Gürkan Arıkan [3], Meftun Çulpan [1]

[1] Department of Urology, Ataşehir Memorial Hospital, Istanbul, Türkiye
[2] Department of Urology, Üsküdar University, Faculty of Medicine, Istanbul, Türkiye
[3] Department of Urology, Private İskenderun Gelişim Hospital, Hatay, Türkiye

Submitted: *2024-09-16*
Accepted: *2025-04-03*

Corresponding Author;
Prof. Dr. Basri Çakıroğlu, M.D.
Address: Department of Urology, Üsküdar University, Faculty of Medicine
E-mail: basri.cakiroglu@uskudar.edu.tr

ORCID
A.E.A 0000-0001-7656-3238
B.Ç. 0000-0001-5337-5226
M.G.A. 0000-0002-9707-596X
M.Ç. 0000-0001-8573-1192

Abstract

Objective: This study aimed to evaluate the efficacy and safety of 200 IU of onabotulinumtoxinA in patients with idiopathic overactive bladder (OAB) and urinary incontinence who had previously shown no response to anticholinergic treatment. This study also sought to examine the impact of a reduction in bladder wall thickness (BWT) on treatment outcomes.

Material and Methods: A retrospective analysis was conducted on patients treated between January 2016 and June 2022. Baseline symptoms and quality of life data were compared with those obtained six months post-treatment. Baseline ultrasound (US)-measured post-void residual urine (PVR) and BWT were recorded. Patients with a history of neurological disorders, anticholinergic-naive patients, those diagnosed with bladder cancer, and those with bladder outlet obstruction were excluded.

Results: This study included 60 patients (41 females and 19 males) with a mean age of 36.05 years. At six months, statistically significant improvements were observed in OAB symptoms, including average urination frequency, nocturia, and incontinence episodes ($p<0.001$). Noteworthy reductions in BWT were also observed (median and mean values decreased from 5.25 mm and 5.22 mm to 4.60 mm and 4.66 mm, respectively). Two patients experienced urinary tract infections, and none required clean intermittent catheterization (CIC).

Conclusions: OnabotulinumtoxinA demonstrated substantial improvements in symptoms and patient-reported outcomes in patients who previously failed to respond to anticholinergic treatment. BWT reduction may be a valuable parameter for evaluating treatment success, although further research with statistical analysis is necessary.

Keywords: botulinum toxin type A, onabotulinumtoxinA, overactive bladder, randomized controlled trial, urinary incontinence, bladder wall thickness

Cite; Avci AE, Cakıroglu B, Arikan MG, Culpan M. Efficacy of 200 IU OnabotulinumtoxinA (Botulinum Toxin Type A) in Patients with Idiopathic Overactive Bladder Resistant to Anticholinergic Treatment: A Retrospective Analysis. New J Urol. 2025;20(2):64-70. **doi:** https://doi.org/10.33719/nju1550632

INTRODUCTION

Overactive bladder (OAB) is commonly characterized by urinary urgency, frequency, and nocturia, which may or may not be accompanied by urge incontinence in the absence of a urinary tract infection. The International Continence Society (ICS) classifies OAB into two subgroups: neurogenic OAB and idiopathic (non-neurogenic) OAB (1). With an estimated prevalence of 12–19%, OAB significantly impacts the quality of life and is associated with a physical, psychological, social, and economic burden comparable to chronic conditions such as cancer, diabetes mellitus, and heart disease (2-5).

Initial management of OAB typically involves behavioral therapy and lifestyle modifications, as recommended by the American Urological Association (AUA) and European Association of Urology (EAU) guidelines (6). First-line pharmacotherapy—using antimuscarinic agents and β3 agonists—often follows; however, adverse effects and limited efficacy may necessitate alternative treatments (6, 7). In such cases, more invasive interventions, including intravesical botulinum toxin (BTX) injections, neuromodulation (pudendal or sacral), and augmentation cystoplasty, are considered. Among these, BTX injections are favored for their relatively minimally invasive nature and proven efficacy in reducing incontinence episodes and improving quality of life (8-12).

While previous randomized controlled trials support BTX doses of 100 IU for idiopathic OAB and 200 IU for neurogenic OAB (4, 13-15), no study to date has evaluated the impact of BTX on bladder wall thickness (BWT) in this patient population. Given that increased BWT—possibly due to fibrosis, edema, or inflammation—may correlate with OAB symptoms (16-18), the present study was designed to fill this gap.

The primary objective of this study is to assess the efficacy of 200 IU onabotulinumtoxinA in alleviating symptoms and improving quality of life in patients with idiopathic OAB and urge incontinence who are refractory to conventional medical therapy. The secondary objective is to evaluate the impact of BTX therapy on bladder wall thickness (BWT).

In addition, this study reveals a novel injection protocol in which 200 IU onabotulinumtoxinA is delivered via 20 injection sites rather than the manufacturer's recommended 30 points. This modified approach is examined to determine if it offers comparable or enhanced outcomes.

MATERIALS AND METHODS

This retrospective study analyzed 60 patients diagnosed with idiopathic OAB and urge incontinence for at least six months, all of whom had failed to respond to a minimum of two antimuscarinic agents and/or a β3 agonist over three months or more.

Patient Selection:

Inclusion Criteria:

- Diagnosis of idiopathic OAB with ≥6 months of urge incontinence
- Refractoriness to at least two antimuscarinic agents and/or a β3 agonist administered for at least three months

Exclusion Criteria:

- Neurological disorders
- Patients naive to anticholinergic therapy
- History of bladder cancer
- Bladder outlet obstruction

Non-neurogenic OAB was confirmed through a detailed clinical history, neurological examination, and, when indicated, imaging studies. Additionally, urodynamic tests were performed to differentiate non-neurogenic OAB from neurogenic bladder dysfunction. Patients with any neurological abnormality identified through clinical evaluation or imaging were excluded from the study.

Intervention:

Patients received 200 IU of onabotulinumtoxinA administered via cystoscopically guided injections at 20 sites (10 IU per site), differing from the manufacturer's recommended distribution of 30 injection points. Sedation or local anesthesia was provided, and cystoscopy was utilized to ensure that injections avoided the ureteral orifices and trigone, thereby minimizing the risk of complications.

Bladder Wall Thickness Measurement:

BWT was measured using a standardized ultrasound protocol. Patients were positioned in a seated position, and measurements were taken using a designated ultrasound

device with defined settings (e.g., probe frequency and measurement landmarks) to ensure reproducibility and accuracy.

Post-Procedure Care and Follow-Up:

- Patients were discharged on the same day following the procedure and prescribed oral ciprofloxacin (500 mg) for three days.
- Anticholinergic therapy was discontinued after BTX administration.
- Follow-up assessments were performed at 4 and 6 weeks post-procedure and included:
  - Bladder diaries to record urinary frequency and incontinence episodes
  - Quality of life questionnaires
  - Ultrasound evaluation of post-void residual (PVR) and BWT

Statistical Analyses:

Statistical analyses were performed using the SPSS software version 26. The variables were investigated using Kolmogorov-Simirnov/Shapiro-Wilk's test to determine whether or not they are normally distributed. Descriptive analyses were presented (using the table of frequencies for the ordinal variables) using medians and interquartile range (IQR) for the non-normally distributed and ordinal variables. Non-parametric tests were conducted to compare these parameters.

RESULTS

The present study comprised a sample of 60 patients, consisting of 41 females and 19 males, with a median age of 35 (IQR 25-45) years. The sample size afforded a comprehensive analysis and provided a representative sample of patients with idiopathic overactive bladder (OAB). The median body mass index (BMI) was 25.56 (IQR 23.28-28.08).

At the 6-month assessment, statistically significant improvements were observed in several OAB symptoms compared to the baseline. Specifically, there was a reduction in the average number of daily urination, nocturnal urination frequency, and incontinence episodes (P <0.001) (see Table 1).

Table 1. Here is the table summarizing the preoperative and postoperative 6th-month evaluation results:

Parameter	Pre-injection Median (IQR)	Pre-injection Mean (SD)	Post-injection Median (IQR)	Post-injection Mean (SD)	p-value
Nocturia	1 (0-2)	1.35 ± 1.56	0 (0-0)	0.20 ± 0.44	<0.001
Frequency	10 (8-10)	10.05 ± 2.22	4 (4-5.75)	4.62 ± 1.07	<0.001
Incontinence	1 (0-3)	1.42 ± 1.82	0 (0-0)	0 ± 0	<0.001
QoL	2 (1-2)	1.92 ± 0.74	4 (3-4)	3.52 ± 0.50	<0.001
Bladder Wall Thickness	5.25 (4.65-6.00)	5.22 ± 0.76	4.60 (4.20-5.15)	4.66 ± 0.58	<0.001
PMR	20 (0-34.25)	20.57 ± 25.47	20 (0-30)	18.10 ± 19.05	0.753
Qmax	30 (26-35)	30.98 ± 5.82	30 (26-35)	31.02 ± 5.80	0.317
Qave	18 (16-20)	18.03 ± 3.47	18 (16-20)	18.17 ± 3.47	0.317

This table provides a clear comparison of the pre-injection and post-injection values along with their statistical significance.

Sex: 19 males 41 females

Age: mean age 36.05 ± 11.72 years; median age: 35 (25 - 45) years

BMI: mean:25.73 ± 3.22 median 25.56 (23.28 – 28.08)

The following significant improvements in OAB symptoms were observed:

1. Urination Frequency: A statistically significant reduction in the average number of daily urinations was observed ($p<0.001$).
2. Nocturia: A statistically significant reduction in the frequency of nocturnal urination ($p<0.001$).
3. Incontinence Episodes: A statistically significant reduction in the number of incontinence episodes ($p<0.001$).
4. Bladder Volume Reductions: Median bladder weight (BWT) decreased from 5.25 mm (IQR 4.65-6.00) to 4.60 mm (IQR 4.20-5.15). (see Table 1).

Two patients developed urinary tract infections. Their post-void residual (PVR) measurements were 50 cc at week 4 and 60 cc during the early postoperative period. None of the patients required clean intermittent catheterization (CIC). Both patients with infections were prescribed antibiotics for two weeks and were symptom-free after treatment.

DISCUSSION

Previous studies have demonstrated that the use of 200 IU of onabotulinumtoxinA (BTX) leads to significant improvements in the quality of life and symptoms of overactive bladder (OAB) in patients who do not respond to anticholinergic medications. These results are consistent with previous research suggesting a link between bladder wall thickness (BWT) and OAB pathophysiology. However, this study did not investigate any disparities in BWT between men and women, which should be the focus of future studies. All patients were informed of the off-label use of BTX and provided consent prior to receiving the injections. Even though the study design was retrospective and the sample size was small, the findings were consistent with those of previous randomized controlled trials.

Comparisons with Previous Studies

The study results were reinforced by the analysis of larger datasets and more recent randomized controlled trials, offering further evidence of the effectiveness of the intervention. For instance, in a randomized controlled trial conducted by Tincello et al., 200 IU BTX was administered to 240 patients with idiopathic OAB, resulting in a significant decrease in the frequency of urge incontinence episodes from 6.20 to 1.67 at month 6 compared to baseline, which supports the findings of our study (15). Concurrent improvements in the urinary frequency were also consistent with our results. Another randomized controlled study involving 34 patients found improvements in the urinary frequency and frequency of urinary incontinence episodes after receiving 200 IU BTX injections, similar to our findings (11).

Quality of Life and Symptom Improvement

Our study findings indicate that the mean quality of life (QoL) score significantly improved from 1.92 ± 0.74 to 3.52 ± 0.50 ($p<0.001$) following the treatment, suggesting a positive impact on the participants' quality of life. To assess the quality of life of patients with OAB or urinary incontinence (UI), questionnaires such as the Incontinence Quality of Life (I-QoL) and Health-Related QoL (HRQoL) have been utilized in previous studies, reporting improvements similar to our study (4, 14, 17). Additional measures, such as the Overactive Bladder Symptom Score (OAB-SS) and Patient Global Impression of Improvement (PGI-I), have also shown comparable enhancements in patient outcomes (15, 16). Although our study participants reported improvements in their quality of life using a self-report 0–4 rating scale, future studies may benefit from incorporating both self-report and objective measures to obtain a more comprehensive understanding of the impact of interventions on QoL.

Dose-Response Relationships and Adverse Effects

While there is no definitive consensus on the optimal dose of botulinum toxin for treating idiopathic OAB or UI, a study by Dmochowski et al. investigated the relationship between dose response and adverse effects in both male and female patients. Statistically significant improvements in QoL scores and UI episodes were observed at doses of 150 IU or higher (14). These findings suggest that the optimal dose of BTX for the treatment of overactive bladder syndrome may be 150 IU or higher. However, higher doses are associated with an increased need for CIC. In our study, administering BTX at a dose of 200 IU resulted in significant improvements in UI symptoms and QoL without requiring CIC. The efficacy of the intervention was consistent with that of other studies, and the lower incidence of adverse effects may be attributed to the smaller sample size.

The most common adverse effects associated with botulinum toxin injections include the need for CIC due to increased

post-void residual (PVR) and urinary retention, followed by urinary tract infections (UTIs) (10). The incidence of these adverse effects is dose-dependent, with urinary retention rates ranging from 16% to 43% and UTI rates ranging from 8.6% to 44% in studies examining botulinum toxin injections at a dose of 200 IU (11,12,15,22). None of our patients experienced urinary retention or increased PVR necessitating CIC, while only two patients developed UTIs. This observation may be due to the small sample size, which limits the analysis of the adverse effects..

Injection Technique and Bladder Wall Thickness

Botulinum toxin is administered to the detrusor muscle while avoiding the ureteral orifices and trigones to prevent vesicoureteral reflux or urinary tract infections (2). A study advocating injections in regions rich in neurons, such as the trigone and floor of the bladder, indicated that this approach prevented an increase in PVR during the follow-up after treatment (23). In our study, the trigone and ureteral orifices were spared, and no cases of urinary retention or increased PVR requiring CIC were observed after the injections.

Bladder wall thickness is known to increase due to fibrosis, edema, or inflammation and plays a crucial role in the pathophysiology of OAB. Previous studies have utilized ultrasound as an affordable, noninvasive, and widely accessible diagnostic tool to measure bladder wall thickness and diagnose OAB. These studies have demonstrated statistically significant reductions in bladder wall thickness following anticholinergic therapy compared with baseline (16, 17, 24). In our study, we observed statistically significant reductions in bladder wall thickness at the month 6 visit after BTX injections. Comperat et al. reported a lower level of bladder fibrosis in patients who received BTX injections than in those who did not, consistent with our findings (18).

Limitations

The limitations of this study include its retrospective design, absence of a control group, small sample size, and reliance on self-reported measures of quality of life. Future research should incorporate prospective studies with control groups to validate these findings and examine the dose-response relationship. Additionally, investigations should incorporate longitudinal designs to understand the temporal dynamics of these relationships better and assess potential confounding variables that may influence observed outcomes.

CONCLUSION

The use of onabotulinumtoxinA has demonstrated promising results in improving the symptoms and overall well-being of patients who do not respond to anticholinergic therapy. Decreased bladder wall thickness may be a reliable indicator of treatment efficiency. To validate its effectiveness further, more substantial and comprehensive long-term clinical trials are necessary.

Funding: This research received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability Statement: All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding authors.

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

Informed Consent: Written informed consent was obtained from all participants (or their parent/legal guardian/next of kin) to participate in this study.

Ethical Approval: Ministry of Health Hisar Hospital Medical and Ethical Advisory Board Date: 10.11.2023 Protocol: 23/54. This study was conducted in accordance with the Declaration of Helsinki of the World Medical Association.

Author Contributions: All authors contributed to the conception and design of this study. Material preparation, data collection, and analysis were performed by Ali Egemen Avci, Basri Çakıroğlu,Mehmet Gürkan Arikan, and Meftun Culpan. The first draft of the manuscript was written by Ali Egemen Avci, and all the authors commented on the previous versions of the manuscript. All authors have read and approved the final manuscript.

REFERENCES

1. Haylen BT, De Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/ International Continence Society (ICS) joint report on

the terminology for female pelvic floor dysfunction. Int Urogynecol J. 2010 Jan;21(1):5-26. https://doi.org/10.1007/s00192-009-0976-9

2. Hsieh PF, Chiu HC, Chen KC, et al. Botulinum toxin A for the Treatment of Overactive Bladder. Toxin (Basel). 2016 Feb 29;8(3):59. https://doi.org/10.3390/toxins8030059
3. Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. World J Urol. 2003;20(6):327-36. https://doi.org/10.1007/s00345-002-0301-4
4. Chapple C, Sievert KD, Macdiarmid S, et al. OnabotulinumtoxinA 100 U significantly improves all idiopathic overactive bladder symptoms and quality of life in patients with overactive bladder and urinary incontinence in a randomized, double-blind, placebo-controlled trial. Eur Urol. 2013;64(2):249-56. https://doi.org/10.1016/j.eururo.2013.04.001
5. Tincello DG. Botulinum toxin treatment of overactive bladder and detrusor overactivity in adults. World J Urol. 2012;30(4):451-6. https://doi.org/10.1007/s00345-011-0778-9
6. Herbison P, Hay-Smith J, Ellis G, et al. Effectiveness of anticholinergic drugs compared with placebo in the treatment of overactive bladder: systematic review. BMJ. 2003 Apr 19;326(7394):841-4. https://doi.org/10.1136/bmj.326.7394.841
7. Kelleher CJ, Cardozo LD, Khullar V et al. Medium-term analysis of subjective efficacy of treatment in women with detrusor instability and low bladder compliance. Br J Obstet Gynaecol. 1997;104(9):988-93. https://doi.org/10.1111/j.1471-0528.1997.tb12054.x
8. Lucas MG, Bosch RJL, Burkhard FC, et al. EAU guidelines for the surgical treatment of urinary incontinence. European Association of Urology [Internet]. EAU guidelines on surgical treatment of urinary incontinence. Eur Urol. 2012;62(6):1118-29. https://doi.org/10.1016/j.eururo.2012.09.023
9. Lightner DJ, Gomelsky A, Souter L, et al. Diagnosis and Treatment of Overactive Bladder (non-neurogenic) in Adults: AUA/SUFU Guideline Amendment 2019. J Urol. 2019;202(3):558-563. https://doi.org/10.1097/JU.0000000000000309
10. Duthie JB, Vincent M, Herbison GP, et al. Botulinum toxin injections for adults with overactive bladder syndrome. Cochrane Database Syst Rev. 2011;(12). https://doi.org/10.1002/14651858.CD005493.pub3
11. Sahai A, Khan MS, Dasgupta P. Efficacy of botulinum toxin-A for treating idiopathic detrusor overactivity: results from a single-center, randomized, double-blind, placebo-controlled trial. J Urol. 2007;177(6):2231-6. https://doi.org/10.1016/j.juro.2007.01.130
12. Brubaker L, Richter HE, Visco A, et al. Pelvic floor disorder network. Refractory idiopathic urge urinary incontinence and botulinum A injections. J Urol. 2008;180(1):217-22. https://doi.org/10.1016/j.juro.2008.03.028
13. Rovner E, Kennelly M, Schulte-Baukloh H, et al. Urodynamic results and clinical outcomes with intradetrusor injections of onabotulinumtoxinA in a randomized, placebo-controlled dose-finding study in idiopathic overactive bladder. Neurourol Urodyn. 2011;30(4):556-62. https://doi.org/10.1002/nau.21021
14. Dmochowski R, Chapple C, Nitti VW, et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo-controlled, randomized, dose-ranging trial. J Urol. 2010;184(6):2416-22. https://doi.org/10.1016/j.juro.2010.08.021
15. Tincello DG, Kenyon S, Abrams KR, et al. Botulinum toxin a versus placebo for refractory detrusor overactivity in women: A randomized blinded placebo-controlled trial of 240 women (the RELAX study). Eur Urol. 2012;62(3):507-14. https://doi.org/10.1016/j.eururo.2011.12.056
16. Robinson D, Anders K, Cardozo L, et al. Can ultrasound replace ambulatory urodynamics in women with irritative urinary symptoms? BJOG. 2002;109(2):145-8. https://doi.org/10.1111/j.1471-0528.2002.01021.x
17. Robinson D, Oelke M, Khullar V, et al. Bladder wall thickness in women with symptoms of overactive bladder and detrusor overactivity: Results from a randomized, placebo-controlled shrink study. Neurourol Urodyn. 2016;35(7):819-25. https://doi.org/10.1002/nau.22808

18. Compérat E, Reitz A, Delcourt A, et al. Histologic features in the urinary bladder wall affected from neurogenic overactivity--a comparison of inflammation, oedema and fibrosis with and without injection of botulinum toxin type A. Eur Urol. 2006;50(5):1058-64. https://doi.org/10.1016/j.eururo.2006.01.025

19. Bartoli, S, Aguzzi, G, Tarricone, R. Impact of urinary incontinence and overactive bladder on quality of life: A systematic literature review. Urology. 2010;75(3):491-500. https://doi.org/10.1016/j.urology.2009.07.1325

20. Höfner K, Burkart M, Jacob G, et al. Symptomatic and quality of life response to tolterodine in subgroups of men with overactive bladder symptoms and presumed non-obstructive benign prostatic hyperplasia. World J Urol. 2010;28(3):353-7. https://doi.org/10.1007/s00345-009-0460-7

21. Denys P, Le Normand L, Ghout I, et al. Efficacy and safety of low doses of onabotulinumtoxinA for the treatment of refractory idiopathic overactive bladder: A multicenter, double-blind, randomized, placebo-controlled dose-ranging study. Eur Urol. 2012;61(3):520-9. https://doi.org/10.1016/j.eururo.2011.10.028

22. Flynn MK, Amundsen CL, Perevich M, et al. Outcomes of a randomized, double-blind, placebo-controlled trial of botulinum A toxin for refractory overactive bladder. J Urol. 2009;181(6):2608-15. https://doi.org/10.1016/j.juro.2009.01.117

23. Smith CP, Chancellor MB. Simplified bladder botulinum toxin delivery technique using a flexible cystoscope and 10 injection sites. J Endourol. 2005;19(7):880-2. https://doi.org/10.1089/end.2005.19.880

24. Latthe PM, Champaneria R, Khan KS, et al. A systematic review of the accuracy of ultrasound as a method of measuring bladder wall thickness in the diagnosis of detrusor overactivity. Int Urogynecol J. 2010;21(8):1019-24. https://doi.org/10.1007/s00192-010-1144-y

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1603293

RESEARCH ARTICLE

Association of Apelin Levels with Lymph Node Invasion and Clinical Progression in Obese Patients Undergoing Radical Prostatectomy for Prostate Cancer

Özgür Kazan [1], Kenan Toprak [2], Burak Tüfekçi [1], Samer Hussein Hadi Alhaddad [1], Ferruh Kemal İşman [1], Asıf Yıldırım [1]

[1] Department of Urology, Istanbul Medeniyet University, School of Medicine, Istanbul, Türkiye

[2] Department of Urology, Nizip State Hospital, Gaziantep, Türkiye

Submitted: *2024-12-24*
Accepted: *2025-04-03*

Corresponding Author;
Hüseyin Özgür Kazan, M.D.
Address: Istanbul Medeniyet University, School of Medicine, Department of Urology, Istanbul, Türkiye
E-mail: ozgurkazan@hotmail.com

ORCID

H.Ö.K.	0000-0003-0202-0454
K.T.	0000-0002-8243-6777
B.T.	0000-0002-7029-0109
S.H.H.A	0009-0006-7375-2352
F.K.I.	0000-0003-4278-4651
A.Y	0000-0002-3386-971X

Abstract

Objective: We aimed to determine the relationship between Apelin, an adipocytokine associated with neoangiogenesis, adverse histopathology such as extraprostatic extension, positive surgical margins, lymph node involvement, and high Gleason score, and survival in patients who underwent curative radical prostatectomy due to prostate cancer.

Material and Methods: In this prospective cohort study, 88 patients who underwent radical prostatectomy with curative intent between March 2018 and January 2019 were included. Patients with any treatment for prostate cancer, including androgen deprivation therapy or radiotherapy, were excluded. In the study, Apelin levels in the serum samples of all patients were measured with commercially available ELISA kits (Elabscience, Houston, TX, USA) before radical prostatectomy was performed. The patients were divided into two groups: non-obese and obese, with a BMI of 30 kg/m2 as the limit. Patient characteristics, histopathological differences, prognosis, and Apelin levels were evaluated between the two groups.

Results: In the study, 17 patients were obese, and 71 were non-obese; age, comorbidity index, lipid parameters, and PSA levels were similar. The mean Apelin levels were not different between the two groups (172.9 vs. 146.4, p=0.262). The clinical progression (CP) rate was higher in obese patients (29.4% vs. 2.8%, p=0.001), while the biochemical recurrence rates were similar between the groups. Higher Apelin levels were associated with lymph node invasion in obese patients (180.2 pN1 vs. 122.8 pN0, p=0.027), but this association was not observed in non-obese patients.

Conclusion: The risk of CP following radical prostatectomy was higher in obese patients, and Apelin levels were associated with lymph node invasion in these individuals.

Keywords: apelin, adipokine, biochemical recurrence, clinical progression, obesity, prostate cancer

Cite; Kazan O, Toprak K, Hadi Alhaddad SH, Tufekci B, Isman, FK Yildirim A. Association of Apelin Levels with Lymph Node Invasion and Clinical Progression in Obese Patients Undergoing Radical Prostatectomy for Prostate Cancer. New J Urol. 2025;20(2):71-78. **doi:** https://doi.org/10.33719/nju1603293

INTRODUCTION

Examining the risk factors for prostate cancer, genetic predisposition is considered a cornerstone of its etiology. In addition, metabolic syndrome, hyperlipidemia, diabetes mellitus, and obesity are also considered contributing factors to increased prostate cancer risk (1). Several studies have suggested an association between prostate cancer and obesity (2). Obesity is also linked to a lower risk of developing low-grade prostate cancer but a higher risk of high-grade prostate cancer in the REDUCE study (3). Similarly, a recent study demonstrated that prostate cancer exhibited a more aggressive course in obese men, correlating with adipokines (4).

Adipokines, proteins secreted by adipocytes and the surrounding connective tissue cells, exert autocrine, paracrine, and endocrine effects (5). Among these, apelin has been identified as the natural ligand for the human G protein-coupled receptor APJ (APLNR), a seven-transmembrane receptor related to the angiotensin type 1 receptor. As a result, this newly discovered ligand was named apelin, short for "APJ Endogenous Ligand (6).

Studies indicate that Apelin regulates cardiovascular functions, anterior pituitary functions, and fluid homeostasis. Additionally, it has been implicated in suppressing apoptosis and serves as a co-receptor in human immunodeficiency virus (HIV) infection (7–10). Initial research in mice demonstrated that elevated Apelin expression enhanced vascularization and increased tumor growth (11). Cancer studies have reported that, compared to healthy controls, Apelin levels are significantly higher in cancer patients, with levels rising in correlation with advancing cancer stages (12). The relationship between Apelin and cancer has been studied in lung cancer, gastrointestinal cancers, hepatocellular carcinoma, endometrial cancer, and oral squamous cell carcinoma.

Apelin has been shown to have proliferative effects on the prostate via androgen receptors (13). Another study suggested that the impaired miRNA-224/Apelin axis may play a role in prostate cancer development, potentially contributing to its aggressive progression (14). This study indicated that reduced miRNA-224 expression and increased Apelin expression could lead to the development of prostate cancer.

In this study, we aimed to analyze the relationship between serum Apelin levels and different histopathological features and obesity in patients who underwent curative radical prostatectomy for localized prostate cancer. Secondly, we compared Apelin levels with biochemical recurrence (BCR) and clinical progression (CP) rates.

MATERIALS AND METHODS

In this prospective cohort study, 88 patients who underwent radical prostatectomy with curative intent between March 2018 and January 2019 were included. The study commenced after obtaining ethical approval (Decision No: 2018/0080), and written informed consent was obtained from all participants. Patients with any ISUP grade who underwent radical prostatectomy with curative intent were eligible for inclusion. However, patients who had received prior treatment for prostate cancer, including androgen deprivation therapy or radiotherapy, were excluded. Additionally, individuals with any current cancer diagnosis other than prostate cancer were excluded from the study.

Serum Apelin levels were measured in all participants using commercially available ELISA kits (E-EL-H0456, Human APLN, Elabscience, Houston, TX, USA) before undergoing radical prostatectomy. The cohort was categorized into two groups based on BMI: non-obese (BMI <30 kg/m^2) and obese (BMI ≥30 kg/m^2). Patient characteristics, histopathological differences, prognostic factors, and Apelin levels were analyzed and compared between the two groups. Systemic staging was conducted using whole-body bone scintigraphy and abdominal contrast-enhanced computerized tomography.

Biochemical recurrence was defined as a PSA rise to ≥0.2 ng/mL on at least two consecutive tests following radical prostatectomy. Clinical progression was assessed according to RECIST criteria using bone scans and abdominal CT in response to PSA elevation or the appearance of symptoms.

Statistical Analysis

Data analysis was conducted using SPSS v.25 (SPSS Inc., Chicago, IL, USA). The normal distribution between groups was assessed using the Kolmogorov-Smirnov test, the Shapiro–Wilk test, and graphical evaluations. Descriptives such as mean, standard deviation, median, frequency, ratio,

minimum, and maximum were used in evaluating the data. Categorical variables were compared using the chi-square test, with Bonferroni correction applied for variables involving comparisons larger than 2x2. The independent samples t-test was used to compare two quantitative variables, while one-way ANOVA was applied for comparisons involving more than two groups. A p-value <0.05 was considered statistically significant.

RESULTS

In the cohort, 17 patients were obese, and 71 were non-obese. Both groups had similar ages, comorbidity index, lipid parameters, and PSA levels. The mean Apelin levels in both groups were also identical (172.9 vs. 146.4, p=0.262) (Table 1).

ISUP grades 3 and 4 detected in biopsy specimens were more common among obese patients. This relationship was not detected in radical prostatectomy specimens. Histopathological characteristics were similar in obese and non-obese patients. While similar BCR rates were detected between groups, the rate of CP was higher in obese patients (29.4% vs 2.8%, p=0.001) (Table 2).

We did not detect any relationship between Apelin levels and ISUP grades and T stage in both obese and non-obese patients. Lymphadenectomy was performed in 37 patients. Lymph node involvement was positive in 6 patients. Higher Apelin levels were associated with lymph node invasion in obese men undergoing radical prostatectomy (mean 180.2 in pN1 vs. mean 122.8 in pN0, p=0.027). This association was not observed in non-obese patients (p = 0.624) (Table 3).

Table 1. Study characteristics between non-obese and obese patients

	Non-Obese patients N=71	**Obese patients N=17**	**P**
Age, years Mean±SD	64.01 ± 6.4	61.24±5.9	0.107[t]
CCI Mean±SD	4.10 ± 1.07	4 ± 1.0	0.731[t]
DM n(%)			
-Absent	58 (81.7)	13 (76.5)	
-Present	13 (18.3)	4 (23.5)	0.624[c]
Family history of prostate cancer n(%)			
-Absent	62 (87.3)	17 (100)	
-Present	9 (12.7)	0 (0)	0.121[c]
Waist circumference,cm Mean±SD	92.0 ± 9.3	110.4 ± 10.9	0.001[t]
Total Cholesterol Mean±SD	204.7 ± 45.1	195.5± 28.6	0.426[t]
Triglyceride Mean±SD	157.6 ± 77.07	161.06 ± 63.5	0.866[t]
HDL Cholesterol Mean±SD	43.2 ± 12.7	38.4 ± 5.45	0.131[t]
LDL Cholesterol Mean±SD	135.1 ± 43.1	125 ± 24.2	0.354[t]
Fasting Glucose Mean±SD	110 ± 28	116.7 ± 27.1	0.385[t]
Preoperative PSA, ng/mL Mean±SD	13.5 ± 18.7	14.9±18.9	0.775[t]
PSA density, ng/mL^2 Mean±SD	0.3 ± 0.48	0.29±0.37	0.986[t]
Apelin, pg/mL Mean±SD	172.9 ± 94.6	146.4 ± 37.3	0.262[t]
Follow-up, months Mean±SD	69.6±5.4	68.3±11.7	0.478[t]

CCI: Charlson Comorbidity Index, DM: Diabetes Mellitus, SD: Standard Deviation

Chi-Square Test, Independent samples t-test

Table 2. Clinical features and survival differences between non-obese and obese patients

	Non-Obese patients N=71	**Obese patients N=17**	**P**
Biopsy ISUP n(%)			
-1	32 (45.1) [a]	4 (23.5) [a]	
-2	20 (28.2) [a]	2 (11.8) [a]	
-3	6 (8.5)[a]	5 (29.4)[b]	
-4	5 (7) [a]	5 (29.4) [b]	
-5	8 (11.3) [a]	1 (5.9) [a]	0.006[c]
RRP ISUP n(%)			
-1	17 (23.9)	4 (23.5)	
-2	18 (25.4)	3 (17.6)	
-3	15 (21.1)	4 (23.5)	
-4	7 (9.9)	3 (17.6)	
-5	14 (19.7)	3 (17.6)	0.888[c]
pT n(%)			
-pT2	36 (50.7)	8 (47.1)	
-pT3	35 (49.3)	9 (52.9)	0.614[c]
pN n(%)			
-pN0	25 (83.3)	6 (85.7)	
-pN1	5 (16.7)	1 (14.3)	0.985[c]
Surgical margin n(%)			
-Negative	57 (80.3)	14 (82.4)	
-Positive	14 (19.7)	3 (17.6)	0.846[c]
Biochemical recurrence n(%)			
-Absent	48 (67.6)	9 (52.9)	
-Present	13 (18.3)	5 (29.4)	
-Persistent	10 (14.1)	3 (17.6)	0.497[c]
Clinical Progression n(%)			
-Absent	69 (97.2)	12 (70.6)	
-Present	2 (2.8)	5 (29.4)	0.001[c]

RRP: Retropubic Radical Prostatectomy

Chi-Square Test, a-b: Bonferroni Adjustment

Table 3. Apelin values between different histopathology and prognosis

Non-Obese Patients		
Biopsy ISUP Mean±SD		
-1	162.3±80.3	
-2	169.3±99.9	
-3	233.6±169.9	
-4	165.9±57.0	
-5	182.7±86.4	0.566[A]
RRP ISUP Mean±SD		
-1	141.4±65.0	
-2	202.5±141.4	
-3	175.8±81.0	
-4	156.4±62.8	
-5	177.9±72.5	0.425 [A]

pT Mean±SD		
-pT2b	177.5±105.9	
-pT2c	139.1±32.9	
-pT3a	177.7±105.5	
-pT3b	160.6±45.8	0.870 [A]
pN Mean±SD		
-pN0	167.6 ± 66.5	
-pN1	152.6 ± 11.8	0.624[t]
Biochemical recurrence Mean±SD		
-Absent		
-Present	174.4±107.3	
	157.7±50.2	0.589[t]
Clinical Progression Mean±SD		
-Absent	173.4 ± 95.9	
-Present	153.8 ± 2.9	0.618[t]
Obese patients		
Biopsy ISUP Mean±SD		
-1	165.1±58.5	
-2	140.9±36.7	
-3	139.5±25.8	
-4	138.9±38.3	
-5	154.6	0.871 [A]
RRP ISUP Mean±SD		
-1	155.3±64.5	
-2	144.4±26.8	
-3	132.5±15.5	
-4	140.9±37.1	
-5	160.6±38.7	0.895 [A]
pT Mean±SD		
-pT2b	151.2±44.0	
-pT2c	-	
-pT3a	127.7±15.2	
-pT3b	153.7±38.9	0.543 [A]
pN Mean±SD		
-pN0	122.7 ± 17.1	
-pN1	180.2	**0.027**[t]
Biochemical recurrence Mean±SD		
-Absent		
-Present	143.6±42.4	
	150.9±27.9	0.740[t]
Clinical Progression Mean±SD		
-Absent	143.3 ± 37.8	
-Present	153.7 ± 38.9	0.775[t]

t: Independent samples t-test, A: One-way ANOVA test

DISCUSSION

In the current study, higher Apelin levels were detected in obese patients with positive pathological lymph nodes during radical prostatectomy. Despite similar preoperative PSA levels, radical prostatectomy ISUP grades, and pT stages between obese and non-obese patients, these results suggest that Apelin may play a significant role in lymphangiogenesis. Although numerous recent studies have established a relationship between angiogenesis and Apelin, its role in lymphangiogenesis remains an area requiring further investigation. Additionally, CP rates were found to be higher in obese patients. While obesity has been long studied as a risk factor for prostate cancer and its negative prognostic impact, recent studies have shown that, as in other cancers, Apelin is found at higher serum levels and is expressed at higher histopathological levels in prostate cancer (13,14). Previous studies have supported that this is particularly related to angiogenesis (15,16).

However, fewer studies have examined the relationships among Apelin, lymphangiogenesis, and lymph node involvement. Our study specifically found a relationship between lymph node invasion and high Apelin levels in obese patients. Interestingly, Apelin levels were not higher in obese patients compared to non-obese patients (146.4 vs. 172.9). This proves that Apelin significantly increases lymph node positivity. This finding is notable because Apelin levels were not significantly elevated in other poor prognostic characteristics, such as radical prostatectomy ISUP grade, pT stage, and PSA levels. Berta et al. demonstrated that Apelin is highly expressed in lymphatic endothelial cells. Both in vitro and in vivo studies have shown that high Apelin levels are associated with intratumoral lymphangiogenesis and lymph node metastasis (17). Similarly, Baran et al. indicated in a breast cancer histopathology study that Apelin could be used as a biomarker for lymph node metastasis (18).

We also observed that clinical progression rates were higher in obese patients. A systematic review including 280,199 cases found that obesity is associated with increased disease-specific mortality (19). Kim et al.. identified obesity as a risk factor for biochemical recurrence following radical prostatectomy (20). While we did not observe such a relationship in our study, we did find that obese patients experienced higher levels of CP. Other risk factors were similar between the two groups. A similar study also reported higher biochemical recurrence rates in obese patients (21).

Our study is the first to suggest that Apelin may be associated with lymph node metastasis, specifically in obese prostate cancer patients. A limitation of our study is the small patient cohort. The average follow-up duration was 68 months; however, a 10-year follow-up period would be more suitable for identifying biochemical recurrence and clinical progression. The number of patients undergoing lymph node dissection was also limited. Further studies with more extensive lymph node sampling are needed to confirm Apelin's role in lymph node involvement in prostate cancer. Metastatic samples from metastatic patients could also be analyzed to evaluate the relationship between Apelin levels. In our study, we only measured serum Apelin levels, but histopathological Apelin expression could also be assessed in future studies.

CONCLUSION

Our findings suggest that there is a significantly higher risk of clinical progression following radical prostatectomy in obese patients, with Apelin levels associated specifically with lymph node invasion.

Funding: This research received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability Statement: All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding authors.

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

Informed Consent: Written informed consent was obtained from all participants to participate in this study.

Ethical Approval: Istanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee. Date/Protocol: 21.03.2018 Decision No: 2018/0080.

REFERENCES

1. Amin Al Olama A, Dadaev T, Hazelett DJ, et al. PRACTICAL Consortium; COGS-CRUK GWAS-ELLIPSE (Part of GAME-ON) Initiative; Australian Prostate Cancer BioResource; UK Genetic Prostate Cancer Study Collaborators; UK ProtecT Study Collaborators; Freedman M, Conti DV, Easton D, Coetzee GA, Eeles RA, Kote-Jarai Z. Multiple novel prostate cancer susceptibility signals identified by fine-mapping of known risk loci among Europeans. Hum Mol Genet. 2015;24(19):5589-602. https://doi.org/10.1093/hmg/ddv203
2. Davies NM, Gaunt TR, Lewis SJ, et al. The effects of height and BMI on prostate cancer incidence and mortality: a Mendelian randomization study in 20,848 cases and 20,214 controls from the PRACTICAL consortium. Cancer Causes Control. 2015;26(11):1603-16. https://doi.org/10.1007/s10552-015-0654-9
3. Vidal AC, Howard LE, Moreira DM, et al. Obesity increases the risk for high-grade prostate cancer: results from the REDUCE study. Cancer Epidemiol Biomarkers Prev. 2014;23(12):2936-42. https://doi.org/10.1158/1055-9965.EPI-14-0795
4. Kang M, Byun SS, Lee SE, et al. Clinical Significance of Serum Adipokines according to Body Mass Index in Patients with Clinically Localized Prostate Cancer Undergoing Radical Prostatectomy. World J Mens Health. 2018;36(1):57-65. https://doi.org/10.5534/wjmh.17026
5. Gimble JM. Adipose tissue-derived therapeutics. Expert Opin Biol Ther. 2003;3(5):705-13. https://doi.org/10.1517/14712598.3.5.705
6. Tatemoto K, Hosoya M, Habata Y, et al. Isolation and Characterization of a Novel Endogenous Peptide Ligand for the Human APJ Receptor. Biochemical and Biophysical Research Communications [Internet]. 1998 Oct 20 [cited 2024;251(2):471-6. Available from: https://www.sciencedirect.com/science/article/pii/S0006291X9899489X
7. Katugampola S, Davenport A. Emerging roles for orphan G-protein-coupled receptors in the cardiovascular system. Trends Pharmacol Sci. 2003;24(1):30-5. https://doi.org/10.1016/s0165-6147(02)00007-x
8. Reaux A, De Mota N, Skultetyova I, et al. Physiological role of a novel neuropeptide, apelin, and its receptor in the rat brain. J Neurochem. 2001;77(4):1085-96. https://doi.org/10.1046/j.1471-4159.2001.00320.x
9. Tang SY, Xie H, Yuan LQ, et al. Apelin stimulates proliferation and suppresses apoptosis of mouse osteoblastic cell line MC3T3-E1 via JNK and PI3-K/Akt signaling pathways. Peptides. 2007;28(3):708-18. https://doi.org/10.1016/j.peptides.2006.10.005
10. Cayabyab M, Hinuma S, Farzan M, et al. Apelin, the natural ligand of the orphan seven-transmembrane receptor APJ, inhibits human immunodeficiency virus type 1 entry. J Virol. 2000;74(24):11972-6. https://doi.org/10.1128/jvi.74.24.11972-11976.2000
11. Sorli SC, Le Gonidec S, Knibiehler B, et al. Apelin is a potent activator of tumour neoangiogenesis. Oncogene. 2007;26(55):7692-9. https://doi.org/10.1038/sj.onc.1210573
12. Lacquaniti A, Altavilla G, Picone A, et al. Apelin beyond kidney failure and hyponatremia: a useful biomarker for cancer disease progression evaluation. Clin Exp Med. 2015 Feb;15(1):97-105. https://doi.org/10.1007/s10238-014-0272-y
13. Tekin S, Sandal S, Colak C. Effects of Apelin-13 on Human Prostate Cancer Lines [Insan Prostat Kanseri Hucre Serilerinde Apelin-13'un Etkileri]. Med-Science [İnternet]. 2014;3(3):1427. [cited 2024 Oct 26] Available from: http://www.scopemed.org/fulltextpdf.php?mno=154668
14. Wan Y, Zeng ZC, Xi M, et al. Dysregulated microRNA-224/apelin axis associated with aggressive progression and poor prognosis in patients with prostate cancer. Hum Pathol. 2015;46(2):295-303. https://doi.org/10.1016/j.humpath.2014.10.027
15. Berta J, Kenessey I, Dobos J, et al. Apelin expression in human non-small cell lung cancer: role in angiogenesis and prognosis. J Thorac Oncol. 2010;5(8):1120-9. https://doi.org/10.1097/JTO.0b013e3181e2c1ff
16. Heo K, Kim YH, Sung HJ, Li HY, Yoo CW, Kim JY, Park JY, Lee UL, Nam BH, Kim EO, Kim SY, Lee SH, Park

JB, Choi SW. Hypoxia-induced up-regulation of apelin is associated with a poor prognosis in oral squamous cell carcinoma patients. Oral Oncol. 2012;48(6):500-6. https://doi.org/10.1016/j.oraloncology.2011.12.015

17. Berta J, Hoda MA, Laszlo V, et al. Apelin promotes lymphangiogenesis and lymph node metastasis. Oncotarget. 2014;5(12):4426-37. https://doi.org/10.18632/oncotarget.2032

18. Baran M, Ozturk F, Canoz O, et al. The effects of apoptosis and apelin on lymph node metastasis in invasive breast carcinomas. Clin Exp Med. 2020;20(4):507-514. https://doi.org/10.1007/s10238-020-00635-2

19. Rivera-Izquierdo M, Pérez de Rojas J, Martínez-Ruiz V, et al. Obesity as a Risk Factor for Prostate Cancer Mortality: A Systematic Review and Dose-Response Meta-Analysis of 280,199 Patients. Cancers (Basel). 2021;13(16):4169. https://doi.org/10.3390/cancers13164169

20. Kim SJ, Park MU, Chae HK, et al. Overweight and obesity as risk factors for biochemical recurrence of prostate cancer after radical prostatectomy. Int J Clin Oncol. 2022;27(2):403-410. https://doi.org/10.1007/s10147-021-02058-9

21. Chalfin HJ, Lee SB, Jeong BC, et al. Obesity and long-term survival after radical prostatectomy. J Urol. 2014;192(4):1100-4. https://doi.org/10.1016/j.juro.2014.04.086

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1635892

RESEARCH ARTICLE

Are the Preoperative Systemic Immune-Inflammation (SII) Index and Hematological Inflammatory Parameters Predictors for Systemic Inflammatory Response Syndrome (SIRS) After Retrograde Intrarenal Surgery (RIRS)?

Tugay Aksakallı [1], Ahmet Emre Cinislioğlu [1], Şaban Oğuz Demirdöğen [2], Adem Utlu [1], Fatih Akkaş [1], İbrahim Karabulut [1]

[1] Department of Urology, University of Health Sciences, Erzurum Regional Training and Research Hospital, Erzurum, Türkiye
[2] Department of Urology, Ataturk University Medical Faculty, Erzurum, Türkiye

Submitted: *2025-02-08*
Accepted: *2025-06-14*

Corresponding Author;
Tugay Aksakalli, MD
Address: University of Health Sciences, Erzurum Regional Training and Research Hospital, Department of Urology, Erzurum, Türkiye
E-mail: tugay_daydreamer@hotmail.com

ORCID
T.A. 0000-0001-6781-738X
A.C. 0000-0002-1037-815X
S.O.D. 0000-0002-8697-8995
A.U. 0000-0002-6381-025X
F.A. 0000-0002-4560-7426
İ.K. 0000-0001-6766-0191

Abstract

Objective: The study aimed to evaluate whether there is a relationship between the preoperative values of the platelet lymphocyte ratio (PLR), the neutrophil lymphocyte ratio (NLR), and systemic immune inflammation (SII) index and the development of systemic inflammatory response syndrome (SIRS) in patients undergoing retrograde intrarenal surgery (RIRS) for kidney stones.

Material and Methods: Demographic and laboratory data of patients who underwent RIRS were collected. NLR, PLR, and SII indices were obtained from the complete blood count parameters. Stone characteristics were obtained from preoperative non-contrast computed tomography. Univariate and multivariate analyses were performed to identify risk factors of SIRS.

Results: SIRS was detected in 27 (3.6%) of 748 patients included in the study. Stone volume, Hb level, operation time, and SII index were independent risk factors in predicting SIRS. The established threshold for predicting SIRS based on stone volume is 1589 mm^3, demonstrating a sensitivity of 88.9%, specificity of 70.0%, and an area under the curve (AUC) of 0.863. The hemoglobin level cut-off is 14.9 g/dl, with a sensitivity of 96.3%, specificity of 56.0%, and AUC of 0.198. The SII index threshold is 703, yielding a sensitivity of 81.5%, specificity of 73.5%, and AUC of 0.820. The operation time cut-off is 62.5 minutes, showing a sensitivity of 88.3%, specificity of 93.3%, and AUC of 0.967.

Conclusion: The SII index appears to be an independent, easily accessible, and cost-effective predictor for SIRS following RIRS.

Keywords: renal stones, retrograde intrarenal surgery, SII index, SIRS

Cite; Aksakalli T, Cinislioglu AE, Demirdogen SO, Utlu A, Akkas F, Karabulut I. Are the Preoperative Systemic Immune-Inflammation (SII) Index and Hematological Inflammatory Parameters Predictors for Systemic Inflammatory Response Syndrome (SIRS) After Retrograde Intrarenal Surgery (RIRS)?. New J Urol. 2025;20(2):79-88. **doi:** https://doi.org/10.33719/nju1635892

INTRODUCTION

Retrograde intrarenal surgery (RIRS) is the preferred minimal invasive surgical method for treating kidney stones smaller than 2 cm. It has also been shown to be effective for stones larger than 2 cm in selected cases (1). Compared to percutaneous nephrolithotomy (PNL) and open stone surgery, RIRS is less invasive, resulting in a shorter recovery time and lower complication rates (2). The overall complication rate after RIRS ranges from 9% to 25%, and most complications are classified as Clavien grade I or II (3). Urinary tract infections are the most common complication after RIRS and can lead to urosepsis and subsequent mortality (4).

Older age, diabetes mellitus (DM), ischemic heart disease, positive urine culture, preoperative stent placement, and longer surgical time were reported as risk factors in literature (5). Even without these risk factors, the development of urosepsis after RIRS has generated interest in other predictive markers. The immune system's response to an inflammatory condition can be reflected by changes in the sub-groups of white blood cells (6). Recently, hematological inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and the systemic immune-inflammation (SII) index, which are frequently evaluated in malignancies, infectious diseases, and inflammatory diseases, have shown promising results (7).

The study aims to evaluate whether preoperative NLR, PLR, and SII index can be used to predict systemic inflammatory response syndrome (SIRS) in patients undergoing RIRS for renal stones.

MATERIALS AND METHODS

Patient Selection and Study Design

The Ataturk University Local Ethics Committee approved this study on 30.03.2023 (approval number: B.30.2.ATA.0.01.00/235). The data of patients who underwent RIRS between January-2020 and March-2023 were retrieved from patient files. Patients with congenital anomalies, DM, obesity (BMI>30kg/m2), immunosuppression, systemic inflammatory diseases (familial Mediterranean fever, systemic lupus erythematosus, Behçet's disease, etc.), chronic renal failure, diagnosed malignancy, and hematological disorders were excluded from the study. In addition, patients with the following criteria were also excluded from the study: preoperative positive urine culture results and C-reactive protein (CRP) levels above 5 ng/l, preoperative fever above 38°C, an operation time exceeding 90 minutes, intraoperative infectious findings such as purulent materials, positive stone culture results, a history of previous ESWL, PNL or pyelolithotomy, patients whom a ureteral access sheath (UAS) was not used during RIRS, double J (DJ) stents were not inserted after RIRS (Figure1), and DJ stents placement more than 30 days.

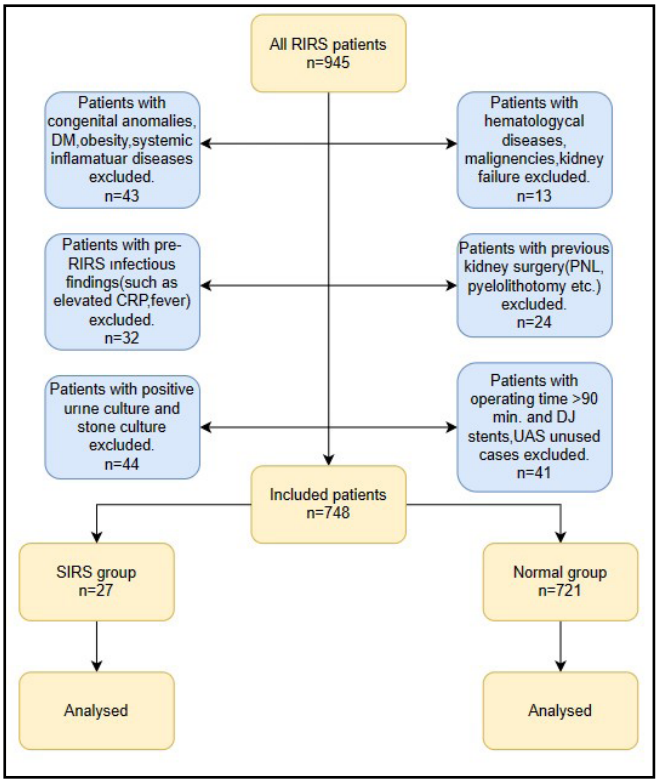


Figure 1. Exclusion criteria and study design

Demographic and clinical data such as age, gender, body mass index (BMI), comorbidities, presence of DJ stent before RIRS, complete blood count parameters obtained before RIRS; white blood cell (WBC) ($\times 10^9$/L), red blood cell (RBC) ($\times 10^{12}$ /L), platelet (Plt) ($\times 10^9$/L), neutrophil ($\times 10^9$/L), lymphocyte ($\times 10^9$/L), hemoglobin (Hb) level (g/dL), SII index (calculated using the formula; SII = platelet count × neutrophil count/lymphocyte count (P x N)/L), Neutrophil/Lymphocyte ratio (NLR), and Platelet/Lymphocyte ratio (PLR), stone characteristics, operation time, presence of SIRS/sepsis after RIRS were retrospectively recorded. The

stone characteristics such as stone diameter, stone volume, Hounsfield unit (HU), laterality, and location were obtained from preoperative non-contrast computed tomography (NCCT). The stone diameter was determined by measuring the largest diameter of the stone, and the stone volume was calculated using the formula (length×width×depth×π×0.167) (8). The Hounsfield Unit (HU) measurement was conducted using a bone window and magnification on the longest stone diameter. The operation time was recorded as the time between the placement of the ureteral access sheath (UAS) and the placement of the DJ stent at the end of the operation. SIRS was defined by the presence of two or more of the following: body temperature above 38°C or below 36°C, heart rate above 90 beats/min, respiratory rate above 20/min, and white blood cell count above 12,000/mm3 or below 4000/mm3. Sepsis is defined, according to the Sepsis-3 criteria, as a life-threatening organ dysfunction caused by a dysregulated host response to infection (9).

Surgical Technique and Clinic Management

In our clinical practice, patients who apply for RIRS are first hospitalized, and laboratory tests such as complete blood count, serum creatinine, and urine culture are routinely performed. Urine culture was obtained using mid-stream urine sample, and urine cultures given 5 days or earlier before the operation were renewed. Surgical prophylaxis is performed intravenously with third-generation cephalosporins 30 minutes before the procedure. The procedure is performed under general anesthesia in the lithotomy position. Preoperative DJ stenting was applied to patients who were unable to insert ureteral access because of a thin ureter and preoperative obstructed, infected kidney because of a ureteral stone. A semi-rigid ureteroscope (URS) was used to reach the bladder and to visualize the ureter. Then, a 0.035-inch guidewire (Boston Scientific Corporation®, Natick MA) was placed through the working channel of the URS to the pelvicalyceal system. URS was removed, and the UAS (9 fr. UAS, Cook Medical Inc., USA) was placed through the guidewire. Then a fiber-optic flexible URS (8 fr. Karl Storz GmbH & Co. KG, Tuttlingen, Germany) was inserted to reach the stone and a Quanta®Litho 30 holmium: yttrium aluminum-garnet (Ho:YAG) laser lithotripter with 272-µm holmium laser used to fragment the stone. After fragmentation, a DJ stent was placed in the pelvicalyceal system. If the ureteral orifice is too narrow to allow the advancement of the URS, a DJ stent is inserted for passive dilatation, and RIRS is performed in the next session.

In the postoperative period, all patients were monitored in the urology service for pain, fever, SIRS, and sepsis. If patients developed fever or SIRS, blood cultures and urine cultures were obtained. In cases of persistent fever or sepsis, antibiotherapy was adjusted based on the recommendations of infectious disease specialists and the results of blood and urine cultures. The patients were discharged once sterile cultures were obtained and when antibiotherapy was completed. Patients who did not develop SIRS or fever were discharged on the first postoperative day. Patients who presented with SIRS findings after discharge were hospitalized and also included in the study. The DJ stents were removed using a flexible cystoscope 3 weeks after the procedure.

Statistical Analysis

All data were analyzed using SPSS, version 23.0 (SPSS Inc, Chicago, Illinois, USA). Categorical variables were given as frequencies and percentages, while continuous variables were presented as mean and standard deviation. The normal distribution of continuous variables was evaluated using the Shapiro-Wilk test. The means of two independent groups showing a normal distribution were compared using the independent samples t-test. In contrast the means of groups not showing a normal distribution were compared using the Mann-Whitney U test. The percentages of categorical variables were compared using Pearson's chi-square test and Fisher's exact test. The predictive values for SIRS were determined using ROC curve analysis. Univariable and multivariable logistic regression tests were used to identify predictive factors for SIRS. A p-value <0.05 was considered statistically significant.

RESULTS

The demographic and clinical characteristics, stone characteristics, and hematological inflammatory parameter values of the 748 included patients are summarized in Table 1. The mean age in our cohort was determined to be 45.6 ± 12.4 years, with a male and female percentage of 65.2% and 34.8%, respectively. Post-RIRS, SIRS was detected in 27 patients, accounting for 3.6% of the total cases. 12 (1.6%) patients were followed in ICU. Sepsis was detected in 5 of

these patients with a percentage of 0.6%, and all sepsis developed patients were followed in the ICU. No mortality was observed during the follow-up of the patients.

Table 1. Demographic data, stone characteristics and hemogram parameters of the whole study sample

	Mean ± SD, (min.- max.)
Age ± SD, (yrs)	45.6 ± 12.4 (19.0-76.0)
Gender, n(%)	
Male	488 (65.2)
Female	260 (34.8)
BMI ± SD, kg/m^2	23.0 ± 2.13 (18.0-28.1)
ASA, n(%)	
ASA 1	347 (46.4)
ASA 2	311 (41.6)
ASA 3	71 (9.5)
ASA 4	19 (2.5)
Stone diameter ± SD, mm	14.9 ± 3.03 (8.0-20.0)
Stone volume ± SD, mm^3	1981 ± 1123 (268.4-4195.0)
Stone density ± SD, HU	965 ± 194
Stone location, n(%)	
Middle calyx	141 (18.9)
Renal pelvis	397 (53.1)
Inferior calyx	146 (19.5)
Superior calyx	64 (8.6)
Presence of DJS preoperatively, n(%)	610 (81.6)
Creatinine value ± SD, mg/dL	0.88 ± 0.16 (0.40-1.21)
WBC count ± SD, µ/L	8.36 ± 2.26 (2.89-24.25)
Lymphocyte count ± SD, µ/L	2.47 ± 0.95 (0.50-18.45)
Neutrophil count ± SD, µ/L	4.99 ± 1.89 (1.21-15.70)
RBC count ± SD, 10^6 µ/L	5.20 ± 0.55 (2.93-7.67)
HGB count ± SD, g/dl	14.9 ± 1.75 (8.0-20.4)
PLT count ± SD, 10^3 µ/L	283 ± 73.3 (107-699)
NLR ± SD	2.27 ± 1.38 (0.21-13.16)
PLR ± SD	125 ± 47.5 (8.83-385.03)
SII ± SD	510 ± 294 (34.5-6045.1)
SIRS rate postoperatively, n(%)	27 (3.6)
ICU patients, n(%)	12 (1.6)
Surgical duration ± SD, min.	41.9 ± 14.4 (14-78)

SD standart deviation, **BMI** body mass index, **ASA** American Society of Anaesthesiology, **HU** Hounsfield Unite, **DJS** double j stent, **WBC** white blood cell, **RBC** red blood cell, **NLR** neutrophil to lymphocyte ratio, **PLR** platelet to lymphocyte ratio, **SIRS** systemic inflammatory response syndrome, **ICU** Intensive care unit

When comparing the SIRS-developing group with the normal group, no statistically significant differences were found in age, gender, BMI, HU, stone localization, preoperative DJ stent presence, mean creatinine, mean WBC, and platelet values. The patients in the SIRS group were found to have significantly higher ASA score ($p < 0.001$), stone diameter (19.4 ± 2.93 vs. 14.8 ± 2.90, $p < 0.001$), stone volume (1438 [1152-3058] vs. 1769 [906-3058], $p < 0.001$), NLR (3.54 ± 0.89 vs. 2.22 ± 1.37, $p < 0.001$), PLR (162 ± 60.1 vs. 123 ± 46.4, $p < 0.001$), SII ındex (957 ± 330 vs. 634 ± 465, $p < 0.001$) and operation time (42 [29-56] vs. 72 [43-86], $p < 0.001$). Additionally, lymphocyte count (1.77 ± 0.45 vs. 2.49 ± 0.95, $p < 0.001$) and hemoglobin level (13.1 ± 1.35 vs. 15.0 ± 1.73, $p < 0.001$) were found to be significantly lower in the SIRS group. The comparison of clinical characteristics between the two groups is summarized in Table 2.

Univariable and multivariable binary logistic regression analyses were conducted to determine the factors predicting SIRS (Table 3). In the univariable analysis, stone volume, lymphocyte count, hemoglobin level, NLR, PLR, SII index, and operation time were identified as significant risk factors. In the multivariable logistic regression, we avoided using the stone diameter and volume, NLR, PLR, SII, RBC, and HGB at the same time because these variables are highly correlated with each other, and this could cause problems of multicollinearity. With this analysis, independent risk factors for SIRS were found to be stone volume, SII index, and operation time.

A Spearman correlation analysis was performed to determine the relationship between SII index, operation duration, stone volume, and hemoglobin level. In the correlation analysis, a weak negative correlation was found between hemoglobin level and operation duration as well as SII index ($r = -0.185$, $r = -0.266$ respectively), which was statistically significant ($p < 0.001$). There was no significant correlation found between the SII index, operation time, and stone volume (Table 4).

Table 2. Comparison of groups normal group and SIRS group

	Normal	**SIRS**	**P value**	
Variables	**Mean ± SD/Median IQR**	**Mean ± SD/Median IQR**		
Number of patients	721	27		
Age, median [IQR], (yrs)	45 [36-56]	50 [32-61]	0.553**	
Gender, n(%)			0.282#	
Male	473 (65.6)	15 (55.6)		
Female	248 (34.4)	12 (44.4)		
BMI, median [IQR] , (kg/m^2)	23.1 [21.5-24.2]	24.1 [21.4-25.2]	0.100**	
ASA, n(%)			<0.001&	1 vs 2 0.333
ASA 1	340 (47.2)	7 (25.9)		1 vs 3 <0.001
ASA 2	300 (41.7)	10 (37.0)		1 vs 4 0.350
ASA 3	62 (8.6)	9 (33.3)		2 vs 3 0.003
ASA 4	18 (2.5)	1 (3.7)		2 vs 4 0.485
				3 vs 4 0.682
Stone diameter ± SD, mm	14.8 ± 2.90	19.4 ± 2.93	<0.001*	
Stone volume, median [IQR], mm^3	1438 [1152-3058]	1769 [906-3058]	<0.001**	
Stone density ± SD, HU	965 ± 194	961 ± 198	0.919*	
Stone location, n(%)			0.931#	1 vs 2 0.599
Middle calyx	135 (18.7)	6 (22.2)		1 vs 3 0.951
Renal pelvis	384 (53.3)	13 (48.1)		1 vs 4 1.000
Inferior calyx	140 (19.4)	6 (22.2)		2 vs 3 0.639
Superior calyx	62 (8.6)	2 (7.4)		2 vs 4 1.000
				3 vs 4 1.000
Presence of DJS preoperatively, n(%)	588 (81.6)	22 (81.5)	0.992#	
Mean creatinine value ± SD, mg/dL	0.88 ± 0.16	0.90 ± 0.20	0.565*	
WBC count , median [IQR] ,(µ/L)	8.08 [6.8-9.5]	8.21 [7.85-8.96]	0.809**	
Lymphocyte count ± SD, µ/L	2.49 ± 0.95	1.77 ± 0.45	<0.001*	
Neutrophil count ± SD, µ/L	4.95 ± 1.90	6.05 ± 1.26	0.003*	
RBC count ± SD, 10^6 µ/L	5.22 ± 0.55	4.84 ± 0.60	<0.001*	
HGB count ± SD, g/dl	15.0 ± 1.73	13.1 ± 1.35	<0.001*	
PLT count ± SD, 10^3 µ/L	284 ± 73.8	269 ± 58.0	0.309*	
NLR ± SD	2.22 ± 1.37	3.54 ± 0.89	<0.001*	
PLR ± SD	123 ± 46.4	162 ± 60.1	<.001*	
SII ± SD	634 ± 465	957 ± 330	<0.001*	
Operation time, median [IQR], min.	42 [32-52]	72 [43-86]	<0.001**	

SD standart deviation, * Independent sample t test, **Mann whitney U test, **#** Pearson chisquare test, **&** Fisher's exact test, **SD** standart deviation, **IQR** Interquartile range, **BMI** body mass index, **ASA** American society of anaesthesiology, **HU** hounsfield unite, **DJS** double j stent, **WBC** white blood cell, **RBC** red blood cell, **NLR** neutrophil to lymphocyte ratio, **PLR** platelet to lymphocyte ratio, **SIRS** systemic inflammatory response syndrome

Table 3. To predict SIRS, univariable and multivariable binary logistic regression analyses were performed

	Univariable			Multivariable		
	OR	**95% CI**	**P value**	**OR**	**95% CI**	**P value**
Age (yr)	1.010	0.979-1.041	0.546			
Gender (female)	1.526	0.703-3.310	0.285			
BMI (kg/m^2)	1.191	.995-1.426	0.057			
Stone diameter (mm)	2.104	1.667-2.655	<0.001			
Stone volume (mm^3)	1.001	1.001-1.002	<0.001	1.001	1.001-1.002	<0.001
Stone density (HU)	0.998	0.992-1.004	0.563			
Stone location	0.956	0.600-1.523	0.851			
Presence of DJS	1.005	0.374-2.702	0.992			
Creatinine value (mg/dL)	1.993	0.190-20.883	0.565			
WBC count (µ/L)	0.916	0.760-1.105	0.360			
Lymphocyte count (µ/L)	0.180	0.088-0.370	<0.001			
Neutrophil count (µ/L)	1.256	1.074-1.469	0.004			
RBC count (10^6 µ/L)	0.308	0.159-0.597	<0.001			
HGB count (g/dl)	0.578	0.467-0.715	<0.001	0.747	0.517-1.080	0.121
PLT count (10^3 µ/L)	0.997	0.991-1.003	0.307			
NLR	1.412	1.200-1.661	<0.001			
PLR	1.011	1.006-1.017	<0.001			
SII	1.001	1.000-1.001	0.003	1.001	1.000-1.002	0.008
Operation time (min.)	1.282	1.189-1.382	<0.001	1.232	1.139-1.333	<0.001

OR odds ratio, **CI** confidence interval, **BMI** body mass index, **HU** hounsfield unite, **DJS** double j stent, **WBC** white blood cell, **RBC** red blood cell, **NLR** neutrophil to lymphocyte ratio, **PLR** platelet to lymphocyte ratio, **SIRS** systemic inflammatory response syndrome, **SII** systemic immune inflamatuar index

Table 4. Correlation analysis between independent risk factors

Spearman's rho		**SII-index**	**OT**	**SV**	**HL**
SII-index	r	1.000	0.050	0.007	-0.266
	p		0.168	0.851	**0.001**
Operation time	r		1.000	0.055	-0.185
	p			0.133	**0.001**
Stone Volume	r			1.000	-0.040
	p				0.277
Hemoglobin level	r				1.000

ROC analysis was performed on the variables identified as independent risk factors in the multivariable regression analysis (Figure 2). For hemoglobin level to predict SIRS, the cut-off value was 14.9 g/dl, with a sensitivity of 96.3%, specificity of 56.0%, and AUC of 0.198 ($p < 0.001$). For the SII index to predict SIRS, the cut-off value was 703, with a sensitivity of 81.5%, specificity of 73.5%, and AUC of 0.820 ($p < 0.001$). For the operation time to predict SIRS, the cut-off value was 62.5 min., with a sensitivity of 88.3%, specificity of 93.3%, and AUC of 0.967 ($p < 0.001$).

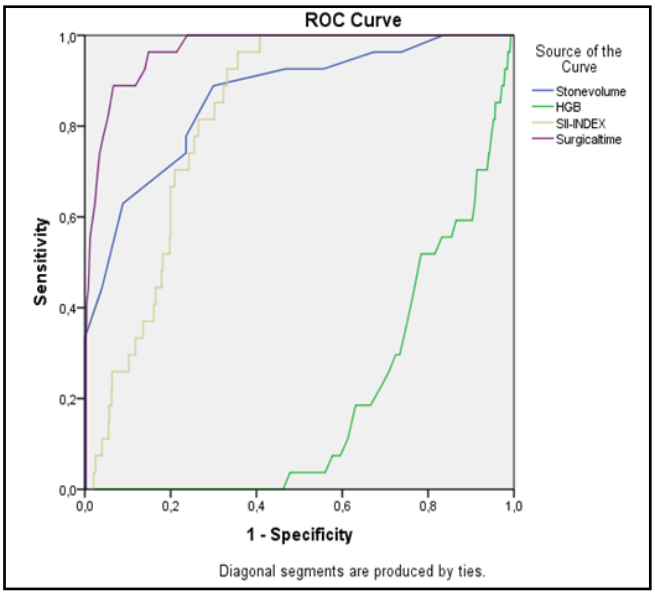


Figure 2. ROC curve for independent variables to predict SIRS post-RIRS

(AUC value: 863, Cut-off value:1589[Sensitivity: 88.9%; specificity: 70.0%] for stone volume; AUC value: 198, Cut-off value:14.9[Sensitivity: 96.3%; specificity: 56%] for Hgb; AUC value: 820, Cut-off value:703[Sensitivity: 81.5%; specificity: 73.5%] for SII index; AUC value: 967, Cut-off value:62.5[Sensitivity: 88.3%; specificity: 93.3%] for surgical time). AUC is the area under the curve.

DISCUSSION

This study emphasizes that patients with prolonged operation time, increased stone volume, and high systemic immune-inflammation index (SII) are at greater risk for developing SIRS after RIRS. These findings highlight the importance of identifying high-risk patients preoperatively and suggest that management strategies targeting modifiable risk factors, such as minimizing operation time and ensuring closer postoperative clinical follow-up, may help reduce the incidence of infectious complications in this population.

Infectious complications are the most commonly encountered and potentially life-threatening complications following RIRS for renal stones. Urosepsis is the most severe form of these complications and can lead to mortality rates ranging from 28.3% to 41.1% (10). In a systematic review conducted by Dybowsk et al., including 17 studies and 8294 patients, the rates of infectious complications after RIRS were reported to range from 2.8% to 7.5% (11). Although the exact rates of urosepsis after RIRS (retrograde intrarenal surgery) are not fully known, a systematic review and meta-analysis conducted by Bhojani et al., including 13 studies and 5597 patients, reported an incidence of urosepsis after URS (ureteroscopy) ranging from 0.2% to 17.8% (12). In the globally conducted multicenter FLEXOR study, fever and infectious complications were identified at a rate of 6.1%, while sepsis was observed at a rate of 1.3% (13). In our study, the incidence of SIRS in patients was 3.6%, and the sepsis rate was 0.6%. We determined that these rates were consistent with the results of the meta-analysis conducted by Bhojani et al. However, the lower rates compared to Dybowski et al. and the FLEXOR study may be attributed to the fact that many of the studies included in these analyses did not exclude patients with diabetes, obesity, hematological diseases, or positive urine cultures. We believe that the exclusion of clinical conditions that could be risk factors for SIRS and patients with positive urine cultures during the preoperative period in our study could explain the lower incidence of SIRS and sepsis rates observed in our study.

Risk factors for sepsis following RIRS include patient-related factors such as female gender, obesity, diabetes mellitus (DM), and stone size, as well as center and surgeon-related factors such as procedure duration, irrigation fluid pressure, stent placement for more than 30 days, and low case volume (14). In the study conducted by Yong Xu et al., positive preoperative urine culture, irrigation rate, and operation duration were reported as independent risk factors for infectious complications (15). In this study, although the authors did not provide specific cut-off values for operation duration and irrigation rate, the operation time should be less than 60 minutes. The association of operative time and infectious complications, which is generally accepted

in the literature, was also observed in our study. We found that operative time was an independent risk factor in the multivariate analysis for the detection of SIRS. In our study, we performed ROC analysis for independent risk factors in predicting SIRS, and the cut-off value for operation time was 62.5 minutes, with 88% sensitivity and 93.3% specificity.

In another study conducted by Moses et al., it was reported that an operation time longer than 120 minutes and preoperative DJ stent placement were independent risk factors for predicting SIRS after RIRS (16). The cut-off values given in this study for the operation duration are stated as longer than our study and other studies. In this study, the identified independent risk factors may have been indirectly influenced by the lack of evaluation of stone characteristics. Additionally, the absence of specifying the timing of DJ stent placement and the high rate of positive preoperative urine cultures can be considered as limitations and reasons for the observed findings. While no relationship was found between stone location and SIRS, stone volume was an independent risk factor for predicting SIRS in our study. Through ROC analysis, we determined a cut-off value of 1589 mm3 for stone volume, with 88.9% sensitivity and 70.0% specificity.

Despite of the recommended practices in current guidelines to minimize risk factors, patients can still develop SIRS and sepsis after RIRS. Hematological inflammatory parameters such as NLR, PLR, and SII index, have been utilized in predicting the prognosis of malignancies such as gastric, cervical, and thyroid cancers, as well as in chronic conditions like hypertension, rheumatoid arthritis, multiple sclerosis, and acute conditions such as COVID-19, acute pancreatitis, acute coronary syndrome, and sepsis (17-22). One of the significant studies evaluating these factors in urolithiasis is the study conducted by Akshay Kriplani et al., which reported that high NLR and PLR ratios were statistically significant in predicting SIRS. Additionally, in this study, the preoperative NLR had a cut-off value of 2.03 with 82% sensitivity and 31% specificity for predicting postoperative SIRS, while the PLR had a cut-off value of 110.62 with 80.2% sensitivity and 50.5% specificity for postoperative SIRS (23). In our study, using multivariate logistic regression analysis, we identified the SII index as an independent risk factor, and through ROC analysis, we determined a cut-off value of 703 for predicting preoperative SIRS with better sensitivity (81.5%) and specificity (73.5%). Similar to the findings of Akshay Kriplani et al., we found that high NLR and PLR were relative risk factors for SIRS after RIRS. However, it is worth noting that Akshay Kriplani et al. did not exclude factors associated with SIRS such as DM, obesity, staghorn stones, and positive preoperative urine culture, which increases the possibility that the observed changes in hematological inflammatory markers may be attributed to these factors rather than being predictive. The cohort in our study was designed to minimize the potential effects of these risk factors on hematological inflammatory parameters. Thus we believe that our study's results are more meaningful compared to those of Akshay et al.

Furthermore, in contrast to Akshay Kriplani et al.'s study, where hemoglobin levels were reported as a relative risk factor. We identified hemoglobin levels as an independent risk factor and determined a cut-off value of 14.9 g/dL with 96.3% sensitivity and 56.0% specificity through ROC analysis. Our study group was formed by excluding patients who had factors that could potentially affect NLR, PLR, and SII index and were at a high risk of postoperative infection. This was conducted to minimize the effect of other related factors on hematological inflammatory parameters and to ensure that the results are more specifically associated with RIRS and urolithiasis.

The main limitations of the study include its retrospective design, the procedure not being performed by a single surgeon, and the small number of patients in the SIRS group within the sample. Another disadvantage of the retrospective design is the inability to evaluate other criteria reported as risk factors in the literature, such as increased intrapelvic pressure, irrigation rate and the preoperative use of DJ stents, which have not been standardized. However, despite all these limitations, we believe that the cut-off we determined for the SII index, which can be calculated from routine complete blood count, could serve as a cost-effective tool for clinicians in considering other factors such as operation time and planning close monitoring in the postoperative period for patients exceeding this value.

CONCLUSIONS

In conclusion, we have identified the SII index as an independent risk factor for predicting SIRS after RIRS.

Clinicians can consider the risk factors for SIRS reported in the literature and adjust their management strategies accordingly, particularly when the SII index exceeds 703. However, for these parameters to be clinically applicable, comparative, large-scale, prospective studies are needed.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest: All authors declare no potential conflict of interest with this publication.

Informed Consent: Informed consent was obtained from all participants in this study.

Ethical Approval: This study was approved by the Ataturk University Local Ethics Committee 30.03.2023 (approval number: B.30.2.ATA.0.01.00/235).

Author's Contribution: TA, and AEC designed the study protocol. SOD, and FA collected the data and did the statystical analysis. IK, and AU revised the manuscript. All authors wrote and revised the main text.

REFERENCES

1. Zeng G, Traxer O, Zhong W, et al. International Alliance of Urolithiasis guideline on retrograde intrarenal surgery. BJU international. 2023;131(2):153-164. https://doi.org/10.1111/bju.15836
2. Sari S, Ozok HU, Cakici MC, et al. A Comparison of Retrograde Intrarenal Surgery and Percutaneous Nephrolithotomy for Management of Renal Stones? 2 CM. Urol J. 2017;14(1):2949-2954.
3. Türk C, Petřík A, Sarica K, et al. EAU Guidelines on Interventional Treatment for Urolithiasis. Eur Urol. 2016;69(3):475-482. https://doi.org/10.1016/j.eururo.2015.07.041
4. Grosso AA, Sessa F, Campi R, et al. Intraoperative and postoperative surgical complications after ureteroscopy, retrograde intrarenal surgery, and percutaneous nephrolithotomy: a systematic review. Minerva urology and nephrology. 2021;73(3):309-332. https://doi.org/10.23736/s2724-6051.21.04294-4
5. Bhojani N, Miller LE, Bhattacharyya S, et al. Risk Factors for Urosepsis After Ureteroscopy for Stone Disease: A Systematic Review with Meta-Analysis. Journal of endourology. 2021;35(7):991-1000. https://doi.org/10.1089/end.2020.1133
6. Zahorec R. Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill. Bratislavske lekarske listy. 2001;102(1):5-14.
7. Han X, Liu S, Yang G, et al. Prognostic value of systemic hemato-immunological indices in uterine cervical cancer: A systemic review, meta-analysis, and meta-regression of observational studies. Gynecologic oncology. 2021;160(1):351-360. https://doi.org/10.1016/j.ygyno.2020.10.011
8. Finch W, Johnston R, Shaida N, et al. Measuring stone volume - three-dimensional software reconstruction or an ellipsoid algebra formula?. BJU Int. 2014;113(4):610-614. https://doi.org/10.1111/bju.12456
9. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). Jama. 23 2016;315(8):801-10. https://doi.org/10.1001/jama.2016.0287
10. Wagenlehner FM, Lichtenstern C, Rolfes C, et al. Diagnosis and management for urosepsis. Int J Urol. 2013;20(10):963-970. https://doi.org/10.1111/iju.12200
11. Dybowski B, Bres-Niewada E, Rzeszutko M, et al. Risk factors for infectious complications after retrograde intrarenal surgery - a systematic review and narrative synthesis. Central European journal of urology. 2021;74(3):437-445. https://doi.org/10.5173/ceju.2021.250
12. Bhojani N, Miller LE, Bhattacharyya S, et al. Risk Factors for Urosepsis After Ureteroscopy for Stone Disease: A Systematic Review with Meta-Analysis. J Endourol. 2021;35(7):991-1000. https://doi.org/10.1089/end.2020.1133

13. Gauhar V, Chew BH, Traxer O, et al. Indications, preferences, global practice patterns and outcomes in retrograde intrarenal surgery (RIRS) for renal stones in adults: results from a multicenter database of 6669 patients of the global FLEXible ureteroscopy Outcomes Registry (FLEXOR). World journal of urology. 2023;41(2):567-574. https://doi.org/10.1007/s00345-022-04257-z

14. Corrales M, Sierra A, Doizi S, et al. Risk of Sepsis in Retrograde Intrarenal Surgery: A Systematic Review of the Literature. European urology open science. 2022;44:84-91. https://doi.org/10.1016/j.euros.2022.08.008

15. Xu Y, Min Z, Wan SP, et al. Complications of retrograde intrarenal surgery classified by the modified Clavien grading system. Urolithiasis. 2018;46(2):197-202. https://doi.org/10.1007/s00240-017-0961-6

16. Moses RA, Ghali FM, Pais VM, et al. Unplanned Hospital Return for Infection following Ureteroscopy-Can We Identify Modifiable Risk Factors? The Journal of urology. 2016;195(4 Pt 1):931-6. https://doi.org/10.1016/j.juro.2015.09.074

17. Zhang J, Zhang L, Duan S, et al. Single and combined use of the platelet-lymphocyte ratio, neutrophil-lymphocyte ratio, and systemic immune-inflammation index in gastric cancer diagnosis. Frontiers in oncology. 2023;13:1143154. https://doi.org/10.3389/fonc.2023.1143154

18. Karadeniz F, Karadeniz Y, Altuntaş E. Systemic immune-inflammation index, and neutrophilto-lymphocyte and platelet-to-lymphocyte ratios can predict clinical outcomes in patients with acute coronary syndrome. Cardiovascular journal of Africa. 2023;34:1-7. https://doi.org/10.5830/cvja-2023-011

19. Gokce SF, Bolayır A, Cigdem B, et al. The role of systemic ımmune ınflammatory ındex in showing active lesion ın patients with multiple sclerosis: SII and other inflamatuar biomarker in radiological active multiple sclerosis patients. BMC neurology. 2023;23(1):64. https://doi.org/10.1186/s12883-023-03101-0

20. Xu JP, Zeng RX, Zhang YZ, et al. Systemic inflammation markers and the prevalence of hypertension: A NHANES cross-sectional study. Hypertension research : official journal of the Japanese Society of Hypertension. 2023;46(4):1009-1019. https://doi.org/10.1038/s41440-023-01195-0

21. Mangalesh S, Dudani S, Malik A. The systemic immune-inflammation index in predicting sepsis mortality. Postgraduate medicine. 2023;135(4):345-351. https://doi.org/10.1080/00325481.2022.2140535

22. Kosidło JW, Wolszczak-Biedrzycka B, Matowicka-Karna J, et al. Clinical Significance and Diagnostic Utility of NLR, LMR, PLR and SII in the Course of COVID-19: A Literature Review. Journal of inflammation research. 2023;16:539-562. https://doi.org/10.2147/jir.S395331

23. Kriplani A, Pandit S, Chawla A, et al. Neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and lymphocyte-monocyte ratio (LMR) in predicting systemic inflammatory response syndrome (SIRS) and sepsis after percutaneous nephrolithotomy (PNL). Urolithiasis. 2022;50(3):341-348. https://doi.org/10.1007/s00240-022-01319-0

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1645041

RESEARCH ARTICLE

The Responses of Artificial Intelligence to Questions About Urological Emergencies: A Comparison of 3 Different Large Language Models

Ubeyd Sungur[1], Yusuf Arıkan[2], Ahmet Tuğrul Türkay[1], Hakan Polat[1]

[1] Department of Urology, University of Health Sciences, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Türkiye
[2] Department of Urology, University of Health Sciences, Tepecik Training and Research Hospital, Izmir, Türkiye

Submitted: *2025-02-22*
Accepted: *2025-05-29*

Corresponding Author;
Ubeyd Sungur, MD
Address: University of Health Sciences Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Department of Urology, Zuhuratbaba Mah, Dr. Tevfik Sağlam Cd No:11, 34147 Bakırköy/İstanbul, Türkiye
E-mail: ubeydsungur@gmail.com

ORCID
U.S. 0000-0002-8910-9859
Y.A. 0000-0003-0823-7400
A.T.T. 0009-0005-4210-8954
H.P. 0000-0003-1525-1243

Abstract

Objective: This study aimed to compare the accuracy and adequacy of responses provided by three different large language models (LLMs) utilizing artificial intelligence technology to fundamental questions related to urological emergencies.

Material and Methods: Nine distinct urological emergency topics were identified, and a total of 63 fundamental questions were formulated for each topic, including two related to diagnosis, three related to disease management, and two related to complications. The questions were posed in English on three different free AI platforms (ChatGPT-4, Google Gemini 2.0 Flash, and Meta Llama 3.2), each utilizing different infrastructures, and responses were documented. The answers were scored by the authors on a scale of 1 to 4 based on accuracy and adequacy, and the results were compared using statistical analysis.

Results: When all question-answer pairs were evaluated overall, ChatGPT exhibited slightly higher accuracy rates compared to Gemini and Meta Llama; however, no statistically significant differences were detected among the groups (3.8 ± 0.5, 3.7 ± 0.6, and 3.7 ± 0.5, respectively; p=0.146). When questions related to diagnosis, treatment management, and complications were evaluated separately, no statistically significant differences were detected among the three LLMs (p=0.338, p=0.289, and p=0.407, respectively). Only one response provided by Gemini was found to be completely incorrect (1.6%). No misleading or wrong answers were observed in the diagnosis-related questions across all three platforms. In total, misleading answers were observed in 2 questions (3.2%) for ChatGPT, three questions (4.7%) for Gemini, and two questions (3.2%) for Meta Llama.

Conclusion: LLMs predominantly provide accurate results to basic and straightforward questions related to urological emergencies, where prompt treatment is critical. Although no significant differences were observed among the responses of the three LLMs compared in this study, the presence of misleading and incorrect answers should be carefully considered, given the evolving nature and limitations of this technology.

Keywords: urological emergencies, artificial intelligence, large language models

Cite; Sungur U, Arikan Y, Turkay AT, Polat H. The Responses of Artificial Intelligence to Questions About Urological Emergencies: A Comparison of 3 Different Large Language Models. New J Urol. 2025;20(2):89-96. **doi:** https://doi.org/10.33719/nju1645041

INTRODUCTION

Urological emergencies are clinical conditions that require immediate initiation of treatment, as delays in patient admission can lead to irreversible consequences (1). While time is critical in testicular torsion, early medical and surgical intervention is essential in conditions such as urosepsis, which can lead to multiorgan dysfunction and the need for intensive care (2,3).

As technology has advanced, both patients and healthcare providers have increasingly turned to the Internet to research the conditions they encounter (4). Large language models (LLM) developed using artificial intelligence (AI) technology have demonstrated the ability to respond to queries and provide rapid data on even highly specialized topics. Over the years, this rapidly evolving technology has led to the development of AI assistants such as ChatGPT, Google Gemini, and Meta Llama AI, each utilizing distinct infrastructures. The use of AI assistants in medical contexts has gained increasing attention in recent years, paving the way for numerous studies (5). Many studies have been published on the efficacy of their application in various diseases (6). However, the adequacy and reliability of the responses provided by these assistants, which are easily accessible to patients in time-sensitive urological emergencies, remain questionable.

This study aimed to evaluate the accuracy and adequacy of responses provided by three different AI-powered platforms to fundamental questions regarding urological emergencies, focusing on diagnosis, treatment management, and complications.

MATERIAL AND METHODS

Nine different topics were identified as urological emergencies: Testicular Torsion, Hematuria, Obstructive Uropathies, Penile Fracture, Urosepsis, Paraphimosis, Fournier's Gangrene, Priapism, and Trauma. For each topic, seven questions were prepared: two related to diagnosis, three related to treatment management, and two related to complications. While preparing the questions, instead of expecting lengthy responses from each AI platform, the command "Can you answer in one paragraph?" was used to request concise answers. The questions were selected focusing on frequently asked fundamental questions. The list of questions is provided in Table 1. Each question was asked separately on new pages to ChatGPT, Gemini, and Meta Llama to prevent any influence from usage history, and responses were documented. The answers were evaluated by the authors participating in the study and scored on a scale of 1 to 4 (1: Completely incorrect, 2: Correct but misleading, 3: Correct but insufficient, 4: Completely correct). The scores were recorded and grouped based on diagnostic questions, treatment management questions, and complication-related questions, followed by statistical analysis. No real patients or patient information were shared in this study. This study was conducted following the Helsinki Declaration.

Statistical Analysis

The mean and deviation, number, and percentage values for the answers given to the questions in three different subgroups and the total for each AI model were documented. Results were analyzed using a non-parametric test. The Friedman test was employed for the comparison of the three groups. A p-value of < 0.05 was considered statistically significant. For the analysis of the study, IBM Statistical Package for Social Sciences SPSS 26.0.1 (IBM, Corp., Armonk, NY, USA) was utilized.

Large Language Models in Artificial Intelligence

ChatGPT-4 is an AI model developed by OpenAI, offering a more comprehensive language understanding and generation capacity compared to its predecessors. It is developed in the USA, with headquarters in San Francisco, California. This model can be utilized across various domains, ranging from everyday conversational language to technical or scientific texts. While interacting with a user, it comprehends the context of the question and generates appropriate responses. Additionally, it seamlessly adapts to multilingual content, enabling smooth communication in different languages.

Gemini 2.0 Flash is an AI model developed by Google DeepMind, with primary facilities located in Mountain View, California. This model is capable of processing visual and textual data simultaneously. This feature allows the model to respond to text-based questions while also interpreting and analyzing visual content. Its most notable characteristic is its ability to integrate information learned from diverse data sources, enabling it to make sense of complex scenarios.

LLama 3.2 is an AI model developed by Meta Llama AI, with major operations based in Menlo Park, California. LLama 3.2 is an AI system that stands out for its efficiency among language models. Its ability to deliver high performance with lower computational power has made it a preferred tool for large-scale projects and diverse applications. The model learns from a vast number of textual sources and provides accurate responses even in complex textual contexts.

RESULTS

When the responses to the 18 diagnosis-related questions were compared, the mean scores for ChatGPT, Gemini, and Meta Llama were calculated as 3.8 ± 0.4, 3.8 ± 0.4, and 3.6 ± 0.5, respectively (p=0.338). ChatGPT provided completely correct answers to 15 (83.3%) questions, while Gemini and Meta Llama provided completely correct answers to 14 (77.8%) and 11 (61.1%) questions, respectively. None of the three platforms provided completely incorrect or misleading answers to any of the diagnosis-related questions.

When the responses to the 27 treatment management-related questions were compared, the mean scores for ChatGPT, Gemini, and Meta Llama were calculated as 3.9 ± 0.5, 3.6 ± 0.8, and 3.8 ± 0.5, respectively (p=0.289). ChatGPT provided completely correct answers to 24 (88.9%) questions, while Gemini and Meta Llama provided completely correct answers to 21 (77.8%) and 22 (81.5%) questions, respectively. Gemini provided a completely incorrect answer to 1 (3.7%) question, while the other platforms had no completely wrong answers. Insufficient and misleading answers were observed in 3 (11.1%), 5 (18.5%), and 5 (18.5%) questions for ChatGPT, Gemini, and Meta Llama, respectively.

When the responses to the 18 complication-related questions were compared, the mean scores for ChatGPT, Gemini, and Meta Llama were calculated as 3.8 ± 0.5, 3.8 ± 0.5, and 3.6 ± 0.6, respectively (p=0.407).

Overall, when considering all topics, the mean scores for ChatGPT, Gemini, and Meta Llama were calculated as 3.8 ± 0.5, 3.7 ± 0.6, and 3.7 ± 0.5, respectively (p=0.146). ChatGPT provided completely correct answers to 54 (85.7%) questions, while Gemini and Meta Llama provided completely correct answers to 50 (79.4%) and 45 (71.4%) questions, respectively. The mean scores and percentages of correct answers for the three platforms are presented in Table 2. The mean scores of three LLMs are shown in Figure 1.

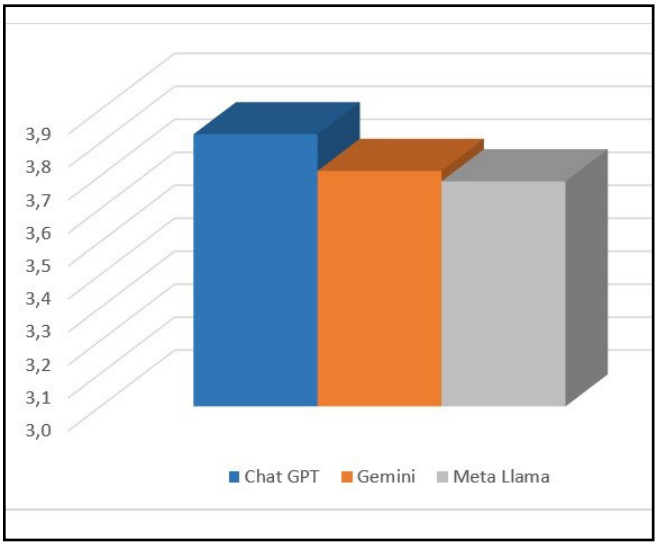


Figure 1. Mean values graph of three different AI models

Table 1. The Questions of Urological Emergencies

1.1.1 What could be the cause of sudden onset scrotal pain?
1.1.2 What is the reason for upward displacement and tenderness of the testicle in the scrotal region?
1.2.1 What is the treatment for testicular torsion, and when should it be performed?
1.2.2 Are there any non-surgical treatment options for testicular torsion?
1.2.3 From which site is surgery for testicular torsion performed?
1.3.1 What are the consequences of delayed treatment in testicular torsion?
1.3.2 Does testicular torsion lead to infertility?
2.1.1 What are the causes of blood in urine?

2.1.2 What could be the reason for black fragments in the urine?
2.2.1 What are the treatments for hematuria?
2.2.2 Is hematuria an emergency, and does it require surgery?
2.2.3 Are there non-surgical treatments for hematuria?
2.3.1 What are the outcomes if hematuria is left untreated?
2.3.2 What complications can occur in individuals with hematuria?
3.1.1 What causes decreased urine output and abdominal distension?
3.1.2 What are the reasons for nausea, vomiting, and severe flank pain?
3.2.1 What are the treatments for acute urinary retention?
3.2.2 What treatments are available for obstruction caused by kidney or ureteral stones?
3.2.3 Is urinary tract obstruction an emergency, and how soon should it be treated?
3.3.1 What complications arise from urinary retention?
3.3.2 What are the consequences of untreated obstruction due to kidney or ureteral stones?
4.1.1 What causes a sound and loss of erection during sexual activity?
4.1.2 What leads to bruising and loss of rigidity in the erect penis?
4.2.1 What is the treatment for penile fracture?
4.2.2 Are there non-surgical treatment options for penile fracture?
4.2.3 When should surgery for penile fracture be performed?
4.3.1 What are the potential complications of penile fracture?
4.3.2 What are the risks if penile fracture repair is not performed?
5.1.1 What causes fever and pain during urination, or perineal pain?
5.1.2 What causes fever in a person passing a kidney stone?
5.2.1 Is acute prostatitis an emergency, and how should it be managed?
5.2.2 How is obstructive pyelonephritis treated?
5.2.3 Are there non-invasive treatment options for fever caused by ureteral stones?
5.3.1 What are the long-term outcomes of urosepsis due to urological disease?
5.3.2 What happens if fever during stone passage is left untreated?
6.1.1 What causes bruising and swelling of the penis in children?
6.1.2 Why does the inability to retract the foreskin occur?
6.2.1 What treatments are available for phimosis-paraphimosis?
6.2.2 Are there non-surgical treatments for paraphimosis?
6.2.3 Does phimosis-paraphimosis require emergency intervention?
6.3.1 Does untreated paraphimosis lead to permanent consequences as the child grows?
6.3.2 What are the outcomes of untreated paraphimosis?
7.1.1 What causes bruising and discharge in the perineal area?
7.1.2 What is the reason for pain, hardness, and discoloration in the scrotum?
7.2.1 Is Fournier gangrene an emergency, and how is it treated?
7.2.2 Are there non-surgical treatments for Fournier gangrene?
7.2.3 How is the surgical area repaired after Fournier gangrene surgery?

7.3.1 What complications may develop in a person with Fournier gangrene?
7.3.2 What are the risks of delayed treatment for Fournier gangrene?
8.1.1 What causes prolonged and persistent penile erection?
8.1.2 How long is persistent erection considered abnormal?
8.2.1 Is priapism an emergency, and what treatments are available?
8.2.2 What are the types of priapism, and how are they diagnosed?
8.2.3 Can priapism be resolved with non-invasive methods or medications?
8.3.1 What are the long-term complications of priapism?
8.3.2 What are the risks of untreated priapism?
9.1.1 How is renal injury diagnosed after a traffic accident?
9.1.2 What causes abdominal distension and flank pain following gynecological surgery?
9.2.1 How is the treatment decision made for blunt or penetrating renal injuries?
9.2.2 What are the treatment types for bladder perforation, and how is the decision made?
9.2.3 How is treatment managed in cases of ureteral injury during surgery?
9.3.1 What complications can arise in conservatively managed renal trauma?
9.3.2 What are the risks of delayed treatment for ureteral injury during surgery?

Table 2. Comparative analysis between the different large language models about urological emergency questions

	Chat-GPT	**Gemini**	**Meta Llama**	
Question Topics, mean ± SD **Answer Proficiency, (n, %)**	**(n = 63)**	**(n = 63)**	**(n = 63)**	**p**
Diagnostic questions	3.8 ± 0.4	3.8 ± 0.4	3.6 ± 0.5	0.338
Completely Correct	15 (83.3)	14 (77.8)	11 (61.1)	
Correct but insufficient	3 (16.7)	4 (22.2)	7 (38.9)	
Correct but misleading	0 (0)	0 (0)	0 (0)	
Completely incorrect	0 (0)	0 (0)	0 (0)	
Questions regarding treatment management	3.9 ± 0.5	3.6 ± 0.8	3.8 ± 0.5	0.289
Completely Correct	24 (88.9)	21 (77.8)	22 (81.5)	
Correct but insufficient	2 (7.4)	3 (11.1)	4 (14.8)	
Correct but misleading	1 (3.7)	2 (7.4)	1 (3.7)	
Completely incorrect	0 (0)	1 (3.7)	0 (0)	
Questions regarding complications	3.8 ± 0.5	3.8 ± 0.5	3.6 ± 0.6	0.407
Completely Correct	15 (83.3)	15 (83.3)	12 (66.7)	
Correct but insufficient	2 (11.1)	2 (11.1)	5 (27.7)	
Correct but misleading	1 (5.6)	1 (5.6)	1 (5.6)	
Completely incorrect	0 (0)	0 (0)	0 (0)	
Total	3.8 ± 0.5	3.7 ± 0.6	3.7 ± 0.5	0.146
Completely Correct	54 (85.7)	50 (79.4)	45 (71.4)	
Correct but insufficient	7 (11.1)	9 (14.3)	16 (25.4)	
Correct but misleading	2 (3.2)	3 (4.7)	2 (3.2)	
Completely incorrect	0 (0)	1 (1.6)	0 (0)	

DISCUSSION

AI applications have advanced rapidly in recent years, becoming an integral part of daily life. In the field of healthcare, they have been the subject of studies in a wide range of areas, including disease diagnosis, treatment management, prediction of complications, and interpretation of imaging and pathology examinations (6). Large language models (LLMs) powered by AI provide rapid responses by interpreting written text, scanning open sources, and summarizing information (7). This capability raises the possibility of their use by both patients and healthcare providers. Although algorithms developed for use by healthcare providers have not yet entered routine practice, their widespread adoption is anticipated in the near future. Meanwhile, the accuracy and adequacy of these platforms, which are used by patients to obtain information, have become a topic of interest. The correctness and adequacy of responses provided by LLMs in patient education have been examined across various subtopics (8). This study aimed to investigate whether the responses generated by LLMs to basic questions in urological emergencies, which may require time-sensitive decision-making, are consistent with the literature, accurate, and reliable.

Urological emergencies encompass a variety of conditions, ranging from testicular torsion, which requires immediate intervention, to hematuria, which may allow for a relatively longer diagnostic window but can still lead to urgent outcomes. The lack of awareness of testicular torsion among patients and their families, delayed hospital presentation, and the potential for organ loss or future infertility can result in devastating consequences. A study investigating the causes of delayed testicular torsion found that only 23.8% of cases underwent timely surgery. Misdiagnosis and the initial consultation with a non-urologist were identified as risk factors for orchiectomy, emphasizing the importance of proper technical training and referral to prevent delays in the diagnosis and treatment of testicular torsion (9). In cases of testicular torsion presenting with scrotal pain, consulting a large language model (LLM) in remote areas with limited healthcare access could potentially reduce the time to initial presentation, thereby preventing orchiectomy.

Another example is urolithiasis, a highly prevalent condition in the general population. Although hospital visits and the need for analgesic treatment due to renal colic are common, patients may prefer to manage the condition without seeking medical attention based on prior experiences or anecdotal information. However, the development of fever and infection during this process may result in complicated urinary tract infections, such as pyelonephritis with obstruction, which, if left untreated, may progress to sepsis and multiorgan failure (10). Therefore, the lack of awareness among patients about the risk of sepsis in cases of renal colic complicated by infection may result in adverse outcomes in individuals who do not seek medical care. A comprehensive study examining factors related to mortality in obstructive pyelonephritis concluded that delayed decompression was associated with increased mortality, with higher rates observed in weekend admissions (11).

Another condition, penile fracture, occurs as an unexpected medical event in men. The dramatic presentation, including an audible snap during sexual intercourse and the appearance of hematoma, often signals the urgency of the situation even to untrained individuals. However, in such acute medical scenarios, the accuracy and reliability of responses provided by a free AI platform, which patients might consult to determine the urgency and potential complications, are of critical importance. In this study, we prioritized evaluating the responses of LLMs for patient education and guidance in these contexts.

Our results demonstrated that AI platforms generally provide accurate and adequate responses to basic questions regarding urological emergencies. While similar responses were predominantly observed across the three different AI assistants, no statistically significant differences were found among the results. The recent study examining the use of ChatGPT for self-diagnosis in orthopedic conditions suggested that, although it could serve as a potential initial step in accessing healthcare, it contained inconsistent results and emphasized the necessity of including clear language encouraging users to seek expert medical opinions (12). Another study investigating the use of AI platforms for emergency medical conditions highlighted that, even if the results are consistent, the ambiguity of sources and the presence of misleading information regarding the timing of medical interventions should be carefully considered due to potential risks (13). Scott et al., in their study evaluating AI-

generated responses to urology patient messages, noted that ChatGPT performed better on simple questions compared to complex ones, suggesting its potential to assist care teams (14). A recent systematic review examining the use of LLMs in patient care underscored the need for caution due to the uncertainties inherent in this technology (15).

Furthermore, ethical considerations must be addressed, particularly concerning the reliance on AI tools without professional Supervision. As AI systems evolve, ensuring transparency in source attribution and decision-making logic becomes essential. Healthcare professionals must be aware of the limitations of these tools and use them as supplementary rather than primary decision-making instruments.

Studies involving LLMs must take into account several limitations. First, the instability of the platforms used, their ongoing development, and their potential for rapid evolution over time highlight the necessity of interpreting findings based on the specific conditions of the platforms at the time of the study. We emphasize that our study focused on basic and straightforward questions, with responses summarized in paragraph form for evaluation. The likelihood of inaccuracies or misleading information may increase with more complex and lengthy responses. Since we aimed to investigate basic questions in emergency scenarios, we believe it would be inappropriate to conclude complex urological emergency conditions based on these questions and answers. Given the continuous advancement and widespread adoption of these platforms, we consider it crucial to assess and research their accuracy and reliability consistently.

CONCLUSION

Three different AI-based LLM models (ChatGPT-4, Google Gemini 2.0 Flash, and Meta Llama 3.2), which are freely accessible to patients, predominantly provided accurate responses to basic and simple questions related to urological emergency conditions. There was no significant difference in the summarized responses among the three platforms. While the use of AI assistants in patient education and guidance is becoming increasingly widespread, it is important to recognize that the current technology is not yet capable of delivering fully qualified and adequate healthcare services, given the potential for misleading or incorrect responses.

Funding: The authors declare that this study received no financial support.

Data Sharing Statement: The results of the study were not published in full or in part in the form of abstracts.

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

Ethical Approval: Chat-GPT, Google Gemini, and Meta Llama are publicly available artificial intelligence models, and there are no animal or human research participants in our study. For these reasons, our study did not require ethics committee approval.

Informed Consent: There is no need for informed consent in this study.

Authorship Contribution: Ubeyd Sungur: Conception and design, Data analysis and interpretation, Drafting the manuscript, Critical revision of the manuscript for the content, Statistical analysis. Yusuf Arıkan: Critical revision of the manuscript for the content and supervision. Ahmet Tuğrul Türkay: Data acquisition, Drafting the manuscript. Hakan Polat: Data acquisition and supervision.

REFERENCES

1. Rosenstein D, McAninch JW. Urologic emergencies. Med Clin North Am. 2004;88:495-518. https://doi.org/10.1016/S0025-7125(03)00190-1
2. Sharp VJ, Kieran K, Arlen AM. Testicular torsion: Diagnosis, evaluation, and management. Am Fam Physician. 2013;88:835-840. https://pubmed.ncbi.nlm.nih.gov/24364548/
3. Wagenlehner FM, Lichtenstern C, Rolfes C, et al. Diagnosis and management for urosepsis. Int J Urol. 2013;20:963-970. https://doi.org/10.1111/iju.12200
4. Stoumpos AI, Kitsios F, Talias MA. Digital Transformation in Healthcare: Technology Acceptance and Its Applications. Int J Environ Res Public Health. 2023;20:3407. https://doi.org/10.3390/ijerph20043407
5. Topol EJ. High-performance medicine: the convergence

of human and artificial intelligence. Nat Med. 2019;25:44-56. https://doi.org/10.1038/s41591-018-0300-7

6. Jiang F, Jiang Y, Zhi H, et al. Artificial intelligence in healthcare: Past, present and future. Stroke Vasc Neurol. 2017;2:230-243. https://doi.org/10.1136/svn-2017-000101

7. Alowais SA, Alghamdi SS, Alsuhebany N, et al. Revolutionizing healthcare: the role of artificial intelligence in clinical practice. BMC Med Educ. 2023;23:689. https://doi.org/10.1186/s12909-023-04698-z

8. Wang D, Zhang S. Large language models in medical and healthcare fields: applications, advances, and challenges. Artif Intell Rev. 2024;57:1-48. https://doi.org/10.1007/s10462-024-10921-0

9. Yi H, Wang D, Wu X, et al. Analysis of factors associated with delayed diagnosis and treatment of testicular torsion in 1005 cases from Chongqing city, China: a cross-sectional study. Sci Rep. 2023;13:1-10. https://doi.org/10.1038/s41598-023-49820-9

10. Hsiao CY, Chen TH, Lee YC, et al. Urolithiasis Is a Risk Factor for Uroseptic Shock and Acute Kidney Injury in Patients With Urinary Tract Infection. Front Med. 2019;6:288. https://doi.org/10.3389/fmed.2019.00288

11. Haas CR, Li G, Hyams ES, Shah O. Delayed Decompression of Obstructing Stones with Urinary Tract Infection is Associated with Increased Odds of Death. J Urol. 2020;204:1256-1262. https://doi.org/10.1097/JU.0000000000001182

12. Kuroiwa T, Sarcon A, Ibara T, et al. The Potential of ChatGPT as a Self-Diagnostic Tool in Common Orthopedic Diseases: Exploratory Study. J Med Internet Res. 2023;25:e47621. https://doi.org/10.2196/47621

13. Yau JYS, Saadat S, Hsu E, et al. Accuracy of Prospective Assessments of 4 Large Language Model Chatbot Responses to Patient Questions About Emergency Care: Experimental Comparative Study. J Med Internet Res. 2024;26:e60291. https://doi.org/10.2196/60291

14. Scott M, Muncey W, Seranio N, et al. Assessing Artificial Intelligence-Generated Responses to Urology Patient In-Basket Messages. Urol Pract. 2024;11:793-798. https://doi.org/10.1097/UPJ.0000000000000637

15. Busch F, Hoffmann L, Rueger C, et al. Current applications and challenges in large language models for patient care: a systematic review. Commun Med. 2025;5:26. https://doi.org/10.1038/s43856-024-00717-2

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1649999

RESEARCH ARTICLE

Intravesical Prostatic Protrusion and Surgical Outcomes in Benign Prostatic Hyperplasia: A Magnetic Resonance Imaging-Based Evaluation

Emre Uzun [1], Kazım Ceviz [1], Hüseyin Gültekin [1], Hasan Batuhan Arabacı [1], Giray Özgirgin [1], Samet Şenel [1]

[1] Department of Urology, Ankara City Hospital, Ankara, Türkiye

Submitted: *2025-03-07*
Accepted: *2025-05-24*

Corresponding Author;
Emre Uzun, MD
Address: Department of Urology, Ankara City Hospital, Türkiye, Ankara Ankara City Hospital Oncology Building Çankaya, Ankara, Türkiye
E-mail: emr.uzun.7@gmail.com

ORCID
E.U. 0000-0002-1929-0074
K.C. 0000-0001-6343-383X
H.G. 0000-0003-2763-0777
H.B.A. 0000-0002-0138-9092
G.Ö. 0009-0000-6364-2148
S.Ş. 0000-0003-2280-4192

Abstract

Objective: This study aimed to investigate the impact of preoperative intravesical prostatic protrusion (IPP) measurements obtained via magnetic resonance imaging (MRI) on postoperative outcomes in patients undergoing transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH).

Material and Methods: A retrospective review was performed on 160 patients who underwent monopolar TURP at our clinic between January 2021 and December 2023. IPP was measured on sagittal MRI images as the vertical distance from the bladder base to the tip of the prostate protruding into the bladder. Patients were divided into three groups according to IPP length: Group A (IPP <5 mm, n=25), Group B (5 mm ≤ IPP <10 mm, n=30), and Group C (IPP ≥10 mm, n=38). Preoperative and postoperative data, including prostate-specific antigen (PSA) levels, International Prostate Symptom Score (IPSS), average urinary flow rate (Qavg), and maximum urinary flow rate (Qmax), were collected and analyzed across the groups.

Results: The mean age of the patients was 65.3 ± 6.7 years. PSA levels were significantly higher in Group C compared to Group A (p=0.014). Prostate volume and the volume of resected tissue were significantly greater in Group C than in Groups A and B (p<0.001). Postoperatively, all groups showed significant decreases in PSA and IPSS values, along with significant increases in Qmax and Qavg. The improvement in Qmax after TURP was significantly greater in Groups B and C compared to Group A (p=0.019). However, the reduction in IPSS scores did not differ significantly among the groups (p=0.727).

Conclusion: IPP correlates positively with prostate volume, PSA levels, and the amount of resected tissue. TURP significantly improves urinary function and symptom scores regardless of IPP length. However, the improvement in Qmax is more pronounced in patients with a higher IPP. IPP measurement may serve as a useful parameter in the surgical decision-making process for BPH patients.

Keywords: intravesical prostatic protrusion, benign prostatic hyperplasia, transurethral resection of the prostate, magnetic resonance imaging, urinary function.

Cite; Uzun E, Ceviz K, Gultekin H, Arabaci HB, Ozgirgin G, Senel S. Intravesical Prostatic Protrusion and Surgical Outcomes in Benign Prostatic Hyperplasia: A Magnetic Resonance Imaging-Based Evaluation. New J Urol. 2025;20(2):97-103. **doi:** https://doi.org/10.33719/nju1649999

INTRODUCTION

Benign prostatic hyperplasia (BPH) is a histological diagnosis characterized by the proliferation of stromal and epithelial cells. It is found in more than half of men over the age of 60 and in almost all men over the age of 80. It is the most common cause of bladder outlet obstruction (BOO), leading to lower urinary tract symptoms (LUTS) in men over 50 years of age (1,2).

For patients with mild to moderate symptoms, initial management of BPH includes observation and medical treatment (3). Surgical options are primarily considered for patients who do not benefit from conservative treatment (careful monitoring and lifestyle modifications) or medical therapy and have severe symptoms (4). Although alternative treatments have emerged in the last 20 years with advancing technology, transurethral resection of the prostate (TURP) has traditionally been considered the gold standard for surgical treatment of BPH due to its low complication rates and high satisfaction rates (5).

Intravesical prostatic protrusion (IPP) is defined as the anatomical extension of the median or lateral lobes of the prostate into the bladder. Several studies have shown that IPP measurement affects the success of medical treatment, catheter-free follow-up of patients with acute urinary retention (AUR), and surgical outcomes (6,7,8).

This study aims to evaluate the effect of IPP measurement using multiparametric magnetic resonance imaging (MRI) of the prostate on postoperative outcomes following TURP.

MATERIAL AND METHODS

The data of 160 patients who underwent monopolar transurethral resection of the prostate (M-TURP) at Ankara Bilkent City Hospital between January 2021 and December 2023 were retrospectively analyzed after institutional review board approval (TABED 2-24-605). Patients with a history of prostate or urethral surgery (n=15), those diagnosed with neurogenic bladder (n=2), and those without multiparametric prostate MRI or detectable IPP on MRI (n=50) were excluded. A total of 93 patients were included in the study.

Multiparametric prostate MRI was performed using a 3T system (Verio, Erlangen, Siemens, Germany) with an empty bladder. IPP was measured by a specialized urologist on sagittal multiparametric prostate MRI images as the vertical distance from the protruding tip of the prostate to the bladder base (Figure 1). The patients were divided into three groups according to IPP measurements, taking as an example the studies conducted by Topazio L. and Oshagbemi AO. et al.: Group A (IPP <5mm, n=25), Group B (5mm < IPP <10mm, n=30) and Group C (IPP >10mm, n=38)(7, 8).

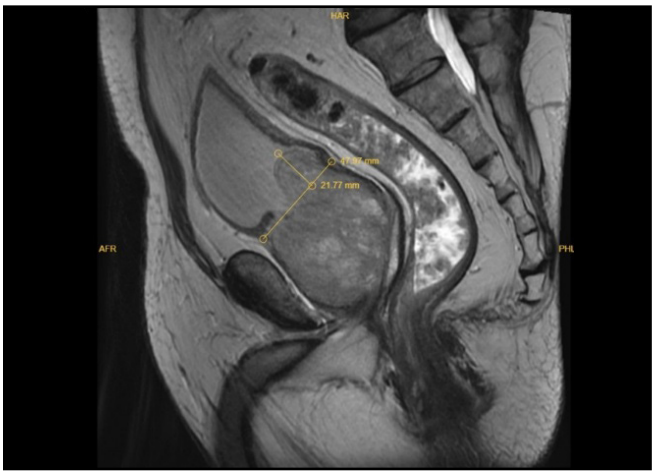


Figure 1. Prostate MRI sagittal section image, IPP measurement

Patient demographics, comorbidities (hypertension, diabetes mellitus, coronary artery disease, neurological diseases), history of hematuria and urinary retention, preoperative parameters (prostate-specific antigen [PSA] level, International Prostate Symptom Score [IPSS], maximum urinary flow rate [Qmax], mean urinary flow rate [Qavg], prostate volume [PV]) were recorded.

Surgical indications included acute urinary retention, Qmax <15 ml/s, and upper urinary tract dilation. All procedures were performed by experienced urologists specializing in endoscopic prostate surgery.

PSA levels, IPSS, Qmax, and Qavg were recorded six months postoperatively, and changes were analyzed.

Surgical Technique

TURP was performed by experienced urologists using a 26Fr resectoscope, monopolar electrocautery, and a continuous irrigation system with 5% mannitol following conventional techniques.

Statistical Analysis

Statistical analyses and data coding were performed using SPSS 22 software (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The Shapiro-Wilk test was used to evaluate the normality of variable distributions. Variables with normal distribution are reported as mean ± standard deviation, while non-normally distributed variables are expressed as medians (interquartile ranges). Categorical variables were compared using the Chi-square or Fisher's exact test, and numerical variables were compared using the Kruskal-Wallis variance analysis. Wilcoxon or Paired Samples tests were used to compare preoperative and postoperative parameters. The two-way mixed ANOVA test was used to evaluate differences in Qmax and IPSS changes among groups. Statistical significance was set at $P < 0.05$ significance.

RESULTS

The mean patient age was 65.3±6.7 years. The clinical, preoperative, and postoperative data of the patients are presented in Table 1. The median IPP was 4mm in Group A, 7.2mm in Group B, and 15.9mm in Group C. The median PSA level in Group C was significantly higher than in Group A (p=0.014). While the prostate volume and resected tissue mass were similar in Groups A and B, they were significantly higher in Group C (p<0.001). Postoperatively, PSA levels and IPSS scores significantly decreased, whereas Qmax and Qavg significantly increased in all groups. The increase in Qmax post-TURP was significantly higher in Groups B and C than in Group A ($F(2,90)=137.499$, p=0.019) (Figure 2). However, there was no significant difference in IPSS reduction among the three groups postoperatively ($F(2,90)=241.122$, p=0.727) (Figure 3).

Table 1. Grouping of patients who underwent TURP for BPH according to IPP length and their clinical, preoperative and postoperative characteristics

	Group A (n=25, % 26.9)	**Group B (n=30, % 32.3)**	**Group C (n=38, % 40.8)**	**p**	**p (Pairwise Comparisons)**
Age (Years) (Mean±SD)	63.9±6.6	66.4±7.2	65.3±6.2	0.266[k]	
Comorbodities					
DM, n (%)	5 (20)	6 (20)	14 (36.8)	0.198[c]	
HT, n (%)	13 (52)	12 (40)	18 (47.4)	0.663[c]	
CAD, n (%)	7 (28)	11 (36.7)	7 (18.4)	0.239[c]	
COPD, n (%)	1 (4)	2 (6.7)	0 (0)	0.267[f]	
Neurological Diseases, n (%)	1 (4)	1 (3.3)	1 (2.6)	0.955[f]	
Hypothyroidism, n (%)	2 (8)	1 (3.3)	3 (7.9)	0.759[f]	
Clinical Data					
History of Hematuria, n (%)	1 (4)	3 (10)	7 (18.4)	0.256[f]	
History Of Urinary Retantion, n (%)	5 (20)	5 (16.7)	9 (23.7)	0.774[c]	
Preoperative Data					
Preoperative PSA (ng/dL) (Median [IQR])	1.7 (0.9-3.1)	2.7 (1-6.5)	3.7 (2.1-6.3)	**0.019[k]**	[*]0.33 [**]0.687 [***]**0.014**
Postoperative PSA (ng/dL) (Median [IQR])	1.2 (0.5-2.1)	1.4 (0.7-1.9)	1.9 (1-3.6)	0.069[k]	
P	**0.007[w]**	**0.001[w]**	**<0.001[w]**		
Preoperative Qmax (mL/sec) (Median [IQR])	11.3 (8.1-15.5)	10.8 (8.3-16.3)	7.9 (6.4-12.9)	0.072[k]	

Postoperative Qmax (mL/sec) (Median [IQR])	17.5 (14.9-20.4)	23.2 (16.7-29.6)	20.5 (14.8-30.2)	**0.047**[k]	*__0.047__ **0.296 ***0.985
P	**<0.001**[p]	**<0.001**[p]	**<0.001**[p]		
Preop Qavg (mL/sec) (Median [IQR])	4 (3.3-5.9)	4.7 (3.1-7.3)	3.2 (2.6-4.6)	0.13[k]	
Postop Qavg (mL/sec) (Median [IQR])	8.5 (7.2-13.1)	8.2 (6.7-9.5)	9.2 (5.9-11.1)	0.414[k]	
P	**<0.001**[p]	**<0.001**[p]	**<0.001**[p]		
Preoperative Voided Volume(cc) (Median [IQR])	255 (182-375)	214 (172-299)	185 (154-268)	**0.02**[k]	*0.662 **0.364 ***__0.017__
Postoperative Voided Volume (cc) (Median [IQR])	285 (222-362)	290 (187-371)	249 (172-325)	0.437[k]	
P	0.753[w]	**0.037**[p]	**0.018**[p]		
Preoperative IPSS (Median [IQR])	21 (17-25)	23.5 (19-29)	22.5 (18.7-25.2)	0.313[k]	
Postoperative IPSS (Median [IQR])	13 (8-15.5)	12 (7.5-17)	9.5 (7-16.2)	0.705[k]	
P	**<0.001**[p]	**<0.001**[p]	**<0.001**[p]		
Prostate Volume (cc) (Median [IQR])	45 (32-62)	55 (47-64)	70 (56-90)	**<0.001**[k]	*0.548 **__0.014__ ***__<0.001__
IPP (mm) (Median [IQR])	4 (3.3-4.2)	7.2 (6.1-8.8)	15.9 (13-17.8)	**<0.001**[k]	*__<0.001__ **__<0.001__ ***__<0.001__
Preoperative PVR (cc) (Median [IQR])	42 (28-92)	105 (43-191)	105 (78-170)	**0.019**[k]	*0.194 **0.999 ***__0.018__
Amount of Tissue Resected (gr) (Median [IQR])	12 (6.5-17.5)	15 (11.5-21)	24 (20-30)	**<0.001**[k]	*<0.295 **__0.004__ ***__<0.001__

***SD**: Standard Deviation, **IQR:** Interquartile Range, **DM:** Diabetes Mellitus, **HT:** Hypertension, **CAD:** Coroner Arter Disease, **COPD:** Chronic Obstructive Pulmoner Disease, **PSA:** Prostate Specific Antigen, **IPP:** Intravesical Prostatic Protrusion, **IPSS:** International Prostate Symptom Score**, Qmax:** Maximal Urinary Flow Rate, **Qavg:** Average Urinary Flow Rate,**PVR**: Post-void Residual Volume [k]**:** Kruskal Wallis Analysis Of Variance, [c]: Chi-square Test, [f]: Fisher's exact test, [w]**:** Wilocoxon Test, [p]**:** Paired Samples Test*

[*] *Difference Between Group A and Group B*

[**] *Difference Between Group B and Group C*

[***] *Difference Between Group A and Group C*

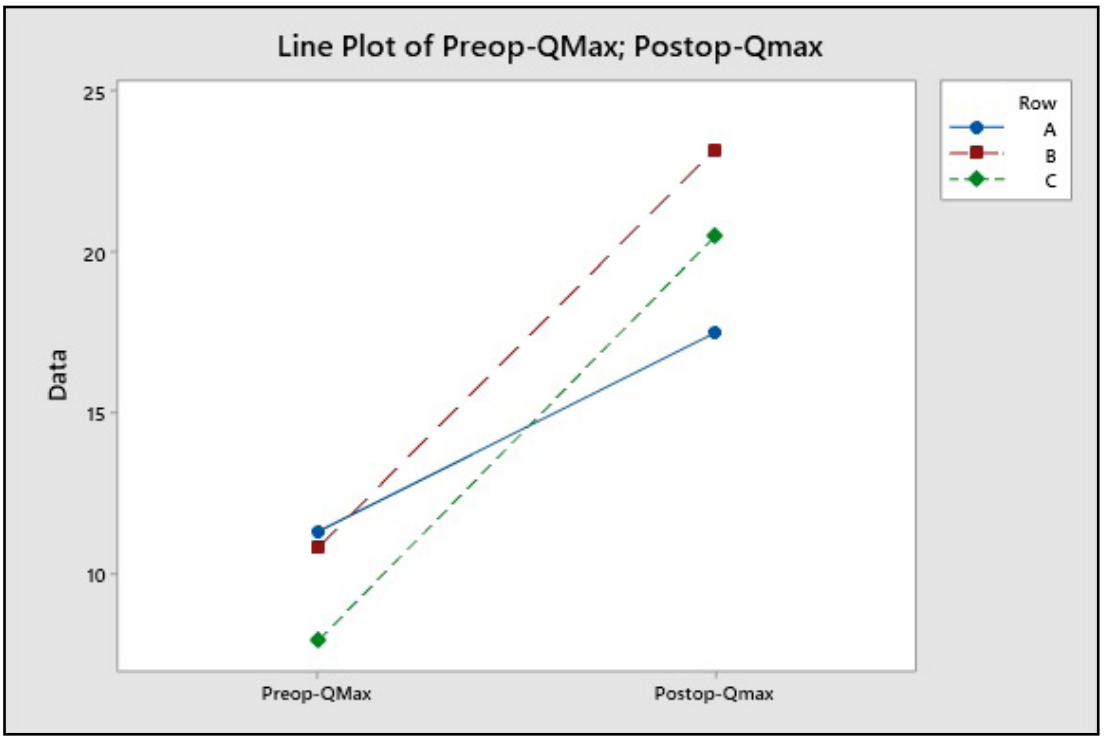


Figure 2. Comprasion of Qmax changes between groups.

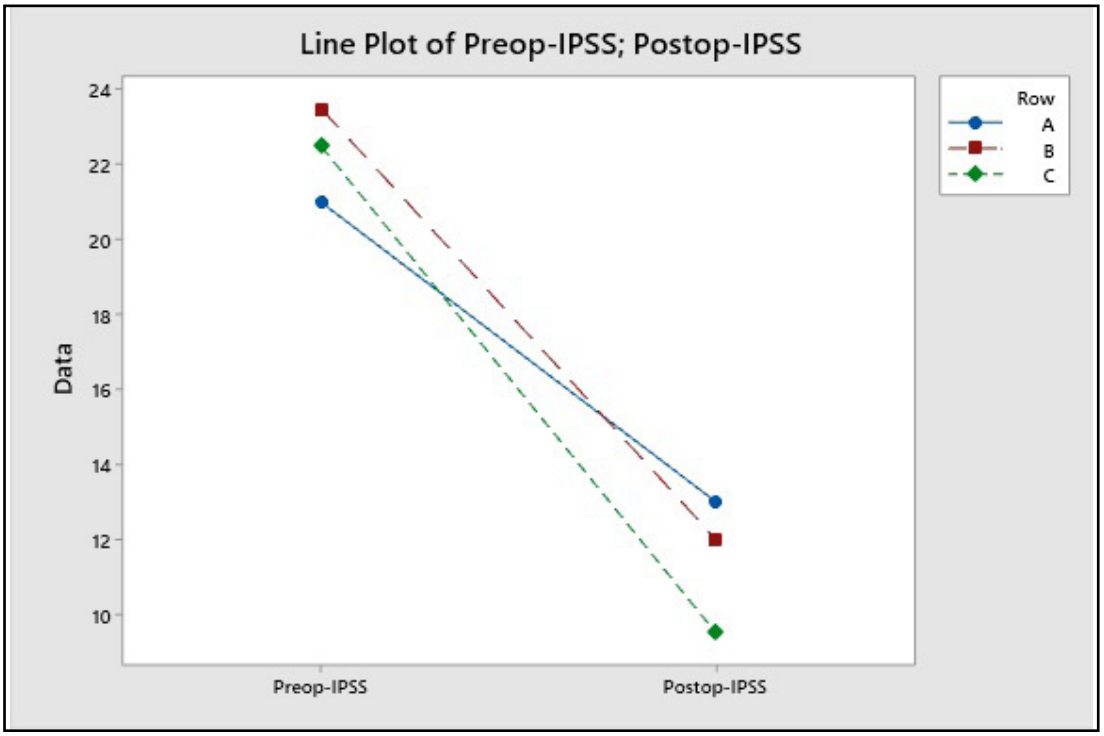


Figure 3. Comprasion of IPSS changes between groups.

DISCUSSION

Various parameters, including uroflowmetry, patient age, preoperative IPSS, prostate volume, and IPP, have been used to determine surgical candidacy and predict surgical success in BPH (8). Foo et al. (9) reported that lower preoperative IPP measurements might rule out BPH. The role of IPP in BPH-related BOO, its predictive value for medical treatment response, its association with bladder stone formation, its link to overactive bladder, and its potential as a prognostic factor for prostate cancer have been investigated (10). However, there is no consensus regarding the effects of IPP on surgical outcomes.

Several studies have reported a strong correlation between IPP and PV, supporting IPP as a non-invasive predictor of BOO and correlating IPP length with PSA levels (11). Our study found significantly higher PSA levels in Group C (p=0.019), particularly in comparison to Group A (p=0.014). The increased prostate volume in Group C may explain this finding. IPP contributes to LUTS and may lead to AUR due to high post-void residual (PVR) volume (12). However, Kadihasanoglu et al. (13) found no relationship between IPP length and AUR incidence. In our study, preoperative PVR differed significantly among groups (p=0.019), with significantly higher values in Group C than in Group A, although AUR incidence was not significantly different among groups.

Our study has several limitations, including its retrospective design and limited sample size. Another limitation is the lack of urodynamic assessment for detrusor activity. Additionally, the six-month follow-up period prevents long-term outcome evaluation and assessment of TURP-related side effects (e.g., urgency, erectile dysfunction). However, compared to other studies, the use of MRI instead of ultrasound for IPP measurements provides a more accurate assessment. Due to this case, this study can be considered as unique.

CONCLUSION

IPP may be considered an important parameter in assessing BOO due to BPH and is associated with improved postoperative voiding function. Given the larger prostate volume and greater resected tissue mass in patients with longer IPP, preoperative IPP measurement should be considered in surgical planning. However, TURP effectively provides symptomatic improvement regardless of IPP length, making it a viable surgical option for all patients.

Funding: No financial support was received for this study.

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

Informed Consent: Informed consent was obtained from all participants involved in the study.

Ethical Approval: The study was approved by the Ethics Committee of Ankara Bilkent City Hospital (Approval No: TABED 2-24-605).

Author Contributions: Concept and Design: HG, EU, Supervision: EU, SŞ, Data Collection and/or Analysis: GÖ, HBA, Analysis and/or Interpretation: KC, HG, HBA, Literature Search: EU, KC, Writing: EU, KC, Critical Review: EU, SŞ.

REFERENCES

1. Miernik A, Gratzke C. Current treatment for benign prostatic hyperplasia. Dtsch Arztebl Int. 2020;117(49):843-854. https://doi.org/10.3238/arztebl.2020.0843
2. Launer BM, McVary KT, Ricke WA, et al. The rising worldwide impact of benign prostatic hyperplasia. BJU Int. 2021;127(6):722-728. https://doi.org/10.1111/bju.15286
3. Shvero A, Calio B, Humphreys MR, et al. HoLEP: the new gold standard for surgical treatment of benign prostatic hyperplasia. Can J Urol. 2021;28(S2):6-10.
4. Franco JV, Jung JH, Imamura M et al. Minimally invasive treatments for lower urinary tract symptoms in men with benign prostatic hyperplasia: a network meta-analysis. Cochrane Database Syst Rev. 2021;7(7):CD013656. https://doi.org/10.1002/14651858
5. Marcon J, Keller P, Pyrgidis N et al. Trends and perioperative outcomes of surgical treatments for benign prostatic hyperplasia in Germany: results from the Grand study. Eur Urol Focus. 2025. https://doi.

org/10.1016/j.euf.2025.01.002

6. Lee JW, Ryu JH, Yoo TK, et al. Relationship between intravesical prostatic protrusion and postoperative outcomes in patients with benign prostatic hyperplasia. Korean J Urol. 2012;53(7):478-482. https://doi.org/10.4111/kju.2012.53.7.478
7. Topazio L, Perugia C, De Nunzio C et al. Intravesical prostatic protrusion is a predictor of alpha blockers response: results from an observational study. BMC Urol. 2018;18(1):6. https://doi.org/10.1186/s12894-018-0320-0
8. Oshagbemi AO, Ofoha CG, Akpayak IC, et al. The predictive value of intravesical prostatic protrusion on the outcome of trial without catheter in patients with acute urinary retention from benign prostatic hyperplasia at Jos University Teaching Hospital, Nigeria: a prospective observational study. Pan Afr Med J. 2022;42:246. https://doi.org/10.11604/pamj.2022.42.246.30685
9. Chia SJ, Heng CT, Chan SP, et al. Correlation of intravesical prostatic protrusion with bladder outlet obstruction. BJU Int. 2003;91(4):371-4. https://doi.org/10.1046/j.1464-410x.2003.04088.x
10. Okedere TA, Idowu BM, Onigbinde SO. Ultrasonographic intravesical prostatic protrusion in men with benign prostatic hyperplasia in Southwest Nigeria. J West Afr Coll Surg. 2023;13:16-22. https://doi.org/10.4103/jwas.jwas_270_22
11. Lim KB, Ho H, Foo KT, et al. Comparison of intravesical prostatic protrusion, prostate volume and serum prostatic-specific antigen in the evaluation of bladder outlet obstruction. Int J Urol. 2006;13(12):1509-1513. https://doi.org/10.1111/j.1442-2042.2006.01611.x
12. Tsai CH, Lee WC, Shen YC, et al. The role of intravesical prostatic protrusion in the evaluation of overactive bladder in male patients with LUTS. Int Urol Nephrol. 2020;52(5):815-820. https://doi.org/10.1007/s11255-019-02370-4
13. Kadihasanoglu M, Aydin M, Taskiran M, et al. The Effect of Intravesical Prostatic Protrusion in Patients with Benign Prostatic Hyperplasia: Controlled, Clinical Study. Urol Int. 2019;103(2):180-186. https://doi.org/10.1159/000499437
14. Lieber MM, Jacobson DJ, McGree ME, et al. Intravesical prostatic protrusion in men in Olmsted County, Minnesota. J Urol. 2009 Dec;182(6):2819-2824. https://doi.org/10.1016/j.juro.2009.08.086
15. Keqin Z, Zhishun X, Jing Z, et al. Clinical significance of intravesical prostatic protrusion in patients with benign prostatic enlargement. Urology. 2007;70(6):1096-1099. https://doi.org/10.1016/j.urology.2007.08.008

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1694756

RESEARCH ARTICLE

Novel Hematologic Markers for Risk Stratification in Bladder Cancer Patients Receiving BCG Treatment

Kemal Kayar [1], Rıdvan Kayar [1], Buğrahan Buhur Özdemir [1], İlker Artuk [1], Emre Tokuç [2], Çağatay Tosun [1], Metin İshak Öztürk [1], Ömer Ergin Yücebaş [1]

[1] Department of Urology, University of Health Sciences, Haydarpaşa Numune Training and Research Hospital, Istanbul, Türkiye

[2] Department of Urology, University of Bahçeşehir, Medical Park Göztepe Hospital, Istanbul, Türkiye

Submitted: *2025-05-07*
Accepted: *2025-06-11*

Corresponding Author;
Kemal Kayar, M.D., FEBU

Address: University of Health Sciences, Haydarpasa Numune Training and Research Hospital, Department of Urology. Tibbiye Street. No: 23 34668 Uskudar, Istanbul, Türkiye

E-mail: kemal.kayar@hotmail.com

ORCID

K.K.	0000-0003-0731-9877
R.K.	0000-0002-1765-919X
B.B.Ö.	0000-0003-3498-0628
İ.A.	0000-0002-7889-4943
E.T.	0000-0002-5885-9278
Ç.T.	0000-0001-8221-8158
M.İ.Ö.	0000-0002-1868-2316
Ö.E.Y.	0000-0002-8161-4068

Abstract

Objective: In order to evaluate the predictive role of novel hematologic markers in recurrence and progression among non-muscle invasive bladder cancer (NMIBC) patients undergoing intravesical BCG therapy.

Material and Methods: A total of 182 patients diagnosed with NMIBC and treated with transurethral resection of bladder tumor (TUR-BT) followed by BCG therapy were included. Patients were stratified into intermediate-, high- and very high-risk groups per the EAU 2024 guidelines. Preoperative hematologic parameters were recorded. In addition, CLR, CAR, and IBI were calculated. Recurrence and progression were assessed through follow-up cystoscopies. ROC curve analysis was used to determine the predictive value of the biomarkers.

Results: Recurrence and progression occurred in 15% and 8% of patients, respectively. Multifocal tumors showed a notable association with recurrence ($p = 0.006$), and carcinoma in situ (CIS) predicted progression ($p < 0.001$). CAR (AUC = 0.695, $p = 0.013$) and CLR (AUC = 0.660, $p = 0.040$) significantly predicted progression. IBI was a strong predictor in the very high-risk group (AUC = 0.920, $p < 0.001$).

Conclusion: CLR, CAR, and IBI are promising markers for identifying patients at higher risk of progression during BCG therapy. IBI shows strong prognostic utility in very high-risk NMIBC patients. Further prospective, multicenter studies are needed for clinical validation.

Keywords: BCG, hematologic inflammatory markers, non-muscle invasive bladder cancer, progression, recurrence

Cite; Kayar K, Kayar R, Ozdemir BB, Artuk I, Tokuc E, Tosun C, Ozturk MI, Yucebas OE. Novel Hematologic Markers for Risk Stratification in Bladder Cancer Patients Receiving BCG Treatment. New J Urol. 2025;20(2):104-112. **doi:** https://doi.org/10.33719/nju1694756

INTRODUCTION

Approximately 75% of bladder cancer cases are non-muscle invasive (NMIBC), and 25% are muscle-invasive (MIBC). NMIBC patients typically undergo transurethral resection followed by intravesical therapies with various therapeutic agents. The specific treatment being chosen based on the patient's risk of progression (1). Accurate prediction of short- and long-term probabilities of disease recurrence and progression in NMIBC patients, post-transurethral resection is essential for guiding adjuvant treatment recommendations and organizing effective surveillance programs. Risk stratification has been widely employed to inform treatment strategies and estimate the likelihood of developing muscle-invasive bladder cancer (2). The European Organization for Research and Treatment of Cancer (EORTC) risk classification system consolidates six factors: previous recurrences, maximum tumor diameter, number of tumors, tumor stage, World Health Organization (WHO) 1973 and 2004/2016 grading classifications, and presence of concomitant carcinoma in situ. Additionally, three clinical risk factors are considered: age greater than 70 years, presence of multiple papillary tumors, and tumor diameter exceeding 3 cm (1-3).

The immune system, including both the inflammatory response and the tumor microenvironment, significantly influences the clinical course, biological features, and outcomes of bladder cancer (4). During an inflammatory response, various immune cells, including neutrophils, lymphocytes, monocytes, and platelets, undergo alterations alongside C-reactive protein (CRP) and albumin. Several of these inflammatory markers have demonstrated potential as valuable indicators for assessing cancer prognosis. Immune-related biomarkers, including the monocyte/lymphocyte ratio (MLR), the pan-immune inflammation value (PIV), systemic inflammatory response index (SIRI), neutrophil/lymphocyte ratio (NLR), systemic immune inflammation index (SII) and platelet/lymphocyte ratio (PLR), have been studied to forecast the prognosis of bladder cancer patients (5-7).

Current studies point out the prognostic significance of CRP to lymphocyte ratio (CLR), inflammatory burden index (IBI), and CRP to albumin ratio (CAR) in both non-metastatic and metastatic cancers. Elevated levels of these markers in colorectal and oral mucosal cancers have been linked to adverse cancer prognosis (8-10). To date, however, no studies or meta-analyses have investigated the association of CLR, CAR, and IBI with recurrence and progression in NMIBC. Our study endeavors to ascertain the correlation between CLR, CAR, and IBI and the risk of recurrence and progression in NMIBC patients undergoing Bacillus Calmette-Guérin (BCG) therapy.

MATERIAL AND METHODS

Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee Date: 29.02.2024 Land No: HNEAH/KAEK-2024/KK/9 Study activities adhered to the principles outlined in the Declaration of Helsinki. All participating patients signed the informed consent in writing and agreed to the anonymous use of their data.

Patients were selected based on the inclusion criteria, which required a diagnosis of NMIBC confirmed by histopathological evaluation. Eligible patients had received at least one induction cycle of BCG therapy and had a minimum follow-up period of 12 months post-BCG therapy with documented recurrence and progression status. Adequate BCG therapy is when a patient has received at least five of six induction installations and at least one maintenance (two of three installations) in 6 months (11). Patients were also required to have available preoperative hematologic laboratory data, including CRP, albumin, and complete blood count parameters. Two hundred fifty patients with primary bladder cancer undergoing transurethral resection of bladder tumor (TUR-BT) at our tertiary referral uro-oncology clinic between January 2015 and June 2023 were enrolled. Sixty-eight patients with a history of secondary malignancy (n=5), immune system failure (n=3), pathology results contraindicating BCG therapy (n=41), non-adherence to BCG follow-up protocols (n=14) or follow-up conducted at other centers (n=5) were excluded from the study. Following these exclusions, our study group comprised 182 patients.

Demographic information (age, sex, comorbidities, smoking status) and clinical parameters were collected. Pre- and postoperative biochemical markers, including CRP (mg/L), albumin (g/L), and complete blood count values (monocyte count, lymphocyte count, platelet count, neutrophil count) (10^9/L), were recorded within a two-week window surrounding surgery. The following calculated indices were

derived from the collected data: neutrophil/lymphocyte as NLR, CRP x NLR as IBI, CRP/albumin as CAR, CRP/lymphocyte as CLR**,** monocyte × neutrophil × platelet) / lymphocyte as PIV, monocyte/lymphocyte as MLR, platelet/lymphocyte as PLR, monocyte x NLR as SIRI, platelet x NLR as SII.

The date of TUR-BT surgery, postoperative pathology results, T stage, low-grade/high-grade (LG/HG) grade, and presence of carcinoma in situ (CIS) were retrieved from the hospital database. Patients were risk-stratified into three groups (intermediate, high, very high) based on the updated prognostic risk group for NMIBC according to the European Association of Urology (EAU) 2024 guidelines. Follow-up cystoscopies were performed at intervals determined by each patient's risk category in accordance with the surveillance schedule outlined in the follow-up section of the EAU guidelines for NMIBC. Tumor recurrence or progression observed during these evaluations was duly recorded.

Disease-free survival time, progression time (if applicable), and progression-free survival time were calculated in months. Patients were followed for a maximum of 114 months and a minimum of 12 months.

The association between the presence of postoperative recurrence and/or progression and the above-mentioned hematologic inflammatory variables was evaluated. The relationships between these variables and the outcomes of interest were examined to assess their prognostic significance.

Statistical analysis was carried out using IBM SPSS version 25 (IBM Corp, Armonk, NY, USA). Continuous variables were presented as medians with interquartile ranges (IQR), where appropriate. Categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using the chi-square test for categorical variables and the Mann-Whitney U test for continuous variables, based on normality distribution (assessed by the Shapiro-Wilk test). The predictive performance for recurrence and progression was evaluated using ROC curve analysis, and the optimal cut-off values were determined using the Youden Index. Statistical significance was set at $p < 0.05$.

RESULTS

In our study, 63% of patients were younger than 70 years old, and 87% were male. Smoking prevalence was 79%. Additionally, 33% of patients had diabetes, 45% had hypertension, and 9% had chronic obstructive pulmonary disease (COPD). CIS was observed in 15% of cases. Single tumor lesions were present in 59% of patients, while 41% had two or more lesions. Tumor size was ≥3 cm in 62% of patients. Risk categorization revealed that 27% had intermediate risk, 59% had high risk, and 14% had very high risk. Recurrence and progression rates were 15% and 8%, respectively. Detailed demographic and clinical characteristics are presented in Table 1.

The median follow-up duration was 52.2 ± 27 months (range: 12–114 months). Evaluation of recurrence and progression according to age, tumor size, tumor multiplicity, and presence of CIS revealed that age group, tumor size, and CIS were not significantly associated with recurrence ($p = 0.133$, $p = 0.268$, and $p = 0.929$, respectively). However, a statistically significant association was observed between recurrence and tumor multiplicity ($p = 0.006$). Recurrence was notably more frequent in patients with multifocal lesions (24.3%) than in those with unifocal disease (9.3%) (Table 2).

In the analysis of progression, only the presence of CIS demonstrated a significant association ($p < 0.001$) with progression observed in 25.9% of patients with CIS, compared to 5.2% in those without. Age group, tumor size, and number of lesions were not significantly associated with progression ($p = 0.058$, $p = 0.703$ and $p = 0.957$, respectively) (Table 2).

When stratified by EAU 2022 risk groups, recurrence rates were 8.2%, 18.5%, and 16% in intermediate-, high- and very high-risk groups, respectively. This difference was not statistically significant ($p = 0.248$). However, a significant difference in progression was noted among risk groups ($p = 0.029$), with progression rates of 2% in the intermediate-risk group, 8.3% in the high-risk group, and 20% in the very high-risk group, as demonstrated in Table 2**.**

Hematologic markers were assessed in relation to recurrence and progression. No statistically significant associations were found between any of the tested indices (CAR, CLR,

IBI, SIRI, SII, PIV, NLR, MLR, and PLR) and recurrence ($p > 0.05$ for all). However, CAR ($p = 0.013$) and CLR ($p = 0.040$) were significantly associated with progression in the overall cohort (Table 3). ROC analysis confirmed that CAR provided superior predictive accuracy compared to CLR, with an AUC of 0.695 versus 0.660. The cut-off value for CAR was determined to be 0.56 (sensitivity = 63.5%, specificity = 66.7%, $p = 0.013$). In comparison, CLR had a cut-off of 1.26 (sensitivity = 59.9%, specificity = 60%, $p = 0.040$), as presented in Table 4 and illustrated in Figure 1-A.

Among patients in the very high-risk group, CLR ($p = 0.025$) and IBI ($p = 0.004$) were significantly associated with progression (Table 3). ROC curve analysis demonstrated the superior discriminative performance of IBI with an AUC of 0.920, a cut-off value of 9.56, and sensitivity and specificity, both at 80% ($p < 0.001$). CLR yielded an AUC of 0.830, with a cut-off of 1.57, sensitivity and specificity of 80%, and a p-value of 0.032 (Table 4, Figure 1-B).

Table I. Patient Demographics and Clinical Characteristics

Variables		n (%)
Age Group	Age ≤ 70	114 (63)
	Age > 70	68 (37)
Sex	Female	24 (13)
	Male	158 (87)
Smoking	None	38 (21)
	Yes	144 (79)
DM	None	122 (67)
	Yes	60 (33)
HT	None	100 (55)
	Yes	82 (45)
COPD	None	166 (91)
	Yes	16 (9)
CIS	None	155 (85)
	Yes	27 (15)
Tumoral lesion	Solitary	108 (59)
	Multifocal	74 (41)
Tumor size	< 3 cm	69 (38)
	≥ 3 cm	113 (62)
Risk categories	Intermediate Risk	49 (27)
	High Risk	108 (59)
	Very High Risk	25 (14)
Recurrence	None	154 (85)
	Yes	28 (15)
Progression	None	167 (92)
	Yes	15 (8)

DM: Diabetes mellitus; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; CIS: Carcinoma in situ

Table 2. EAU 2022 Statistical Evaluation of Risk Factors of NMIBC and Presence of CIS in Terms of Recurrence and Progression

Risk Factor		Recurrence	No Recurrence	p*	Progression	No Progression	p*
Age	≤ 70	14 (%12.3)	100 (%87.7)	0.133	6 (%5.3)	108 (%94.7)	0.058
	> 70	14 (%20.6)	54 (%79.4)		9 (%13.2)	59 (%86.8)	
Tumoral lesion	Solitary	10 (%9.3)	98 (%90.7)	**0.006**	9 (%8.3)	99 (%91.7)	0.957
	Multifocal	18 (%24.3)	56 (%75.7)		6 (%8.1)	68 (%91.9)	
Tumor Size	< 3 cm	8 (%11.6)	61 (%88.4)	0.268	5 (%7.2)	64 (%92.8)	0.703
	≥ 3cm	20 (%17.7)	93 (%82.3)		10 (%8.8)	103 (%91.2)	
CIS	None	24 (%15.5)	131 (%84.5)	0.929	8 (%5.2)	147 (%94.8)	**<0.001**
	Yes	4 (%14.8)	23 (%85.2)		7 (%25.9)	20 (%74.1)	
Risk Groups	Intermediate Risk	4 (%8.2)	45 (%91.8)	0.248	1 (%2)	48 (%98)	**0.029**
	High Risk	20 (%18.5)	88 (%81.5)		9 (%8.3)	99 (%91.7)	
	Very High Risk	4 (%16)	21 (%84)		5 (%20)	20 (%80)	

*: Chi-square, CIS: Carcinoma in situ

Table 3. Analysis of Hematologic Parameters and Statistical Evaluation in Terms of Recurrence and Progression

	Overall Group			Very High-Risk Group			High- and Very High-Risk Group		
	Mean (IQR)	p*	p**	Mean (IQR)	p*	p**	Mean (IQR)	p*	p**
CAR	0.89 (0.43-0.96)	0.529 [a]	**0.013 [a]**	1.18 (0.44-1.13)	0.138 [a]	0.077 [a]	0.92 (0.43-0.97)	0.372 [a]	**0.017 [a]**
CLR	1.67 (1.06-1.62)	0.205 [a]	**0.040 [a]**	2.07 (0.86-2.48)	0.088 [a]	**0.025 [a]**	1.73 (0.71-1.74)	0.224 [a]	0.092 [a]
IBI	9.01 (3.16-8.66)	0.950 [a]	0.088 [a]	11.32 (3.32-10.59)	0.630 [a]	**0.004 [a]**	9.28 (3.17-9.17)	0.872 [a]	**0.036 [a]**
SIRI	1.39 (0.72-1.58)	0.246 [a]	0.114 [a]	1.75 (0.69-1.93)	0.683 [a]	0.185 [a]	1.39 (0.73-1.65)	0.348 [a]	0.225 [a]
SII	590.62 (342.46-739.05)	0.801 [a]	0.139 [a]	759.47 (366.41-964.21)	0.999 [a]	0.541 [a]	606.27 (355.85-762.28)	0.888 [a]	0.294 [a]
PIV	360.06 (161.08-374.52)	0.530 [a]	0.157 [a]	523.36 (174.70-526.80)	0.882 [a]	0.497 [a]	363.03 (173.79-387.29)	0.972 [a]	0.199 [a]
NLR	2.36 (1.54-2.80)	0.450 [a]	0.248 [a]	2.83 (1.39-3.74)	0.795 [a]	0.197 [a]	2.41 (1.56-2.85)	0.431 [a]	0.562 [a]
MLR	0.24 (0.16-0.28)	0.977 [a]	0.147 [a]	0.27 (0.19-0.34)	0.710 [a]	0.276 [a]	0.24 (0.17-0.28)	0.812 [a]	0.297 [a]
PLR	114.61 (83.79-137-32)	0.215 [a]	0.409 [a]	134.64 (93.13-156.80)	0.154 [a]	0.541 [a]	115.58 (86.71-141.19)	0.361 [a]	0.676 [a]

*: Statistical analysis by recurrence, **: Statistical analysis by progression, [a]: Mann-Whitney U Test. IQR: Interquartile range. CAR: Crp albumin ratio, IBI: Inflammation burden index, SIRI: Systemic inflammatory response index, SII: Systemic immune-inflammation index, PIV: Pan immune inflammation value, NLR: Neutrophil lymphocyte ratio, MLR: Monocyte lymphocyte ratio, PLR: Platelet lymphocyte ratio, CLR: Crp lymphocyte ratio

Table 4. ROC Analysis Results for Predicting Progression

	AUC (95%)	Cut-Off	p	Sensitivity (%)	Specificity (%)
Overall Group					
CAR	0.695(0.572-0.817)	0.56	**0.013**	63.5	66.7
CLR	0.660(0.508-0.812)	1.26	**0.040**	59.9	60
Very High-Risk Group					
IBI	0.920(0.802-1.000)	9.56	**<0.001**	80	80
CLR	0.830(0.529-1.000)	1.57	**0.032**	80	80
High- and Very High-Risk Group					
IBI	0.672(0.526-0.817)	6.66	**0.021**	63.9	64.3
CAR	0.696(0.566-0.825)	0.56	**0.003**	63.9	64.3

AUC: Area under curve; CAR: Crp albumin ratio; CLR: Crp lymphocyte ratio; IBI: inflammation burden index.

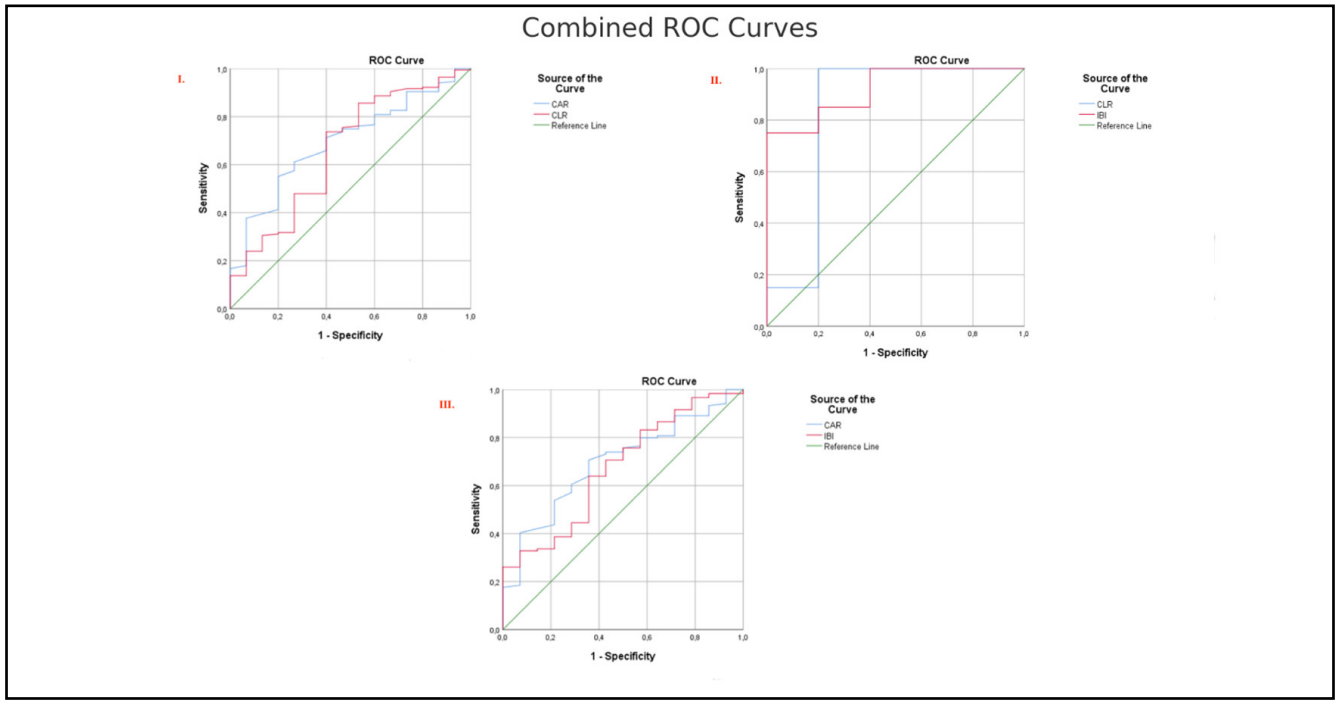


Figure 1. ROC Curve Analysis of Inflammatory Markers for Predicting Progression **(A)** CAR and CLR in the overall cohort (AUC: CAR = 0.695; CLR = 0.660). **(B)** IBI and CLR in the very high-risk subgroup (AUC: IBI = 0.920; CLR = 0.830). **(C)** IBI and CAR in the combined high- and very high-risk cohort (AUC: IBI = 0.672; CAR = 0.696). Dashed diagonal line represents the reference (AUC = 0.5).

In the combined high- and very high-risk cohort, both CAR (p = 0.017) and IBI (p = 0.036) were significantly associated with progression (Table 3). ROC analysis showed comparable predictive value for both parameters. CAR had an AUC of 0.696, a cut-off of 0.56, a sensitivity of 63.9%, and a specificity of 64.3% (p = 0.003). IBI demonstrated an AUC of 0.672, with a cut-off of 6.66, sensitivity of 63.9%, specificity of 64.3%, and a p-value of 0.021 (Table 4, Figure 1-C).

DISCUSSION

This study investigated the prognostic value of novel hematologic indices—CAR, CLR, and IBI—in predicting recurrence and progression in NMIBC patients undergoing BCG therapy. Among these, CAR and CLR emerged as relevant predictors of progression across the entire cohort, while IBI emerged as a particularly strong predictor in the very high-risk group.

While evaluating patient- and tumor-related factors as predictors of recurrence, the presence of a multifocal tumor was notably linked with increased recurrence risk (p = 0.006). At the same time, no statistically significant differences were observed for advanced age, increased tumor size, or CIS (p = 0.133, p = 0.268, p = 0.929, respectively). In predicting progression, as demonstrated by Daher et al. in 2010, the presence of CIS was a significant predictor (p = 0.000). In contrast, advanced age, multifocality, and increased tumor size did not demonstrate meaningful associations (p = 0.058, p = 0.957, p = 0.703, respectively) (12). As noted by Sylvester et al., when defining the current risk classification, progression rates in the very high-risk patient group were observed to increase from 12% to 40-44% in 5-year follow-up compared to the high-risk group in the previous classification (2). In our study, progression rates were 2% in the medium-risk group, 8.3% in the high-risk group, and 20% in the very high-risk group, demonstrating a significant difference (p=0,029).

Our findings align partially with prior literature evaluating systemic inflammatory markers in bladder cancer. While indices such as NLR, SII, and PLR have been linked to recurrence or progression in earlier studies (5, 13, 14), these associations were not observed in our cohort. This discrepancy may reflect differences in study population characteristics, BCG regimen consistency, or inflammatory marker thresholds. Notably, Deng-Xiong et al. identified SII as a predictor during BCG induction, whereas we found no significant role for SII in any subgroup (13). Similarly, Kun Ye et al. highlighted SIRI as a predictive factor that did not reach significance in our analysis (7).

The most compelling result of our study was the high predictive accuracy of IBI in very high-risk patients (AUC: 0.920). As a composite index reflecting CRP and NLR, IBI appears to reflect the systemic inflammatory burden more effectively than individual components (9). To our knowledge, this is the first study to assess IBI in the context of intravesical BCG therapy for NMIBC. Its predictive power in high-risk settings suggests potential utility in refining patient stratification beyond current risk models.

The role of CLR, a ratio combining CRP and lymphocyte count, has been validated in various malignancies, including colorectal and gastric cancer (15-17). In our study, CLR was significantly elevated among patients with disease progression, particularly in the very high-risk group. These findings echo previous reports linking CLR to tumor aggressiveness and immune evasion (18).

CAR also demonstrated prognostic value for progression, consistent with studies in pancreatic and muscle-invasive bladder cancer (19, 20). However, its lack of association with recurrence underscores that distinct inflammatory profiles may underpin early recurrence versus invasive transformation.

To the best of our knowledge, this is the first study to comprehensively evaluate IBI, CLR, and CAR in the context of intravesical BCG therapy among NMIBC patients stratified according to the updated 2024 EAU risk groups. While prior studies have assessed inflammatory markers such as NLR, SII, and PLR (5, 13, 14), the application of IBI—a composite index integrating CRP and NLR—in very high-risk NMIBC patients has not been previously reported. This novel approach provides a low-cost, accessible prognostic tool that may complement traditional risk classification systems and improve individualized follow-up strategies.

Importantly, none of the markers evaluated in our study were predictive of recurrence, including the more widely used indices such as NLR and PLR (21). This observation aligns with previous evidence suggesting that recurrence may be influenced more by tumor biology or localized immunologic factors in the bladder microenvironment rather than systemic inflammation (22).

Our study has several limitations. Its retrospective design and single-center setting limit generalizability. In addition, despite an adequate overall sample size, subgroup analyses—particularly for the very high-risk group—may be underpowered. Nonetheless, the consistent association of IBI and CLR with progression highlights the potential of these markers in supplementing current risk stratification models.

In clinical practice, integrating such low-cost, readily accessible biomarkers could aid in tailoring surveillance intensity and therapeutic strategies, especially in patients at heightened risk of progression. Prospective multicenter validation is warranted to confirm these findings and to

explore their role in guiding treatment decision-making.

CONCLUSION

Accurate estimation of bladder cancer prognosis is essential for guiding treatment decisions and improving patient outcomes. Preoperative inflammatory markers offer a cost-effective and non-personalized approach to prognostication. This study provides valuable insights that may inform future prospective, multicenter studies with larger patient groups, contributing to a more comprehensive understanding of prognostic markers in non-muscle invasive bladder cancer.

Funding: This study was not supported by any source. No financial or commercial interests from any drug company or others were taken and there is no relationship of authors that may pose conflict of interest.

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

Data Availability Statement: The data that support the findings of this study are available from all authors, upon reasonable request.

Ethical Approval: Haydarpaşa Numune Training and Research Hospital Clinical Research Ethics Committee Date: 29.02.2024 Land No: HNEAH/KAEK-2024/KK/9

Authorship Contribution: KK: Conceptualization; methodology; data analysis; statistical analysis; manuscript writing. RK: Conceptualization; methodology; data analysis; statistical analysis; manuscript writing. BBÖ: Data acquisition. İA: Data acquisition, resources. ET: Manuscript writing and editing, critical supervision. ÇT: Manuscript editing. MİÖ: Critical Supervision. ÖEY: Supervision.

REFERENCES

1. Babjuk M, Burger M, Comperat EM, et al. European Association of Urology Guidelines on Non-muscle-invasive Bladder Cancer (TaT1 and Carcinoma In Situ) - 2019 Update. Eur Urol. 2019;76(5):639-657. https://doi.org/10.1016/j.eururo.2019.08.016
2. Sylvester RJ, Rodriguez O, Hernandez V, et al. European Association of Urology (EAU) Prognostic Factor Risk Groups for Non-muscle-invasive Bladder Cancer (NMIBC) Incorporating the WHO 2004/2016 and WHO 1973 Classification Systems for Grade: An Update from the EAU NMIBC Guidelines Panel. Eur Urol. 2021;79(4):480-488. https://doi.org/10.1016/j.eururo.2020.12.033
3. Comperat EM, Burger M, Gontero P, et al. Grading of Urothelial Carcinoma and The New "World Health Organisation Classification of Tumours of the Urinary System and Male Genital Organs 2016". Eur Urol Focus. 2019;5(3):457-466. https://doi.org/10.1016/j.euf.2018.01.003
4. Mbeutcha A, Shariat SF, Rieken M, et al. Prognostic significance of markers of systemic inflammatory response in patients with non-muscle-invasive bladder cancer. Urol Oncol. 2016;34(11):e17-e24. https://doi.org/10.1016/j.urolonc.2016.05.013
5. Vartolomei MD, Porav-Hodade D, Ferro M, et al. Prognostic role of pretreatment neutrophil-to-lymphocyte ratio (NLR) in patients with non-muscle-invasive bladder cancer (NMIBC): A systematic review and meta-analysis. Urol Oncol. 2018;36(9):389-399. https://doi.org/10.1016/j.urolonc.2018.05.014
6. Kayar R, Bastug Y, Tokuc E, et al. Pan-immune-inflammation value as a prognostic tool for overall survival and disease-free survival in non-metastatic muscle-invasive bladder cancer. Int Urol Nephrol. 2024;56(2):509-518. https://doi.org/10.1007/s11255-023-03812-w
7. Ye K, Xiao M, Li Z, et al. Preoperative systemic inflammation response index is an independent prognostic marker for BCG immunotherapy in patients with non-muscle-invasive bladder cancer. Cancer Med. 2023;12(4):4206-4217. https://doi.org/10.1002/cam4.5284
8. Nakamura Y, Shida D, Boku N, et al. Lymphocyte-to-C-Reactive Protein Ratio Is the Most Sensitive Inflammation-Based Prognostic Score in Patients With Unresectable Metastatic Colorectal Cancer. Dis Colon Rectum. 2021;64(11):1331-1341. https://doi.org/10.1097/DCR.0000000000002059

9. Xie H, Ruan G, Ge Y, et al. Inflammatory burden as a prognostic biomarker for cancer. Clin Nutr. 2022;41(6):1236-1243. https://doi.org/10.1016/j.clnu.2022.04.019

10. Yamagata K, Fukuzawa S, Ishibashi-Kanno N, et al. Association between the C-reactive protein/albumin ratio and prognosis in patients with oral squamous cell carcinoma. Sci Rep. 2021;11(1):5446. https://doi.org/10.1038/s41598-021-83362-2

11. Kamat AM, Sylvester RJ, Bohle A, et al. Definitions, End Points, and Clinical Trial Designs for Non-Muscle-Invasive Bladder Cancer: Recommendations From the International Bladder Cancer Group. J Clin Oncol. 2016;34(16):1935-1944. https://doi.org/10.1200/JCO.2015.64.4070

12. Chade DC, Shariat SF, Godoy G, et al. Clinical outcomes of primary bladder carcinoma in situ in a contemporary series. J Urol. 2010;184(1):74-80. https://doi.org/10.1016/j.juro.2010.03.032

13. Deng-Xiong L, Qing-Xin Y, De-Chao F, et al. Systemic Immune-inflammation Index (SII) During Induction has Higher Predictive Value Than Preoperative SII in Non-muscle-invasive Bladder Cancer Patients Receiving Intravesical Bacillus Calmette -Guerin. Clin Genitourin Cancer. 2023;21(3):e145-e52. https://doi.org/10.1016/j.clgc.2022.11.013

14. Wu R, Li D, Zhang F, et al. Prognostic Value of Platelet-to-Lymphocyte Ratio in Non-Muscle Invasive Bladder Cancer Patients: Intravesical Bacillus Calmette-Guerin Treatment After Transurethral Resection of Bladder Tumor. Front Surg. 2022;9:907485. https://doi.org/10.3389/fsurg.2022.907485

15. Okugawa Y, Toiyama Y, Yamamoto A, et al. Lymphocyte-C-reactive Protein Ratio as Promising New Marker for Predicting Surgical and Oncological Outcomes in Colorectal Cancer. Ann Surg. 2020;272(2):342-351. https://doi.org/10.1097/SLA.0000000000003239

16. Lu LH, Zhong C, Wei W, et al. Lymphocyte-C-reactive protein ratio as a novel prognostic index in intrahepatic cholangiocarcinoma: A multicentre cohort study. Liver Int. 2021;41(2):378-87. https://doi.org/10.1111/liv.14567

17. Cheng CB, Zhang QX, Zhuang LP, et al. Prognostic value of lymphocyte-to-C-reactive protein ratio in patients with gastric cancer after surgery: a multicentre study. Jpn J Clin Oncol. 2020;50(10):1141-9. https://doi.org/10.1093/jjco/hyaa099

18. Zhang H, Wang Y, Ni J, et al. Prognostic Value of Lymphocyte-C-Reactive Protein Ratio in Patients Undergoing Radical Cystectomy for Bladder Cancer: A Population-Based Study. Front Oncol. 2021;11:760389. https://doi.org/10.3389/fonc.2021.760389

19. Kuroda K, Tasaki S, Horiguchi A, et al. Postoperative C-reactive protein-to-albumin ratio predicts poor prognosis in patients with bladder cancer undergoing radial cystectomy. Mol Clin Oncol. 2021;14(3):54. https://doi.org/10.3892/mco.2021.2216

20. Shirakawa T, Makiyama A, Shimokawa M, et al. C-reactive protein/albumin ratio is the most significant inflammatory marker in unresectable pancreatic cancer treated with FOLFIRINOX or gemcitabine plus nab-paclitaxel. Sci Rep. 2023;13(1):8815. https://doi.org/10.1038/s41598-023-34962-7

21. Chen H, Wu X, Wen Z, et al. The Clinicopathological and Prognostic Value of NLR, PLR and MLR in Non-Muscular Invasive Bladder Cancer. Arch Esp Urol. 2022;75(5):467-71. https://doi.org/10.56434/j.arch.esp.urol.20227505.68

22. de Arruda Camargo GC, Oliveira G, Santos BNS, et al. Modulation of the tumor microenvironment in non-muscle-invasive bladder cancer by OncoTherad(R) (MRB-CFI-1) nanoimmunotherapy: effects on tumor-associated macrophages, tumor-infiltrating lymphocytes, and monoamine oxidases. Med Oncol. 2024;41(11):287. https://doi.org/10.1007/s12032-024-02533-z

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1608073

CASE REPORT

Hundreds of Ileal Condylitis Stones

Ahmet Turhan[1], Mert Başaranoğlu[1], Ali Nebioğlu[2], Erdem Akbay[1]

[1] Department of Urology, Mersin University Faculty of Medicine, Mersin, Türkiye

[2] Department of Urology, Mersin City Training and Research Hospital, Mersin, Türkiye

Submitted: *2024-12-27*
Accepted: *2025-02-12*

Corresponding Author;
Ahmet Turhan, MD
Address: Department of Urology, Mersin University Faculty of Medicine, Mersin, Türkiye
E-mail: drturhanahmet@gmail.com

ORCID

A.T. 0009-0008-4933-0808
M.B. 0000-0002-9873-4920
A.N. 0000-0001-6325-1534
E.A. 0000-0001-7669-414X

Abstract

One of the long-term complications of urinary diversion, urolithiasis, is influenced by factors such as bacterial colonization, urinary stasis, mucus, and anatomical abnormalities. Stones are typically observed in the upper urinary tract, and they are rarely seen in the ileal conduit. Although endoscopic surgery can be used for the treatment of stones in the ileal conduit, it is predominantly treated with open surgery. We report a 28-year-old male patient with 282 urinary stones, the largest of which measures 8 cm, found in the ileal conduit. The case is evaluated in terms of treatment and surgical approaches.

Keywords: ileal conduit, lithotripsy, urolithiasis, urinary diversion

INTRODUCTION

Urinary diversion, which is frequently preferred by surgeons today to ensure urine output following radical cystectomy, was first described by Bricker in 1950. (1) Urolithiasis, one of the late complications of urinary diversion, occurs in 3-43% of patients with urinary diversion, and its etiology is typically associated with factors such as anatomical abnormalities, urinary stasis, bacterial colonization, and mucus. (2) Due to anatomical differences in these patients and factors such as intra-abdominal adhesions, although endoscopic surgery can be used to manage stones, open surgery is generally preferred (3).

Our case is a rare patient with Bricker urinary diversion who has 282 urinary stones, the largest of which is 8 cm.

CASE REPORT

A 28-year-old male patient underwent cystectomy and Bricker urinary diversion 15 years ago due to vesical exstrophy. The patient has a history of recurrent urinary tract infections (Proteus and Escherichia coli) over the last 10 years, with repeated antibiotic use. He presented with right upper quadrant pain, a firm mass on the right side, and continuous mucus discharge from the urostomy.

Cite; Turhan A, Basaranoglu M, Nebioglu A, Akbay E. Hundreds of Ileal Condylitis Stones. New J Urol. 2025;20(2):113-116. **doi:** https://doi.org/10.33719/nju1608073

On physical examination, multiple incision scar marks were noted on the abdomen, and a naturally observed ostomy was found in the right lower quadrant. The patient's renal function (creatinine: 1.36 mg/dL, urea: 29 mg/dL) and urinalysis (nitrite negative, leukocytes negative, pH 6.5, culture-negative) were within normal limits. Computed tomography revealed a hypoplastic left kidney (80 mm), a normal right kidney, and no stones or dilation in the upper urinary system. The patient had a Bricker urinary diversion extending to the right lower quadrant, with multiple stones, the largest measuring 8 cm (Figure 1a,b,c). Multiple stones were observed on the plain radiograph (Figure 1d).

The patient underwent laparotomy through a right paramedian incision. The stones were completely removed by opening from the anti-mesenteric side while preserving the ileal conduit and ureteral anastomosis (Figure 2). The ileal conduit was closed with two layers.

Postoperative computed tomography images were obtained (Figure 3). The patient had the drain removed on the third postoperative day and was discharged on the ninth day.

At the one-year follow-up, no recurrence was observed in the patient. No changes in renal function were detected. Urinary tract infection prophylaxis was administered. The stones' analysis was not done.

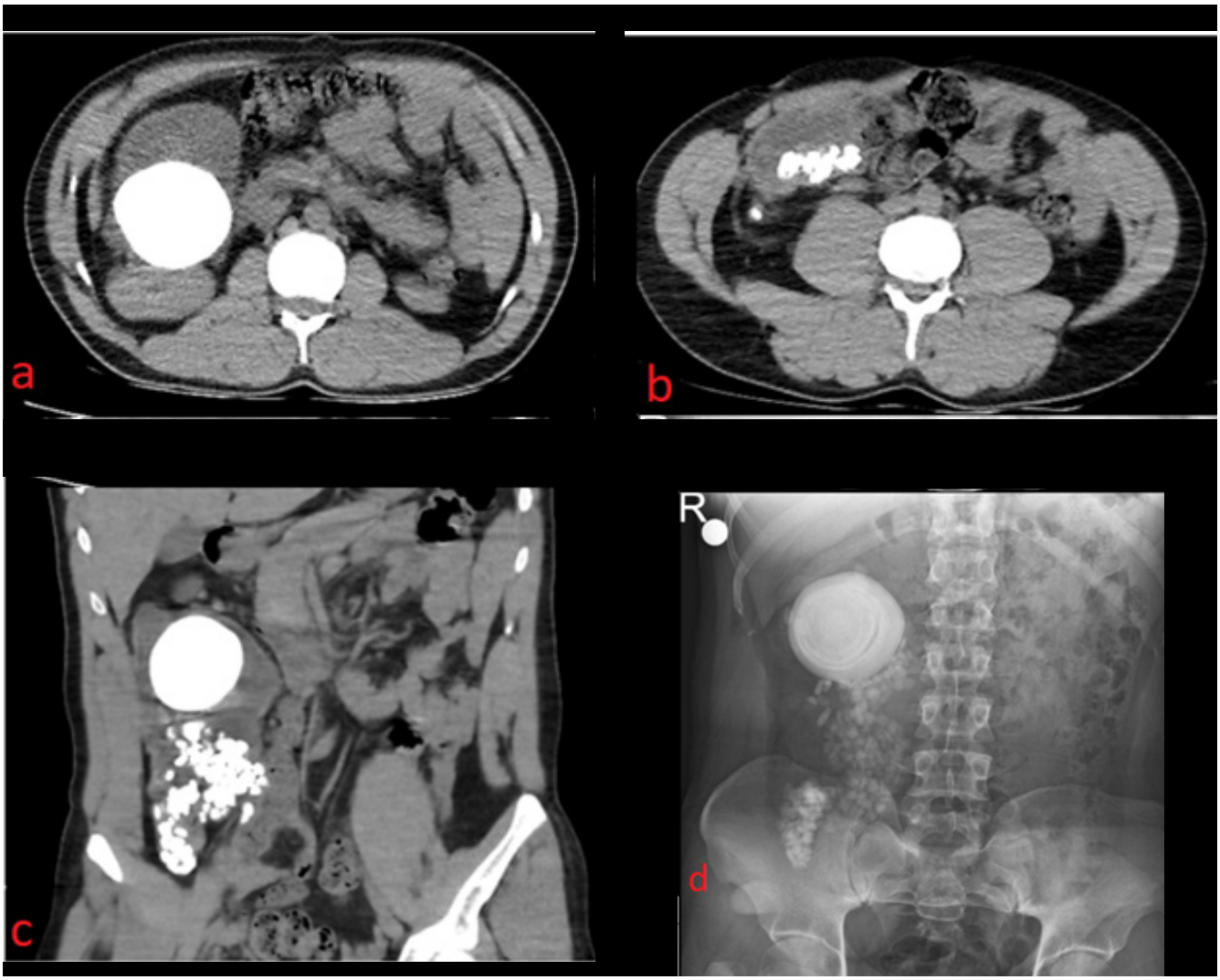


Figure 1.a. Axial computed tomography at the level of L1, **b**: Axial computed tomography at the level of L3, **c**: Coronal computed tomography, **d**: Plain urinary system radiograph

Figure 2. 282 stones removed from the ileal conduit.

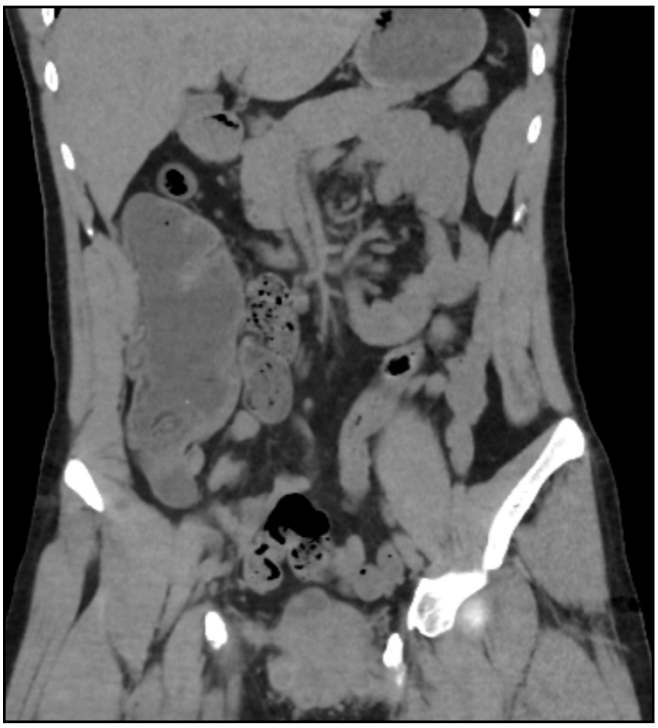


Figure 3. Postoperative computed tomography images

DISCUSSION

Radical cystectomy and urinary diversion are the main treatment modalities for muscle-invasive bladder cancer. Ileal conduit, a type of urinary diversion, is associated with early postoperative complications such as urinary infections, urinary or fecal leaks from the anastomosis, wound infections, and ileus. Urolithiasis within the ileal conduit is one of the late complications and is typically observed in the upper urinary system, though it is rarely seen within the ileal conduit itself (3,4,5). Risk factors for stone formation in the ileal conduit include bacterial colonization, mucus secreted by the ileum into the urine, metabolic reactions, and stapler-related issues secondary to surgery. Additionally, urinary stasis, which arises due to anatomical differences depending on the type of urinary diversion, is a factor that influences the frequency of urinary stones (2).

In patients with urinary diversion, bacteriuria is observed in a range of 14-96%, with the majority being asymptomatic. These bacteria typically possess urease enzymes, and the breakdown of urea leads to the production of ammonia, which increases the urine pH and contributes to the formation of magnesium phosphate stones (2). The prevention of urostomy stoma stenosis contributes to reducing bacterial colonization by ensuring the complete drainage of urine from the ileal conduit. In patients with infection-related stone formation, prophylactic antibiotic use is recommended (2,5).

Another cause is hyperoxaluria, which develops due to the length of the ileal segment. The length of the ileal segment should be 15-20 cm; if it is longer, the patient's ability to absorb bile acids and fatty acids decreases. In this case, bile and fatty acids cannot be absorbed and combined with calcium, which would normally bind with oxalate. As a result, ionized oxalate remains in the intestines, leading to the development of hyperoxaluria (2).

In patients with urinary diversion, various endoscopic and open surgical methods are applied depending on the anatomical location of the stone. The surgical approach for stones in the upper urinary system is managed in the same way as in normal patients. However, for ileal conduit stones, endoscopic surgery is not preferred due to a 50% recurrence rate and anatomical differences (6).

Despite the fact that postrenal failure due to ileal stones has been reported in the literature, in our patient, renal function was only partially affected, and no changes were observed

during follow-up after surgery (7). While cases involving ileal conduit stones have been reported in the literature, the removal of such a large number of stones is rare, making this case a significant contribution to the literature.

In all patients with urolithiasis, high oral fluid intake, and dietary modifications, such as reducing animal protein consumption, are advised. Additionally, it is essential to identify the underlying etiological factors contributing to stone formation and implement appropriate treatment strategies (2,5).

CONCLUSION

Ileal conduit stones are rare complications following cystectomy. In patients with a history of radical cystectomy, urolithiasis should be considered in the presence of recurrent urinary tract infections and persistent mucus in the urine. The definitive treatment for urolithiasis is surgery, with open surgery being preferred over endoscopic surgery in most cases. The use of prophylactic antibiotics in these patients is of great importance.

Funding: This study , being a case report, did not require any funding.

Conflict of Interest: The author declares that they have no conflicts of interest.

Informed Consent: Written informed consent was obtained from the patients for publication of these reports and accompanying images.

Ethical Approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Authors' Contributions: EA performed the diagnosis, treatment, surgery and follow-up of the patient. AT, MB, AN and EA made significant contributions to the writing of the case report. All authors read and approved the final draft.

REFERENCES

1. Bricker EM. Bladder substitution after pelvic evisceration. Surg Clin North Am. 1950;30(5):1511-1521. https://doi.org/10.1016/s0039-6109(16)33147-4
2. Okhunov Z, Duty B, Smith AD, et al. Management of urolithiasis in patients after urinary diversions. BJU Int. 2011;108(3):330-336. https://doi.org/10.1111/j.1464-410X.2011.10194.x
3. Espinheira Santos V, Costa Borges EV, de Oliveira Carneiro J, R et al. Giant Stone in Ileal Conduit. Urol Int. 2020;104(1-2):163-166. https://doi.org/10.1159/000499091
4. Cicione A, De Nunzio C, Lombardo R, et al. Complications and quality of life of ileal conduit, orthotopic neobladder and ureterocutaneostomy: systematic review of reports using the Clavien-Dindo Classification. Minerva Urol Nefrol. 2020;72(4):408-419. https://doi.org/10.23736/S0393-2249.20.03641-3
5. Cohen J, Giuliano K, Sopko N, et al. Cystolitholapaxy in Ileal Conduit. Urol Case Rep. 2015;3(6):185-187. https://doi.org/10.1016/j.eucr.2015.07.005
6. Hertzig LL, Iwaszko MR, Rangel LJ, et al. Urolithiasis after ileal conduit urinary diversion: a comparison of minimally invasive therapies. J Urol. 2013;189(6):2152-2157. https://doi.org/10.1016/j.juro.2012.12.003
7. Gómez Pascual JA, del Rosal Samaniego JM, García Galisteo E, et al. Litiasis gigante en derivación urinaria tipo Bricker. Uropatía obstructiva como forma de presentación. Actas Urol Esp. 2003;27(3):240-243.

The New Journal of Urology
eISSN 3023-6940
doi: https://doi.org/10.33719/nju1630050

CASE REPORT

A Rare Case of Bladder Tumor: Squamous Cell Papilloma

Görkem Akça [1], Hakkı Uzun [1], Hasan Güçer [2], Eyüp Dil [1], Selim Yazar [1], Erdem Orman [1]

[1] Recep Tayyip Erdoğan University Training and Research Hospital, Department of Urology, Rize, Türkiye

[2] Recep Tayyip Erdoğan University Training and Research Hospital, Department of Pathology, Rize, Türkiye

Submitted: *2025-01-30*
Accepted: *2025-04-08*

Corresponding Author;
Görkem Akça, MD
Address: Recep Tayyip Erdoğan University Training and Research Hospital, Department of Urology, Rize, Türkiye
E-mail: gakca7@hotmail.com

ORCID

G.A.	0000-0002-7019-4264
H.U.	0000-0002-5189-3166
H.G.	0000-0002-9122-379X
E.D.	0000-0001-7739-4253
S.Y.	0000-0002-9843-9008
E.O.	0000-0003-1422-7137

Abstract

Squamous cell papilloma of the bladder is an exceedingly rare benign lesion. It is often identified incidentally during imaging studies performed for unrelated reasons and may mimic urothelial carcinoma of the bladder. The definitive diagnosis of this lesion, which can present with varying clinical symptoms, is established through pathological examination. Here, we report a case of squamous cell papilloma in a 56-year-old asymptomatic male patient. The patient underwent cystoscopy after a suspicious lesion was observed on full-abdominal CT imaging, raising concern for a bladder tumor. During cystoscopy, transurethral resection was performed on calcified exophytic lesions observed in the bladder, achieving complete resection of all lesions. Histopathological analysis revealed the lesion to be a squamous cell papilloma, and the patient was placed under follow-up. The etiology and clinical significance of these lesions, which are rarely reported in the literature, remain unclear. In this article, we summarize the case of squamous cell papilloma of the bladder while reviewing the relevant literature. We believe that this report contributes to the literature by emphasizing the importance of accurate pathological evaluation for urologists and preventing overly aggressive treatments for patients.

Keywords: papilloma, squamous, bladder

INTRODUCTION

Bladder lesions are frequently observed, particularly in older individuals. The urothelial lining of the bladder typically gives rise to lesions of urothelial origin, the majority of which are malignant urothelial tumors. Benign lesions are less common, accounting for less than 1% of all bladder tumors (1). Among benign tumors, urothelial papilloma and inverted papilloma are the most commonly encountered. Squamous lesions of the bladder are even rarer. Squamous cell carcinoma represents approximately 3–5% of all malignant bladder tumors (2). However, benign, non-invasive squamous lesions, such as squamous cell papilloma, are exceedingly rare, with only a limited number of cases reported in the literature (3). These tumors are characterized endoscopically by a calcified mass-like appearance and microscopically by benign proliferative lesions composed of papillary cores

Cite; Akca G, Uzun H, Gucer H, Dil E, Yazar S, Orman E. A Rare Case of Bladder Tumor: Squamous Cell Papilloma. New J Urol. 2025;20(2):117-120. **doi:** https://doi.org/10.33719/nju1630050

lined with squamous epithelium, devoid of cellular atypia or dysplasia (4). Other rare benign squamous lesions of the bladder include keratinized squamous metaplasia, verrucous squamous hyperplasia, and condyloma acuminatum.

In this report, we present a case of squamous cell papilloma of the bladder, diagnosed following cystoscopy and transurethral resection performed for a suspected bladder tumor.

CASE PRESENTATION

A 56-year-old male patient was referred to the urology outpatient clinic after abdominal computed tomography (CT) performed in the emergency department revealed atrophy in the right kidney. The patient had no active urinary complaints. His medical history was unremarkable except for a previous open cystolithotomy. There were no identifiable risk factors for urothelial cell carcinoma, including no smoking history or occupational exposures to urothelial carcinogens. There was no history of cancer in his family. Physical examination findings were unremarkable. Laboratory tests showed serum creatinine: 1.27 mg/dL, eGFR: 58 mL/min/1.73m^2, glucose: 81 mg/dL, hemoglobin: 13.8 g/dL, PSA: 0.67 ng/mL, and CRP: 1.32 mg/dL. Urinalysis revealed microscopic hematuria without increased inflammatory cells, and urine culture was negative. Abdominal CT imaging revealed minimal atrophy and a millimetric calculus in the mid-portion of the right kidney, as well as suspicious calcified lesions with wall thickening in the anterior bladder wall (Figure 1).

Diagnostic cystoscopy revealed widespread, slightly exophytic, white plaque-like lesions with calcifications on the anterior and posterior bladder wall mucosa (Figure 2). These lesions were considered highly suspicious for urothelial carcinoma. Transurethral resection (TUR) was performed under spinal anesthesia, and all lesions were completely resected. The postoperative course was uneventful, and the patient was discharged on postoperative

Histopathological examination revealed dense keratin lamellae, some with calcifications, along with papillary structures lined with squamous epithelium, some of which were free-floating. In contrast, others were connected to the lamina propria and muscle layer (Figure 3). Mild chronic inflammation and congestion were also seen in the stroma. No mitotic figures, koilocytosis, dysplasia, or stromal invasion were observed. Immunohistochemical analysis showed squamous epithelial cells positive for p63, focally positive for p16, and displaying a wild-type staining pattern for p53. Ki-67 expression was localized to the basal layer with increased levels. These findings were consistent with squamous cell papilloma.

There was no mitosis, koilocytosis, or dysplasia in the epithelium with a distinct granular layer. No stromal invasion was seen.

No additional treatment was considered, and the patient was followed up. The patient's last follow-up was 6 months after resection, and there were no urinary symptoms and no evidence of recurrence of the lesion on CT urography imaging.

DISCUSSION

The majority of bladder lesions originate from the urothelium. Squamous cell lesions are rare and can be either benign or malignant (1). Malignant squamous lesions of the bladder include squamous cell carcinoma, squamous differentiation in urothelial carcinoma, and in situ squamous cell carcinoma (5). Benign squamous lesions include keratinized squamous metaplasia, squamous cell papilloma, verrucous squamous hyperplasia, and condyloma acuminatum.

Squamous cell papilloma localized in the bladder is extremely rare. A review of the literature reveals only three case reports published to date (5,6,7). In a study by Guo et al. (2006), 29 cases of non-invasive squamous lesions of the bladder were examined, five of which were identified as squamous cell papillomas (3). A case of a 74-year-old patient presenting with hematuria and LUTS in 2013 is presented (5). In a case report published in 2022, a case of squamous papilloma accompanied by a bladder stone was treated with TURB (7). The case reported in 2020 involved a 76-year-old woman (6). Sengupta et al. (2021) also reported a case of squamous cell papilloma localized in the urethra (4).

In clinical practice, these lesions can present with atypical symptoms such as hematuria, lower urinary tract symptoms, or suprapubic pain, but they may also be incidentally discovered. Due to its rarity, the etiology of squamous cell

papilloma remains unclear. Risk factors include smoking, exposure to aromatic amines, and a history of bladder stones, as observed in our case (4). In the study conducted by Cheng et al. in 2000, no relationship was found between squamous papilloma and HPV infection (8). However, the relationship between oral squamous papilloma and HPV has been demonstrated in some studies (9).

The differential diagnosis should exclude other benign and malignant lesions of the bladder, primarily urothelial carcinoma. On cystoscopy, squamous cell papilloma typically appears as a calcified mass, which is often indistinguishable from urothelial carcinoma. Diagnosis is established through accurate pathological evaluation of tissue obtained via excisional biopsy or transurethral resection. Histologically, squamous cells are characterized by parallel alignment to the surface, abundant eosinophilic cytoplasm, and a spindle-shaped morphology, whereas urothelial cells typically exhibit moderate clear or basophilic cytoplasm and a perpendicular alignment to the surface. Squamous cell papilloma is described as a papillary, exophytic, non-invasive lesion with extensive keratinization on the surface. Immunohistochemically, p63 positivity and focal p16 positivity are significant for diagnosing squamous papilloma.

Squamous papilloma should be differentially diagnosed with keratinizing squamous metaplasia, which is considered an important risk factor for invasive carcinoma. Keratinizing squamous metaplasia, clinically known as leukoplakia, is a pathologic response to chronic inflammatory stimulation such as from infection, indwelling catheters, stones, and parasite eggs. Marked hyperkeratosis, parakeratosis, and elongation of the rete pegs were present in verrucous squamous hyperplasia. The condyloma would be larger than the papilloma, would have a broader base, and would appear pink-to-red as a result of less keratinization. HPV infection should be ruled out by the absence of morphological koilocytic features or through molecular methods (8). In cases of nuclear atypia, mitotic activity, or irregular cell clusters within the stroma suggestive of invasion, malignant tumors must be considered.

Due to its rarity and limited data in the literature, the clinical significance of squamous cell papilloma remains unclear. It is considered a benign lesion, and recurrence is believed to be rare following surgical excision (3). In the study conducted by Guo et al., 5 cases of squamous papilloma were identified and followed up for 21 months, with recurrence observed in only one case (3). In the case reported by Takei et al., recurrence was observed in the third month, but no recurrence was noted in the following 2.5 years (6). In the case reported by Miliaras et al., no recurrence was observed after 6 months of follow-up, while the follow-up duration in the case reported by Mohamed et al. was not specified (5,7). In the case of urethral squamous papilloma, no recurrence was observed after 9 months of follow-up (4). The paucity of reported cases and the short follow-up periods makes it challenging to establish follow-up recommendations.

In conclusion, squamous cell papilloma of the bladder is a rare benign lesion with characteristic microscopic and immunohistochemical features that mimic malignant bladder tumors endoscopically. Its etiology and clinical significance remain uncertain. This case emphasizes the importance of accurate pathological evaluation for urologists and underscores the need to avoid overly aggressive treatments for patients.

Ethics Approval and Consent to Participate

Our institution (Recep Tayyip Erdoğan University) does not require any ethical approval for reporting individual cases or case series. Our study is following the Declaration of Helsinki. Written informed consent for the publication of identifying images or other personal or clinical details was obtained from the patient. The photographs are completely unidentified, and personal details are not mentioned in the text. The authors are accountable for all aspects of the work and for ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Acknowledgements: Thank the patient for their willingness to participate in this case report.

Funding: The authors declared that this study received no financial support.

Conflict of Interests: No conflict of interest was declared by the authors.

Informed Consent: Written informed consent for publication of identifying images or other personal or clinical details was obtained from the patient. The photographs are completely unidentified, and personal details are not mentioned in the text.

Data Sharing Statement: All data generated or analysed during this study are included in this published article. The authors are accountable for all aspects of the work and for ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval: Our institution (Recep Tayyip Erdoğan University) does not require any ethical approval for reporting individual cases or case series. Our study is in accordance with the Declaration of Helsinki.

Authorship Contributions: Surgical and Medical Practices: G.A. and E.O., Concept: G.A. and H.U., Design: G.A., H.G. and H.U., Data Collection or Processing: G.A., E.O. and H.G., Analysis or Interpretation: G.A. and H.G, Literature Search: G.A., E.D. and S.Y., Writing:G.A.

REFERENCES

1. Busch C, Johansson SL. Urothelial papilloma. In: Eble JN, Sauter G, Epstein JI, Sesterhenn IA, editors. Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs. 3rd edition. Lyon, France: IARC Press; 2004. p. p. 113.
2. Brown JT, Narayan VM, Joshi SS, et al. Challenges and opportunities in the management of non-urothelial bladder cancers. Cancer Treat Res Commun. 2023;34:100663. https://doi.org/10.1016/j.ctarc.2022.100663
3. Guo CC, Fine SW, Epstein JI. Noninvasive squamous lesions in the urinary bladder: a clinicopathologic analysis of 29 cases. Am J Surg Pathol. 2006;30(7):883-891. https://doi.org/10.1097/01.pas.0000213283.20166.5a
4. Sengupta S, Basu S, Ghosh K, et al. Urethral squamous papilloma with multiple bladder diverticulum: A case report and literature review. Urol Case Rep. 2021;37:101638. Published 2021 Mar 13. https://doi.org/10.1016/j.eucr.2021.101638
5. Miliaras D, Vakalopoulos I, Anagnostou E. Squamous cell papilloma of the urinary bladder endoscopically mimicking cancer. Case Rep Pathol. 2013;2013:486312. https://doi.org/10.1155/2013/486312
6. Takei K, Otsuki Y. Hinyokika Kiyo. 2020;66(11):403-406. https://doi.org/10.14989/ActaUrolJap_66_11_403
7. Mohamed A, Khalil IA, Aldeeb M, et al. Squamous cell papilloma a rare urinary bladder tumor, case report and operative video. Urol Case Rep. 2022;43:102074. https://doi.org/10.1016/j.eucr.2022.102074
8. Cheng L, Leibovich BC, Cheville JC, et al. Squamous papilloma of the urinary tract is unrelated to condyloma acuminata. Cancer. 2000;88(7):1679-1686. https://doi.org/10.1002/(sici)1097-0142(20000401)88:7<1679::aid-cncr23>3.0.co;2-k
9. Jaju PP, Suvarna PV, Desai RS. Squamous papilloma: case report and review of literature. Int J Oral Sci. 2010;2(4):222-225. https://doi.org/10.4248/IJOS10065

eISSN 3023-6940

THE
NEW JOURNAL
OF UROLOGY

AUTHOR GUIDELINES

AIM

The New Journal of Urology (New J Urol) is a scientific, referred, open access publication of the Eurasian Uro-oncological Association. The society is a non-profit organization and it aims to increase the standards in the field of urology including education of the academicians, professionals and public. The New Journal of Urology aims to create or make contributions for the development of technical, scientific and social facilities and it also cooperates with any and all related institutions, organizations, foundations and societies from the national and international area for this purpose.

The journal' s financial expenses are covered by the Eurasian Uro-oncological Association. The journal is published quarterly – three times a year- in February, June and October, respectively and the language of the journal are English and Turkish.

The purpose of the New Journal of Urology is to contribute to the literature by publishing urological manuscripts such as scientific articles, reviews, letters to the editor, case reports, reports of surgical techniques, surgical history, ethics, surgical education and articles of forensic medicine.

The target group of the journal consists of academicians working in the field of urology, urologists, residents of urology and all other fields of expertise and practitioners interested in urology.

Urology specialists, medical specialty fellows and other specialists who are interested in the field of urology are the journal's target audience.

SCOPE

The New Journal of Urology has been indexed by TUBITAK ULAKBIM-TR DİZİN, Google Schoolar, Scilit, EBSCO, SOBIAD Citation Index, J-GATE, İdeal Online, Turkish Citation Index, and TurkMedline (National Health Sciences-Periodicals Database).

Yeni Üroloji Dergisi/The New Journal of Urology ceased printing in 2024 (ISSN: 1305-2489, eISSN: 2687-1955).

The New Journal of Urology is now only published online with the eISSN: 3023-6940.

The journal is integrated with ORCID and CrosReff DOI.

All published content is available for free at https://newjournalurology.com/archive.

All manuscripts submitted to the journal should be submitted via the online submission system, which is available at the link.

Instructions for authors, including technical information and required forms, can be found at https://newjournalurology.com/author-guidelines.

Editorial and publication processes of the journal are shaped in accordance with the guidelines of the international organizations such as the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE). Our journal follows the principles of transparency and best practices for scholarly publishing as identified by the Committee on Publication Ethics (COPE), the Directory of Open Access Journals (DOAJ), the Open Access Scholarly Publishing Association (OASPA), and the World Association of Medical Editors (WAME).

COPE DOAJ OASPA WAME. Principles of Transparency and Best Practice in Scholarly Publishing — English.

https://doi.org/10.24318/cope.2019.1.12

The statements and/or opinions indicated at the articles which are published at the journal reflect the views of the author, not the opinions of the editors, editorial board and / or the Publisher. Editors and publishers do not accept any responsibility for such materials.

No fee is required for submitting articles, evaluation, processing or publishing process from the authors.

Authors' credentials and e-mail addresses are in no way used for other purposes.

The journal will allow the authors to retain publishing rights without restrictions.

The New Journal of Urology is an open access journal, which means that all content is freely available without charge to the user or his/her institution. Users are allowed to read, download, copy, distribute, print, search, or link to the full texts of the articles, or use them for any other lawful purpose, without asking prior permission from the publisher or the author. This is in accordance with the BOAI definition of open access.

eISSN 3023-6940

THE
NEW JOURNAL
OF UROLOGY

AUTHOR GUIDELINES

INFORMATION ABOUT JOURNAL

The New Journal of Urology is an international, scientific, open access, online/published journal in accordance with independent, unbiased, and double-blinded peer-review principles, published three times a year on February, June and October. The New Journal of Urology is indexing in both international and national indexes and the publication language is English.

The New Journal of Urology has been indexed by TUBITAK ULAKBIM-TR DİZİN, Google Schoolar, Index Copernicus, Scilit, EBSCO, EuroPub, SOBIAD Citation Index, OAJI, J-GATE, İdeal Online, Turkish Citation Index, and TurkMedline (National Health Sciences-Periodicals Database).

Yeni Üroloji Dergisi/The New Journal of Urology ceased printing in 2024 (ISSN: 1305-2489, eISSN: 2687-1955).

The New Journal of Urology is now only published online with the eISSN: 3023-6940.

The New Journal of Urology publishes papers on all aspects of urology and related topics. In addition to original articles, review articles, case reports and letters to the editor are also published.

The scientific board guiding the selection of the papers to be published in the journal consists of elected experts of the journal and if necessary, are selected from national and international authorities.

The authors should guarantee that the manuscripts have not been previously published and/or are under consideration for publication elsewhere. Only those data presented at scientific meetings in form of an abstract may be accepted for consideration, however, the date, name and place of the meeting in which the paper was presented should be stated. The signed statement of scientific contributions and responsibilities of all authors, and statement on the absence of conflict of interests are required. All manuscripts are reviewed by the editor and at least two experts/reviewers.

Manuscript format should be in accordance with Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication (available at https://www.icmje.org/). The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Council of Medical Journal Editors (ICMJE). The journal conforms to the Principles of Transparency and Best Practice in Scholarly Publishing.

The New Journal of Urology does not charge for submitting articles, evaluation, processing or publishing process from the authors.

Authors' credentials and e-mail addresses are in no way used for other purposes.

The journal will allow the authors to retain publishing rights without restrictions.

The New Journal of Urology is an open access journal, which means that all content is freely available without charge to the user or his/her institution. Users are allowed to read, download, copy, distribute, print, search, or link to the full texts of the articles, or use them for any other lawful purpose, without asking prior permission from the publisher or the author. This is in accordance with the BOAI definition of open access.

All the content published in the journal can be accessed free of charge via the following link; https://newjournalurology.com/archive.

All submissions are screened by a similarity detection

eISSN 3023-6940

THE
NEW JOURNAL
OF UROLOGY

PREPARATION OF MANUSCRIPT

software (iThenticate by Crossref). In the event of alleged or suspected research misconduct, e.g., plagiarism, citation manipulation, and data falsification/fabrication, the Editorial Board will follow and act in accordance with COPE guidelines.

The authors should identify the individuals who accept direct responsibility for the manuscript. Each individual listed as an author should fully meet the criteria for authorship and should complete an authorship form (criteria recommended by the International Committee of Medical Journal Editors - www.icmje.org/). The corresponding author should clearly indicate the preferred citation and identify all individual authors.

When using previously published content, including figures, tables, or any other material in electronic formats, authors must obtain permission from the copyright holder. Legal, financial and criminal liabilities in this regard belong to the author(s).

Statements or opinions expressed in the manuscripts published in The New Journal of Urology reflect the views of the author(s) and not the opinions of the editors, the editorial board, or the publisher; the editors, the editorial board, and the publisher disclaim any responsibility or liability for such materials. The final responsibility regarding the published content remains with the authors.

Journal Title:	The New Journal of Urology
Journal Abbreviation:	New J Urol
Frequency:	Tri-annual (February, June, October)
Publisher:	Ali İhsan Taşçı
Language:	English
Publication Date:	2008
Journal History:	Continues: Yeni üroloji dergisi (online) eISSN: 2687-1955 (*2019-2024*) Has other medium version: Yeni üroloji dergisi (printed), ISSN: 1305-2489 (*2008-2024*)
Continued by:	The New Journal of Urology (Online), 3023-6940 (2024-)
DOI Prefix:	10.33719

Broad Subject Term(s):	Oncology Urology & Nephrology
Open Access& Licensing:	OA Creative Commons CC BY, Attribution 4.0 International (http://creativecommons.org/licenses/by/4.0/)
Electronic Links:	https://newjournalurology.com/

GENERAL GUIDELINES

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at the link. Manuscripts submitted via any other medium will not be evaluated. Manuscripts submitted to the journal will first go through a technical evaluation process where the editorial office staff will ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the submitting author with technical correction requests. The editor reserves the right to reject manuscripts that do not comply with the above-mentioned requirements. Editors have the right to make corrections without changing the main text. The ORCID (Open Researcher and Contributor ID) number of the authors should be provided while sending the manuscript. A free registration can be done at https://orcid.org.

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.

eISSN 3023-6940

THE NEW JOURNAL OF UROLOGY

PREPARATION OF MANUSCRIPT

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 ICJME 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

Original Articles

New Journal of Urology adopts the ICMJE's clinical trial registration policy, which requires that clinical trials must be registered in a publicly accessible registry that is a primary register of the WHO International Trials Registry Platform (ICTRP) or in ClinicalTrials.gov. Authors can help improve transparency and accountability in their research by recording clinical trials in a publicly accessible registry.

Original Research Articles should include subheadings below;

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

eISSN 3023-6940

THE
NEW JOURNAL
OF UROLOGY

PREPARATION OF MANUSCRIPT

- 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

Case Reports

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

Letters to the Editor

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.

Keywords

eISSN 3023-6940

THE NEW JOURNAL OF UROLOGY

PREPARATION OF MANUSCRIPT

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

During the initial submission process to The New Journal of Urology, corresponding authors must submit a signed and scanned authorship contribution form. This form is available for download through https://dergipark.org.tr/tr/journal/1455/file/2260/download. The purpose of this requirement is to

eISSN 3023-6940

THE
NEW JOURNAL
OF UROLOGY

PREPARATION OF MANUSCRIPT

ensure appropriate authorship rights and prevent ghost or honorary authorship.

Manuscript Retraction: Authors may withdraw their manuscript from the journal by providing a written declaration.

References

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.

Author Contribution&Copyright Transfer Form

The New Journal of Urology requires corresponding authors to submit a signed and scanned version of the authorship contribution form (available for download through https://dergipark.org.tr/tr/journal/1455/file/2260/download) during the initial submission process to act appropriately on authorship rights and to prevent ghost or honorary authorship.

Manuscript Retraction

For any other reason authors may withdraw their manuscript from the journal with a written declaration.

Revisions

When submitting a revised version of a paper, the author must submit a detailed "Response to the reviewers" that states point by point how each issue raised by the reviewers has been covered and where it can be found (each reviewer's comment, followed by the author's reply and line numbers where the changes have been made) as well as an annotated copy of the main document. If the revised version of the manuscript is not submitted within the allocated time, the revision option may be canceled. If the submitting author(s) believe that additional time is required, they should request this extension before the initial period is over.

AFTER ACCEPTANCE

Accepted manuscripts are copy-edited for grammar, punctuation, and format. A PDF proof of the accepted

eISSN 3023-6940

THE
NEW JOURNAL
OF UROLOGY

PREPARATION OF MANUSCRIPT

manuscript is sent to the corresponding author and their publication approval is requested. The journal owner and the editorial board are authorized to decide in which volume of the accepted article will be printed. Authors may publish their articles on their personal or corporate websites by linking them to the appropriate cite and library rules.

THE
NEW JOURNAL
OF UROLOGY

Volume 20, Issue 2, June, 2025
İstanbul / Türkiye

Pera Publishing Services
Address: Ataköy 3-4-11 Kısım Mah. Dr Remzi Kazancıgil Cd. O-114 N:12 D:7 Bakırköy İstanbul / Türkiye
E-Mail : info@perayayincilik.com