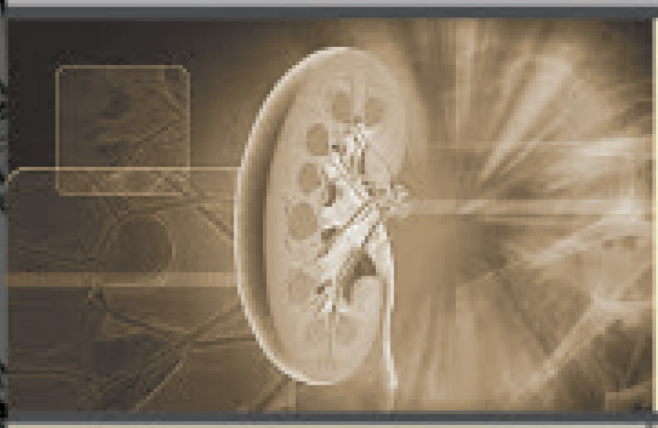
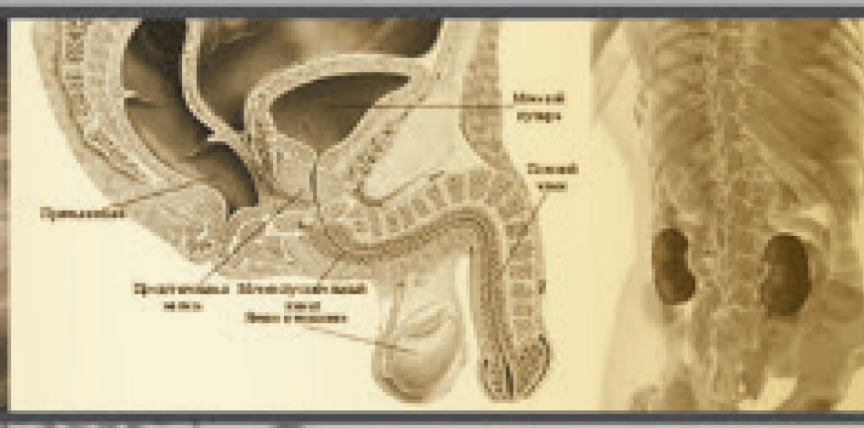
2010
Society of Urological Surgery in Türkiye

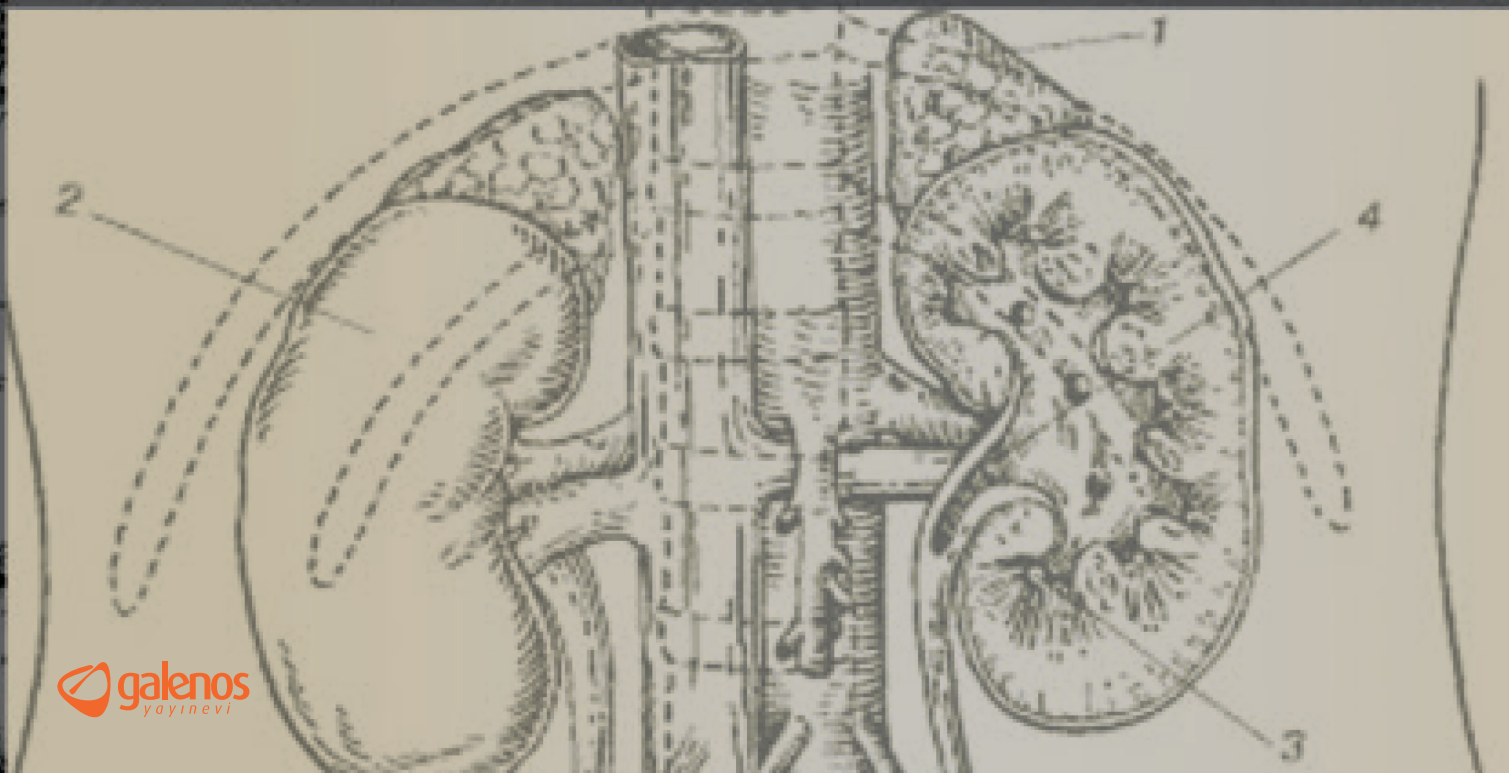
E-ISSN 2148-9580

JOURNAL OF UROLOGICAL SURGERY

Volume 13 / Issue 2 / June 2026 www.jurolsurgery.org







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Journal of Urological Surgery is indexed by **Web of Science-Emerging Sources Citation Index (ESCI), DOAJ, ProQuest, EBSCO, Embase, CINAHL, British Library, Gale, IdealOnline, TUBITAK/ULAKBIM Turkish Medical Database, TurkMedline, Hinari, GOALI, ARDI, OARE, AGORA, J-GATE, CNKI** and **Türkiye Citation Index**.

The journal is published electronically.

Owner: Bülent ÖNAL on Behalf of the Society of Urological Surgery

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Web: www.galenos.com.tr
Publisher Certificate Number: 14521
Publication Date: June 2026
E-ISSN: 2148-9580
International scientific journal published quarterly.

Reviewing the articles' conformity to the publishing standards of the Journal, typesetting, reviewing and editing the manuscripts and abstracts in English and publishing process are realized by Galenos.

Society of Urological Surgery

JOURNAL OF UROLOGICAL SURGERY

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Doi: 10.4274/jus.galenos.2026.2025-11-6
J Urol Surg 2026;13(2):72-79

Clinical Trial Landscape of CAR-engineered Cell Therapies in Renal Cell Carcinoma: Current Status and Future Directions

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Abstract

Renal cell carcinoma (RCC) is a common urologic malignancy with poor outcomes in metastatic disease, despite advances in targeted therapies and immune checkpoint inhibitors. Chimeric antigen receptor (CAR)-engineered cell therapies, particularly CAR-T and CAR-natural killer (CAR-NK) cells, have revolutionized the treatment of hematologic malignancies, but face unique barriers in solid tumors such as RCC, including tumor heterogeneity and an immunosuppressive microenvironment. Using the Trialtrove database with the keywords "CAR" and "oncology: kidney," we identified 44 eligible interventional trials as of June 10, 2025. Most are early-phase and industry-sponsored, and are conducted primarily in China and the United States. CAR-T studies outnumber CAR-NK trials, with cluster of differentiation 70 as the most common target, followed by estimated glomerular filtration rate and programmed cell death protein 1. Combination regimens frequently incorporate lymphodepletion with cyclophosphamide and fludarabine. Preliminary clinical data indicate that CAR therapies for RCC are generally safe and feasible but show limited durable efficacy. Key obstacles include antigen escape and poor persistence of infused cells within the tumor microenvironment. To overcome these challenges, next-generation strategies—such as dual-target CAR constructs, cytokine co-expression (e.g., interleukin-15), and biomarker-guided patient selection—are actively being explored. Regulatory frameworks in the United States and China increasingly support innovation in cellular therapies. Overall, the evolving clinical landscape highlights both the promise and the ongoing challenges of CAR-engineered therapies for RCC, underscoring the need for optimized designs and rational combination approaches to improve patient outcomes.

Keywords: Renal cell carcinoma, CAR-T therapy, CAR-NK therapy, clinical trials, immunotherapy, targeted antigens

Introduction

Renal cell carcinoma (RCC) is the most common malignant tumor of the kidney, originating from the renal tubular epithelium. It accounts for 85-90% of renal malignancies and approximately 2-3% of all solid tumors, with clear cell carcinoma representing the predominant histological subtype (about 70-80%) (1,2). Epidemiological studies show a steady global increase in RCC incidence. According to GLOBOCAN 2020, there are approximately 430,000 new cases and 180,000 deaths annually worldwide, with the highest incidence reported in North America and Europe. In the United States, approximately 80,000 new cases are diagnosed annually. RCC occurs about twice as often in men as in women, and incidence peaks between the ages of 50 and 70 (3).

In China, the incidence of RCC has also risen markedly, with an estimated 70,000-80,000 new cases and approximately 30,000 deaths annually. Among urinary tract malignancies, it ranks second only to bladder cancer and is more prevalent in urban and economically developed regions (4). Established risk factors include smoking, obesity, hypertension, chronic kidney disease, including dialysis, occupational exposures (e.g., cadmium, asbestos, organic solvents), and hereditary syndromes such as von Hippel-Lindau (VHL) disease (5). The widespread adoption of imaging technologies has resulted in increased incidental detection of RCC at earlier stages. For localized RCC, surgical resection can achieve a 5-year survival rate of 70-90%. However, the prognosis for patients with advanced or metastatic disease remains poor, with 5-year survival below 20%. Historically, surgical resection was the only curative

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Received: 11.11.2025 **Accepted:** 13.01.2026 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Lai Y, Chai W, Huang B, Wang Z, Liang H. Clinical trial landscape of CAR-engineered cell therapies in renal cell carcinoma: current status and future directions. J Urol Surg. 2026;13(2):72-79.

option, while radiotherapy and chemotherapy offered minimal benefit (6).

The therapeutic landscape changed with the advent of tyrosine kinase inhibitors (TKIs) targeting the vascular endothelial growth factor (VEGF) pathway (6,7), followed by the development of immune checkpoint inhibitors (ICIs) directed at programmed cell death protein 1 (PD-1)/PD-ligand 1 and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). Combination regimens involving ICIs and TKIs have since become the standard of care (8,9). More recently, chimeric antigen receptor (CAR)-engineered cell therapies—particularly CAR-T and CAR-natural killer (CAR-NK) cells—have transformed the treatment paradigm for hematologic malignancies (10). Nonetheless, their application to solid tumors such as RCC is hindered by challenges including tumor heterogeneity, an immunosuppressive microenvironment, and difficulties in antigen selection (11,12).

To better define current progress and unmet needs, we analyzed the clinical trial landscape of CAR-engineered therapies in RCC. A comprehensive review was conducted using the Trialtrove clinical trial database-the world's largest curated trial repository, encompassing more than 450,000 data sources and over 350,000 global studies. The search strategy used the keywords "chimeric antigen receptor" and "oncology: kidney", with a cut-off date of June 10, 2025. Eligible studies were interventional trials explicitly investigating CAR-T or CAR-NK cell therapies for RCC. Trials without explicit CAR engineering or those with non-interventional designs were excluded. Parameters assessed included temporal trends, trial phase and status, targeted antigens, therapy type (CAR-T vs. CAR-NK), combination regimens, sponsorship, and geographic distribution. Data extraction accuracy was independently validated by multiple reviewers.

1. Treatment Landscape of RCC and Rationale for CAR-based Immunotherapy

RCC is traditionally managed with surgery. Partial nephrectomy is preferred for small, localized tumors to preserve renal function, while radical nephrectomy is reserved for larger or more complex tumors. For frail patients or patients with very small lesions, active surveillance or minimally invasive ablation (cryoablation, radiofrequency ablation) is appropriate. According to the 2025 European Association of Urology guidelines, surgery remains the mainstay in localized disease, with nephron-sparing approaches prioritized when feasible (13).

The advent of systemic therapy has reshaped the management of advanced and metastatic RCC. ICIs—alone or combined with VEGF/TKIs—are now first-line standards of care, exemplified by nivolumab plus ipilimumab or pembrolizumab plus axitinib, which have shown superior survival compared with sunitinib in randomized trials (9,14). Targeted VEGF and mechanistic target of rapamycin inhibitors remain options for selected patients. Nevertheless, many individuals experience primary resistance or eventual relapse, highlighting the limits of current immunotherapy.

VHL-associated RCC follows a similar paradigm: surveillance and nephron-sparing surgery remain key, and the hypoxia-inducible factor-2α inhibitor belzutifan offers a new systemic option, showing durable responses in VHL-associated RCC, including tumor shrinkage in early clinical studies (15). Yet, even with these advances, durable control of progressive disease remains uncommon, underscoring the need for novel immunotherapeutic approaches.

CAR-engineered cell therapies—including CAR-T and CAR-NK cells—directly redirect lymphocytes to tumor-associated antigens, potentially overcoming checkpoint resistance and the immunosuppressive tumor microenvironment (TME). Recent preclinical and early clinical evidence shows promise: cluster of differentiation 70 (CD70) is highly expressed in many RCC tumors and has been targeted successfully by novel CAR-T constructs, with CTX130 (allogeneic CD70-targeting CAR-T) achieving disease control in the majority of advanced/refractory clear cell RCC (ccRCC) patients and at least one durable complete response lasting 3 years (16). Early work has also explored dual-targeted CARs [e.g., carbonic anhydrase IX (CAIX) + CD70] to address antigen heterogeneity. These next-generation, highly personalized therapies aim to address the central challenge of immune evasion in RCC and represent a logical extension of current immunotherapy strategies.

2. Principles of CAR-T and CAR-NK Therapies

2.1. Principles of CAR-T Therapy

CAR-T therapy is a novel form of adoptive cell transfer that involves genetically modifying autologous T-cells to express CARs. These synthetic receptors enable T-cells to recognize and eliminate tumor-associated antigens independently of the major histocompatibility complex (11).

2.1.1. CAR Structure and Design

A CAR comprises several modular domains: an extracellular single-chain variable fragment (scFv) for antigen recognition; a hinge region linking the scFv to the transmembrane domain; a transmembrane domain anchoring the receptor to the T-cell membrane; and intracellular signaling domains. The latter include co-stimulatory domains [e.g., CD28, CD137 (4-1BB)] and the CD3 zeta (CD3ζ) activation domain, which together transmit signals that drive T-cell proliferation and cytotoxic function (Figure 1A) (17). First-generation CARs contained only the CD3ζ signaling domain. These receptors showed limited T-cell activation and persistence due to the absence of co-stimulation. Second-

generation CARs added a single co-stimulatory domain (e.g., CD28 or 4-1BB), which significantly enhanced T-cell activation, persistence, and antitumor activity (10). Third-generation CARs incorporated two co-stimulatory domains, further improving T-cell function and durability. Fourth-generation CARs ("armored" CARs) engineered to secrete cytokines [e.g., interleukin (IL)-12, IL-15] or express chemokine receptors, thereby enhancing persistence, infiltration, and independence from host immune support (Figure 1B) (11).

2.1.2. Manufacturing Process

Cell Collection: T-cells are obtained from patients, typically via leukapheresis (18).

Genetic Modification: Genes encoding the CAR construct are introduced using viral vectors (e.g., lentivirus, γ-retrovirus) or non-viral methods such as transposon systems (10).

***In Vitro* Expansion:** The engineered T-cells are stimulated and expanded *ex vivo* to achieve the therapeutic cell dose (18).

Patient Reinfusion: The expanded CAR-T-cells are administered to the patient by intravenous infusion (Figure 2) (18).

2.1.3. Mechanism of Action

Antigen Recognition: CAR-T-cells identify tumor-specific antigens via their scFv domain (17).

T-cell Activation: Antigen binding triggers signaling through the co-stimulatory and CD3ζ domains, promoting proliferation and cytokine secretion (19).

Tumor Killing: Activated CAR-T-cells destroy tumor cells by releasing perforin and granzymes, while also secreting pro-inflammatory cytokines [e.g., interferon (IFN)-γ, tumor necrosis factor (TNF)-α] that recruit and activate additional immune cells (19).

2.2. Principles of CAR-NK Therapy

CAR-NK therapy applies similar engineering strategies to NK cells, exploiting their intrinsic ability to kill tumor cells via both antigen-dependent and antigen-independent mechanisms (20).

2.2.1. NK Cell Sources

CAR-NK cells can be derived from multiple sources, including peripheral blood, umbilical cord blood, or induced pluripotent stem cells (iPSCs). These diverse origins support the potential for "off-the-shelf" allogeneic applications (21).

2.2.2. CAR Structure and Design

Like CAR-T-cells, CAR-NK constructs feature an antigen-binding domain (scFv), a hinge and a transmembrane domain, and intracellular signaling modules. For NK cells, co-stimulatory

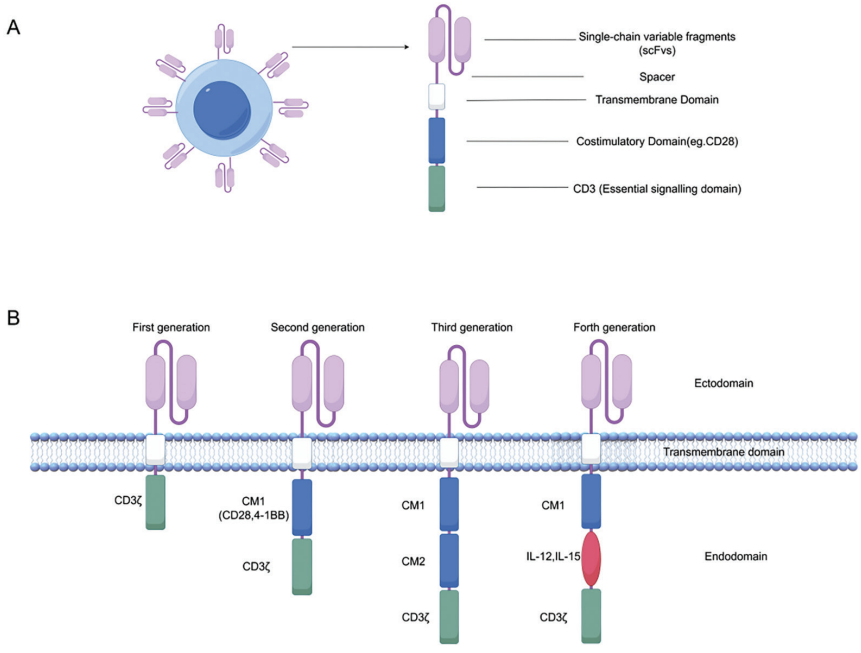

Figure 1. CAR structure domains and generational evolution. (A) The basic structure of a CAR, consisting of an antigen-binding domain (single-chain variable fragment, scFv), a spacer/hinge region, a transmembrane domain, and intracellular signaling domains. (B) The generational evolution of CAR designs: first-generation CARs contain only the CD3ζ activation domain; second-generation CARs incorporate one costimulatory domain (e.g., CD28 or 4-1BB), enhancing persistence and activity; third-generation CARs combine multiple costimulatory domains for amplified signaling; and fourth-generation CARs (also called "armored" CARs) are based on second-generation constructs and engineered to express cytokines (e.g., IL-12, IL-15) or other molecules to modulate the tumor microenvironment and improve efficacy

CAR: Chimeric antigen receptor, scFv: Single-chain variable fragment, CD: Cluster of differentiation, IL: Interleukin

and activation domains tailored to their biology include DNAX-activating protein 10 (DAP10), DAP12, and CD3ζ.

2.2.3. Manufacturing Process

Cell Collection and Isolation: NK cells are isolated from peripheral blood, cord blood, or iPSCs (22).

Genetic Modification: *CAR* genes are introduced using viral vectors or non-viral approaches such as transposons (20).

***In Vitro* Expansion:** Modified NK cells are expanded *ex vivo* to reach therapeutic numbers (22).

Patient Reinfusion: Expanded CAR-NK cells are infused intravenously (22).

2.2.4. Mechanism of Action

Antigen Recognition: CAR-NK cells engage tumor-specific antigens via the scFv domain.

NK Cell Activation: Signal transduction through co-stimulatory and activation domains promotes NK cell proliferation and cytokine secretion (21).

Tumor Killing: Activated CAR-NK cells eliminate tumor cells through perforin- and granzyme-mediated cytotoxicity, cytokine release (e.g., IFN-γ, TNF-α), and apoptosis-inducing pathways via death receptor ligands such as Fas ligand and tumor necrosis factor-related apoptosis-inducing ligand (Figure 2) (23).

3. CAR-T and CAR-NK Therapies in RCC

3.1. Current Status of CAR-engineered Cell Therapy Clinical Studies in RCC

A systematic review of the Trialtrove database was conducted on June 10, 2025, using search terms related to CAR-engineered cell therapies and RCC. This search identified 44 interventional trials meeting the inclusion criteria. Studies lacking CAR engineering or employing non-interventional designs were excluded. Temporal analysis revealed a steady increase in the number of trial initiations from 2010 (n=1) to a peak in 2023 (n=9), followed by a modest decline (Figure 3A).

3.2. Trial Phases and Design

Most trials are early-phase (Phase I or Phase I/II) (Figure 3B), reflecting the exploratory nature of CAR-based therapy in solid tumors. These studies primarily evaluate safety, tolerability, and dose escalation to define the maximum tolerated dose and recommended Phase II dose, and collect preliminary efficacy signals such as objective response rate (ORR), duration of response, and progression-free survival. No Phase III trials

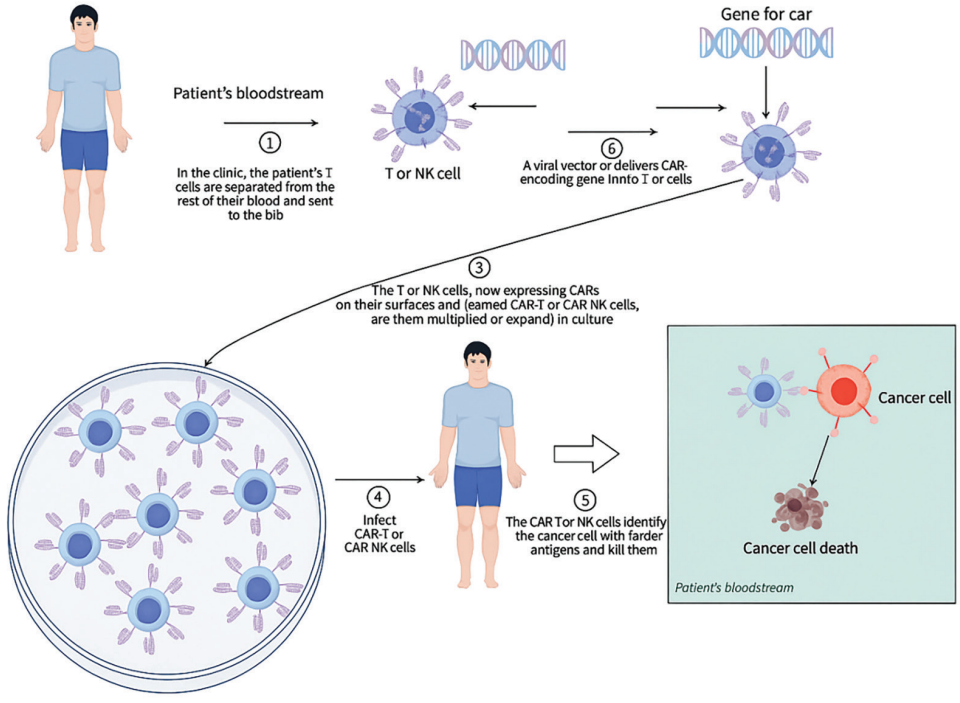

Figure 2. Schematic diagram of the CAR-T or CAR-NK cell therapy process. This figure outlines the key steps of CAR-T or CAR-NK cell therapy: (1) T or NK cells are isolated from the patient's blood; (2) a viral vector is used to deliver the chimeric antigen receptor (*CAR*) gene into the T or NK cells in the laboratory; (3) CAR-expressing T or NK cells are expanded in culture; (4) CAR-T or CAR-NK cells are infused into the patient; (5) CAR-expressing cells recognize and kill cancer cells by binding to target antigens; (6) cancer cell death subsequently occurs

CAR: Chimeric antigen receptor, NK: Natural killer

have yet been initiated, underscoring the need to demonstrate superiority over current standards—TKIs and ICIs—before large-scale randomized evaluation.

A representative example is the multicenter TRAVERSE phase 1a/b trial (NCT04696731), which is testing the allogeneic anti-CD70 CAR-T product ALLO-316 in advanced ccRCC after failure of ICI and VEGF inhibitor therapy (24). At a median follow-up of 6.8 months, the ORR was 20% in CD70-positive patients and 25% in patients with ≥50% CD70 expression; all confirmed responses were ongoing at data cut-off. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were mostly mild, and no Graft-versus-host disease (GvHD) occurred, underscoring a manageable safety profile. Other early-phase candidates include CTX-131 and ADI-270 (CD70-directed), IOMX-0675 (anti-LILRB1/2), and next-generation constructs targeting PD-1, VEGF receptor (VEGFR), CAIX, and c-mesenchymal-epithelial transition factor (c-MET).

3.3. Integration of CAR-NK Platforms

Alongside CAR-T, CAR-NK therapies are emerging as a complementary approach, combining innate cytotoxicity with reduced risk of GvHD. Nearly all ongoing CAR-NK trials are Phase I or I/II and are primarily led by academic centers in China (Figure 3C). Platforms include umbilical cord blood-derived CAR-NK cells (CB-NK), CAR-NKT cells, and the NK-92 cell line, with targets mirroring CAR-T efforts, notably CD70, and extending to NKG2D ligands. Despite small sample sizes and occasional program discontinuations (e.g., fate therapeutics' FT-536), these

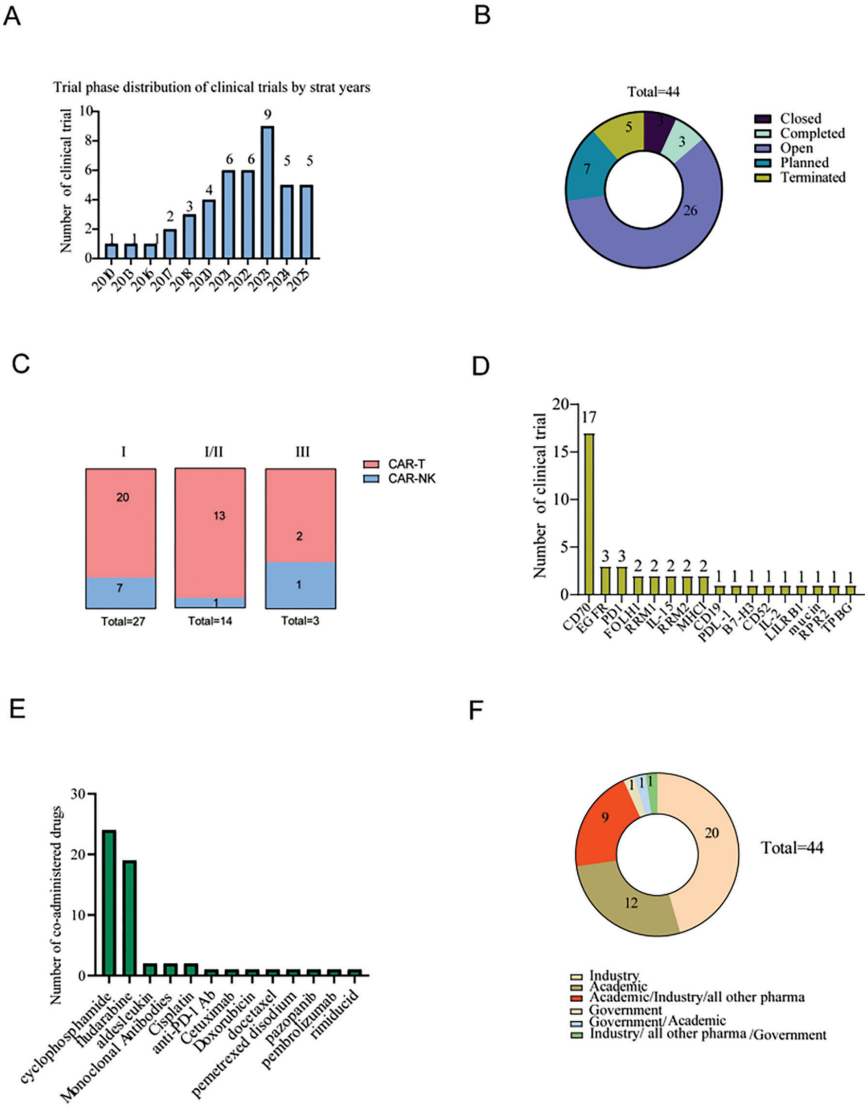

Figure 3. The Clinical Trial landscape of CAR-engineered cell therapies for renal cell carcinoma. (A) Number of trials by start year; (B) trial status distribution; (C) distribution of CAR-T versus CAR-NK trails by clinical phase; (D) number of trials per antigen target; (E) frequency of each co-administered drug with CAR cells; (F) sponsor type distribution

CAR: Chimeric antigen receptor, NK: Natural killer

studies provide important proof-of-concept evidence for NK-based engineering in RCC.

3.4. Antigen Targets and Technological Innovations

Antigen Spectrum (Figure 3D): CD70 is the dominant and most promising antigen (n=17), owing to high expression in ccRCC and minimal expression in normal tissue. Other exploratory targets include B7-H3 (CD276), estimated glomerular filtration rate, prostate-specific membrane antigen, human leukocyte antigen G, VEGFR, CAIX, and c-Met, reflecting diversification beyond CD70.

Technological Platforms: Allogeneic CAR constructs (e.g., ALLO-316, MT-027) shorten manufacturing timelines and reduce cost compared with autologous approaches. Logic-gated CAR designs (for example, A2B-395, which contains a tumor-specific "switch") enhance on-target safety.

Combination Strategies (Figure 3E): Many trials pair CAR cells with checkpoint inhibitors (e.g., pembrolizumab) or with lymphodepleting chemotherapy (cyclophosphamide and fludarabine) to improve CAR-cell persistence and antitumor efficacy.

3.5. Sponsorship and Geographic Landscape

Industry-led trials (n=20) outpace those sponsored by academic institutions (n=12) or mixed collaborations, highlighting robust commercial investment (Figure 3F). China and the United States dominate the global landscape, with Chinese cities such as Shanghai, Chongqing, and Shenzhen emerging as development hubs.

3.6. Key Findings and Challenges

Across both CAR-T and CAR-NK modalities, safety profiles are acceptable, with CRS generally mild; however, efficacy remains modest, with low-to-moderate ORRs and infrequent durable remissions. Major biological barriers include antigen escape, limited CAR-cell tumor infiltration, and a TME.

Overall, CAR-engineered cell therapy in RCC is transitioning from conceptual promise to early clinical reality. While CAR-T trials currently dominate and provide the most robust preliminary efficacy data, CAR-NK programs broaden the therapeutic horizon, potentially offering advantages in off-the-shelf availability, reduced cost, and enhanced safety. Overcoming the hostile TME, improving persistence, and achieving durable responses prior to Phase III validation and eventual clinical adoption.

3.7. Key Clinical Trial Results

Two landmark Phase I trials have defined the current clinical landscape of CD70-targeted CAR therapies in RCC.

The TRAVERSE trial (NCT04696731) evaluated ALLO-316 (allogeneic anti-CD70 CAR-T) in patients with CD70-positive metastatic ccRCC who had progressed on ICIs and VEGF inhibitors. At a median follow-up of 6.8 months, an ORR of 33% was achieved in CD70-positive patients, with a disease control rate (DCR) of 100%, and all responses were ongoing. CRS and ICANS were mild, and no GvHD occurred (24).

The COBALT-RCC trial (NCT04922015) evaluated CTX130 (allogeneic CD70-targeting CAR-T) in patients with advanced ccRCC. It reported a DCR of 81.3%, including one patient achieving complete remission for >3 years with no dose-limiting toxicity (16).

These trials demonstrate the feasibility and preliminary efficacy of CD70-targeted CAR-T therapies in RCC, with acceptable safety profiles. Both studies support the clinical potential of allogeneic platforms to overcome autologous manufacturing limitations and to improve accessibility.

3.8. CAR-Based Therapies in RCC

Emerging CAR-T and CAR-NK therapies show considerable promise for ccRCC. Early clinical studies have shown encouraging activity. Key Phase I trials such as TRAVERSE and COBALT-RCC have demonstrated the feasibility of CD70-targeted CAR-T therapies in RCC, with preliminary efficacy and acceptable safety profiles. Nanobody-based CD70 CAR-T cells effectively eliminated RCC cells *in vitro* and in xenograft models, demonstrating robust expansion and durable antitumor activity (25). CAR-NK therapy is also being investigated in early studies to counteract the TME. Dual-target constructs simultaneously engage CAIX and CD70, thereby enhancing efficacy and safety. Armored CARs incorporate localized release of ICIs (e.g., PD-1/CTLA-4 bispecifics) to remodel the TME. Multi-target and logic-gated designs, as well as allogeneic "off-the-shelf" CAR-NK platforms, aim to overcome antigen heterogeneity, immune escape, and poor cell persistence. Iterative CAR optimization and biomarker-driven patient selection, along with rational combinations with ICIs or TKIs, are key to improving efficacy and long-term survival in RCC.

4. Challenges and Future Directions

The growing body of clinical research on CAR-engineered cell therapies in RCC has established preliminary feasibility and safety, but also highlighted substantial obstacles. CD70-targeted CAR therapies have demonstrated clinical benefit, yet progress is limited by several key issues: antigen heterogeneity and immune escape, the TME, inadequate CAR cell trafficking and persistence, and safety concerns such as CRS and neurotoxicity.

A major obstacle is antigen escape, where tumor cells evade CAR-cell recognition by downregulating or losing expression of

the targeted antigen. This phenomenon, well-documented in hematologic malignancies, also occurs in solid tumors like RCC due to intratumoral heterogeneity and selective pressure from therapy. In RCC, antigen escape contributes to limited long-term efficacy, as observed in early trials in which initial responses were not sustained. Strategies to mitigate this include dual- or multitarget CAR constructs and logic-gated designs that require multiple antigens for activation.

Future efforts should prioritize iterative optimization of CAR designs. Next-generation approaches are justified by the need to address RCC-specific barriers: (1) dual- or multi-target CARs combat antigen heterogeneity and antigen escape, as single-target therapies risk relapse due to antigen loss, (2) Armored CARs secrete cytokines or checkpoint inhibitors to enhance persistence and counteract the immunosuppressive TME, (3) Logic-gated or switchable CARs improve safety by requiring multiple signals for activation, reducing off-tumor toxicity, (4) Allogeneic "off-the-shelf" platforms enable faster access and scalability. These innovations build on promising early data and aim to achieve deeper, more sustained remissions.

In parallel, biomarker-driven patient selection and rational combination approaches with established treatments—such as TKIs and ICIs—are expected to play an increasingly important role. Together, these strategies have the potential to improve efficacy, extend the durability of response, and ultimately enhance long-term survival in RCC patients.

Conclusion

CAR-T and CAR-NK therapies represent an emerging frontier in the treatment of RCC, offering potential solutions to the limitations of current targeted and immune checkpoint therapies. While their clinical efficacy remains modest at present, ongoing advances in CAR engineering, dual- and multi-targeting strategies, and rational combination regimens signal that cell-based therapies are poised to assume a meaningful role in future RCC management. Realizing this potential will require sustained innovation, biomarker-driven patient selection, and rigorous validation through well-designed clinical trials. Ultimately, these efforts may translate into durable responses and improved survival for patients with RCC.

Footnotes

Authorship Contributions

Concept: H.L., Design: Z.W., Data Collection or Processing: Y.L., W.C., Analysis or Interpretation: H.L., Literature Search: H.L., Z.W., Y.L., B.H., Writing: H.L., Z.W., Y.L., W.C., B.H.

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

Financial Disclosure: This work was supported by the Medical Research Project of Shenzhen Longhua Medical Association (2023LHMA01), the Medical Research Project of Shenzhen Longhua Medical Association (2023LHMA01), and the Scientific Research Projects of Medical and Health Institutions of Shenzhen Longhua District (2021055).

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ORIGINAL RESEARCH
General Urology

Doi: 10.4274/jus.galenos.2025.2025-6-10
J Urol Surg 2026;13(2):80-89

Lower Genitourinary Injuries Following Traffic Accidents: Epidemiology, Clinical Characteristics and Outcomes

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What's known on the subject? and What does the study add?

This study investigates lower genitourinary injuries (LGUI), including trauma to the testicles, penis, bladder, urethra, scrotum, vagina, and vulva, resulting from road traffic accidents, using a large trauma registry covering 178,625 cases from 1996 to 2015. Among these, 591 patients (0.33%) presented with LGUI, with motorcyclists and cyclists being the most affected groups (53% and 26.4%, respectively), while 83.9% of these victims were male. The most common injuries involved the testicles (41%) and scrotum (20%). The study aimed to describe the incidence, clinical patterns, and predictive factors of these injuries to improve early detection and management. Using a novel statistical model (DataShared-SepLogit), the study also identified frequent injury associations: Such as testicular injuries with penile trauma among motorcyclists and cyclists and bladder injuries with pelvic fractures in pedestrians and motorists. Analysis of clinical records revealed that testicular injuries were mostly serious and required surgery. Blunt trauma often led to severe outcomes such as hematomas and albuginea ruptures, whereas open wounds, though generally deemed less severe, paradoxically had lower salvage rates after surgery, perhaps due to the nature of the intervention required. Urethral and bladder injuries were often associated with pelvic fractures and required long catheterization or surgery. The study highlights the importance of early identification of LGUI after road accidents and may improve trauma protocols by drawing attention to underdiagnosed injuries with potentially serious consequences.

Abstract

Objective: Traffic accidents are the most frequent cause of genitourinary injuries. There exists a paucity of data on lower genitourinary injuries (LGUI) after traffic accidents. The main objective of our study was to analyze the incidence and clinical patterns of LGUI in traffic accidents. The secondary objective was to determine the LGUI predictive factors, and the associations with lesions.

Materials and Methods: Patient cases were extracted from the trauma registry of the French department of Rhone from 1995 to 2015. We assessed the LGUI presented by each road user category. Injuries were coded with the abbreviated injury scale and the injury severity score. Multivariate prediction models and the DataShared-SepLogit method were used for data analysis.

Results: Of 178,625 victims, 591 (0.33%) presented with LGUI, 53% were motorcyclists, and 26.4% were cyclists. The most commonly injured organ was testicles (41%) followed by scrota (20%) and penises (15%). Among the 312 motorcyclists, testicular (60%) and scrotal (24%) injuries were the most frequent lesions. Among the 156 cyclists, penile injuries were the most frequent (27%). Among the 54 motorists, bladder (46%) and testicle (20%) injuries were the most frequent. For motorcyclists, motorists, and pedestrians, compared to women, a four, three, and two-fold risk of LGUI was observed for men, respectively. For cyclists, being a man was a protective factor. Testicular lesions were strongly associated with penile lesions for motorists and cyclists. Bladder injuries were strongly associated with pelvic fractures for pedestrians and motorists. Within the 78 testicular traumatisms with clinically available records, 69% (54) had an ultrasound examination and 12.5% (16) had an albuginea rupture. The salvage rates for patients who had surgery after blunt testicular trauma were 64% (7 albuginea repairs for 11 albuginea ruptures) and 33% after open wound trauma.

Conclusion: LGUI is an infrequent trauma after traffic accidents, with testicular injuries being the most commonly injured. Physicians must maintain a high awareness of external genitalia injuries in motorcyclists and cyclists.

Keywords: Functional urology, general urology, radiology

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Received: 14.07.2025 **Accepted:** 08.09.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Kara N, Neuville P, Ballout N, Ndiaye A. Lower genitourinary injuries following traffic accidents: epidemiology, clinical characteristics and outcomes. J Urol Surg. 2026;13(2):80-89.

Introduction

Blunt or penetrating trauma of the pelvis or external genitalia can cause significant damage to the lower genitourinary system. This includes bladder, urethra, penis, scrotum, or testicle (1). Although rarely lethal, failure to recognize these lesions at initial management can lead to significant morbidity and persistent genital and urinary dysfunction. Their detection and early management can help limit the occurrence of such complications (2).

Patients with severe trauma due to road traffic accidents and sudden deceleration traumas are particularly prone to urinary genital injuries (2,3). In 2017 in France, 3,600 deaths occurred because of road accidents. Among these deceased patients, 10% had genitourinary lesions (4).

In previous studies (5,6), between 1996 and 2013, a prevalence of 0.59% has been shown (963 out of 162,690) for urinary tract injuries after traffic accidents, including 41% of kidney trauma and 23% of testicular trauma. Most of the victims were motorcyclists.

Kidney trauma epidemiology has been described previously. Hotaling et al. (7) reported 9,002 kidney injuries (0.3%) among 3,247,955 trauma injuries from hospitals in the United States and Puerto Rico, and Bjurlin et al. (8) reported a rate of 0.8% kidney trauma among 466,028 motor vehicle collisions (9,10).

The etiology and clinical patterns of all-cause combined lower genitourinary injuries (LGUI) have also been described previously. Lee et al. (9) reported 74 testicular ruptures and 32 penile fractures among 156 patients with blunt trauma to the external genitalia.

Bjurlin et al. (10) reported 162 (0.57%) penetrating external genital traumas among 28,459 trauma patients in Chicago; gunshot wounds accounted for the most common mechanism of injury (93%) and included 63% of testicular injuries.

Only a few studies reported the specific epidemiology of LGUI following road traffic accidents. Bjurlin et al. (11) found that among 16,585 bicycle injuries, 2.16% of victims presented with LGUI. Kidneys were the predominant organ of injury (75%), followed by bladder and urethra (15%), and penis and scrotum (10%) in 1979. Similarly, in 1979, Hurt (12) described 117 motorcyclists (13%) out of 900 who sustained LGUI, with the majority of these injuries being minor in severity.

Most of the studies concerning LGUI caused by road accidents were retrospective epidemiologic analyses. To the best of our knowledge, no study has thoroughly investigated clinical patterns, management strategies, and clinical outcomes of patients with LGUI following road traffic accidents.

The main objective of our study was to define the incidence and clinical patterns of LGUI occurring after road traffic accidents.

The secondary objective was to determine the predictive factors and associations in lesions, to improve early detection and management of LGUI.

Materials and Methods

This study used recorded data from the official departmental Registry. Since 1996, this association has reported traffic accident cases to the National Institute of Science and Technology for Transport, Development and Networks. The registry covers the department and has been approved by health authorities (National Registry Committee and National Commission for Information Technology and Civil Liberties no: 999211, date: 09.09.2016).

The Registry collects the demographic characteristics of each road traffic casualty type of road user, the characteristics of the crash (time, location, and collision type) and a description of the bodily injuries sustained to help researchers better understand the mechanisms of injury in motor vehicle collisions.

The inclusion criteria were: Road traffic casualty involving at least one vehicle (motorized or not) from 1996 to 2015, occurring in the department, and requiring institutional health care activity. This included 245 health care structures cooperating, including prehospital primary care teams and forensic medicine institutes.

The different populations analyzed were motorists, motorcyclists, cyclists, pedestrians, van drivers, van passengers, bus passengers, and skateboard users.

We assessed different groups of LGUI: Testis, bladder, penis, perineum, scrotum, urethra, vagina, and vulva.

Cases of LGUI were identified using the abbreviated injury scale (AIS) 90 codes in the register, and the severity through injury severity score (ISS) score (1).

Initial medical history, physical examination, radiological exams, and management approach were retrospectively reviewed by utilizing the complete electronic medical records available from 2005 to 2015.

Statistical Analysis

Statistical analyses were performed using SAS (SAS 9.4, SAS Institute Inc., Cary, NC). A p-value ≤ 0.05 was used to indicate statistical significance. The DataShared-SepLogit method was used to estimate conditional associations between bodily injuries in the Registry. This method consists of multiple logistic regressions that include penalties which encourage structured sparsity. Ballout and Viallon (13) described the model's

superiority over other graphical models based on empirical comparisons using synthetic data. It uses well-known methods of binary graphical models, to show association structures among a set of injuries.

Results

A total of 178,625 victims were available for analysis from 1996 to 2015; 591 of whom presented with LGUI (0.33%). More than half (53%) of the victims were motorcyclists, 26.4% were on a bicycle, 9.1% were in a car, 9% were pedestrians, and 4% were involved in other vehicles such as trucks and buses. Overall, 34.0% (201/591) of victims were hospitalized.

The mean (standard deviation) age of victims with LGUI was 26.2 (16.6) years, and 83.9% were males (sex ratio 5.2/1, 496 men and 95 women).

The most commonly injured genitourinary organs were testicles (41%), scrotum (20%), penis (15%), bladder (11%), vagina (7%), urethra (5%), vulva (5%), and perineum (5%).

Among the LGUI victims, 54 (9%) were motorists, and 37% of them were hospitalized. Bladder (46%), testicles (20%), and scrotum (13%) were the most frequently injured organs in this group.

Among the 312 motorcyclist victims with LGUI, testicular (60%) and scrotal (24%) injuries were the most frequent. Additionally, 43% of the victims were hospitalized.

There were 156 cyclists with LGUI for whom penile injuries (27%) were the most frequent.

Among the 42 pedestrians with LGUI, bladder (38%) and perineum (19%) injuries were the most frequent. 52% of pedestrian victims were hospitalized (Table 1).

We found that the mean AIS was 2 and the mean ISS was 13. More than 80% of LGUI were associated with low and moderate ISS; 13% of cases had an ISS of 25 or higher, and the mortality rate was 7% (Table 2).

We found a strong interaction between road user type and age on the presence of LGUI. Therefore, we presented one multivariate model per road user type, using the same factors in each model (Table 3).

Compared to women, the risk of presenting with LGUI in men was 4 times higher for motorcyclists, 3 times higher for motorists, and twice as high for pedestrians ($p<0.05$). Conversely, being a man was a protective factor when considering cyclists [odds ratio (OR) 0.71, 95% confidence interval (CI) (0.50, 0.99)]. In this same group, the risk of LGUI was 3-fold for cyclists aged 15 years or younger compared to those aged 26 to 35 years old [OR 3.34; 95% CI (1.83; 6.11)].

Considering motorists, the odds of presenting with LGUI were 3 times higher in victims between 66 and 75 years old compared to those aged 26 to 35 years [OR 3.5, 95% CI (1.2: 9.8)].

In the case of motorcyclists, crashes on rural roads led to a higher risk of LGUI than crashes on city streets [OR 1.53; 95% CI (1.10, 2.11)].

Injury Associations

The analysis of the distribution of the bodily injuries of the 178,625 victims by the DataShared-SepLogit method, permitted the definition of profiles of injury associations.

The DataShared-SepLogit method is a statistical tool used to study the linking of different factors across several groups of patients. It works in two steps: SepLogit breaks down complex relationships between binary outcomes (yes/no events, such as the presence or absence of an injury) into a series of simple

Table 1. Hospitalization rate and type/frequency of LGUI (skateboard and rollerskate users are not represented for more clarity, <5% of victims)

	Motorists n=54 (9%)		Motorcyclists n=312 (53%)		Cyclists n=156 (26%)		Pedestrians n=42 (7%)		Total
	n	%	n	%	n	%	n	%	
Hospitalization	20	37	135	43	24	15	22	52	201
Penis	2	4	38	12	42	27	4	10	86
Perineum	3	6	8	3	9	6	8	19	28
Scrotum	7	13	75	24	32	21	3	7	117
Testicles	11	20	188	60	36	23	4	10	239
Urethra	6	11	9	3	6	4	6	14	27
Vagina	1	2	5	2	25	16	6	14	37
Vulva	1	2	4	1	20	13	0	0	21
Bladder	25	46	19	6	1	1	16	38	61

LGUI : Lower genitourinary injuries

Table 2. Global injury severity according to maximum AIS and the ISS					
MAIS	**n**	**%**	**ISS**	**n**	**%**
MAIS=1	324	55	1-'8	408	69%
MAIS=2	93	16	9-'15	69	11.7%
MAIS=3	86	15	16-24	36	6.1%
MAIS=4	42	7	>24	78	13.2%
MAIS=5	6	1	Total	591	100%
Death	40	7			
Total	591	100			
AIS: Abbreviated injury scale, ISS: Injury severity score					

logistic regressions. Data-Shared Lasso then compares results across groups, identifying which associations are common to all groups and which are specific to one group. By combining these two ideas, this approach allows researchers to analyze several subgroups at once, highlight both shared and unique patterns, and reduce the risk of missing important signals.

To represent those associations, we used a graphical model. When there was a dependence/association between two injured organs (OR >1, $p<0.05$), we represented it by an edge (line between two organs). If, and only if, the two corresponding organs were independent given the other organ, they were not linked by an edge on the graphic model (Figure 1).

Using this method, we found that testicular lesions were strongly associated with penile lesions for motorists, cyclomotorists, and cyclists. We found that for pedestrians and motorists, bladder injuries were associated with pelvic fractures.

Medical and Radiological Records Analysis

Data from medical and radiological records were electronically registered from 2005, allowing the collection of complete data for 341 patients with LGUI between 2005 and 2015. The data from the more recent accidents were not fully available.

The medical and radiological records of 78 testicular injuries were available for analysis (Table 4).

The mean vehicle speed at the moment of the crash, as reported by patients, was 64.7 (30-110) km/h. The mean hospital length of stay was 11.6 days (range 1-72). Scrotal trauma occurred on the right side in 42% of cases, on the left side in 31%, and was bilateral in 19% of cases (missing data: 8%). Scrotal hematoma and/or hematocele were clinically found in 55% of the cases, and scrotal swelling was found in 76% of the cases.

Of the 78 testicular injuries, 31% were open wounds. In comparison with blunt trauma, we found that open testicular trauma had less hematoma at clinical examination (42% vs. 80%). We found that they also had fewer intratesticular hematomas (25% vs. 79%) and albuginea ruptures (25% vs. 73%) at ultrasound (US) examination.

67% of the patients had a testicular US examination, 12% had a computed tomography (CT) scan, and 23% had no imaging.

The salvage rate for patients who had surgery after blunt or penetrating trauma was 67% (7 albuginea repairs and 4 orchiectomies for 11 albuginea ruptures) and 100% for those who underwent conservative management. The salvage rate for patients who had surgery after open wounded trauma was 33% (1 albuginea repair and 2 orchiectomies for 3 albuginea ruptures). From 11 operative records, a mean length of 2.3 cm for the rupture of tunica albuginea was found.

Thirty-seven patients (47%) were seen at a first follow-up consultation with a mean delay of 1.48 months (0.25-7 months). Sixteen patients (21%) were seen at a second follow-up consultation with a mean delay of 3.9 months after initial treatment.

The records of 15 penile traumas were available, four of them being bruises, eight open wounds, and three fractures. The open wounds were all superficial, with no complications found during the follow-up consultation for the 6 patients who attended. For the 3 penile fractures, no cracking sound or typical eggplant presentation was reported, and one was associated with an open wound. One penile US was performed; showing an albuginea tear at the middle third of the cavernous corpus. During initial management, two penile fractures were complicated by penile curvatures and pain during sexual intercourse at the follow-up consultation, at 5 weeks. One patient underwent surgical management and presented with penile curvature and erectile dysfunction at the follow-up consultation (at 6 weeks).

Fifteen urethral injuries had clinical and radiological records available (Figure 2).

Blood at the meatus was found in 86.7% of cases; 80% of patients had a urinary diversion by suprapubic catheter; and 80% of patients had an associated pelvic fracture (12/15).

A total of 8 cases of anterior urethral injuries were found: 4 complete disruptions (grade 4), 1 partial disruption (grade 3), 1 contusion (grade 2), and 2 unspecified cases. The severity reports of 2 urethral injuries were unavailable. The mean length of catheterization was 77.5 days.

Table 3. Risk factors for LGUI, OR estimated from a multivariate logistic regression

		Motorist				Motorcyclist				Cyclist				Pedestrian			
Factors		**OR**	**95% CI**		**p-value**	**OR**	**95% CI**		**p-value**	**OR**	**95% CI**		**p-value**	**OR**	**95% CI**		**p-value**
					p<0.001				p<0.0001				p<0.05				p<0.05
Sex	Male	3.35	1.75	6.40		4.44	2.43	8.10		0.71	0.50	0.99		2.06	1.07	3.97	
	Female	1				1				1				1			
					p<0.05								p<0.0001				
	0-15	2.32	0.88	6.111						3.34	1.83	6.11					
	16-25	0.73	0.36	1.5						1.23	0.61	2.478					
	26-35	1				1				1				1			
Age	36-45	0.50	0.17	1.525						0.96	0.40	2.28					
	46-55	0.74	0.24	2.252						0.84	0.31	2.229					
	56-65	1,06	0.30	3.71						0.65	0.18	2.3					
	66-75	3.472	1.225	9.838						0.43	0.06	3.32					
	+76	2.236	0.99	10.023						-							
Road network									p<0.01								p<0.01
	City street					1.00				1.00				1.00			
	Highway					1.30	0.72	2.33						4.66	1.10	19.68	
	Rural road					1.53	1.10	2.11						4.75	1.67	13.55	
	Other					0.72	0.2	1.00						0.69	0.27	1.77	
Time of accident					p<0.01												
	0 to 3:00 am	3.639	1.282	10.333													
	4:00 to 7:00 am	2.535	0.934	6.88													
	8:00 to 11:00 am	1.03	0.357	2.976													
	midnight to 3:00 pm	1.376	0.531	3.569													
	4:00 to 7:00 pm	1				1				1				1			
	8:00 to 11:00 pm	3.311	1.359	8.067													
	Unknown	0.432	0.114	1.0637													
Antagonist									p<0.0001				p<0.05				
	Motorist					1				1				1			
	None					0.199	0.143	0.28		2.194	1.174	4.099					
	Van/bus					0.813	0.381	1.74		6.788	1.867	24.68					
	Fixed obstacle					0.754	0.5	1.14		2.632	1.189	5.828					
	Other					0.375	0.209	0.67		1.49	0.596	3.723					

CI: Confidence interval, OR: Odds ratio, LGUI: Lower genitourinary injuries

Among the 4 cases of posterior urethral injuries, 3 of these were complete ruptures, associated with bladder neck injury (grade 5), and were linked to pelvic fractures and intra-abdominal injuries. The mean length of catheterization was 71.3 days. The average delay in retrograde urethrography control was not available.

Among the 17 bladder lesions with clinically and radiologically available records, 15 had a CT cystography, 6 hematomas and 9 perforations were found. 82% of the patients (n=14) had simultaneous pelvic fracture, and 71% (n=12) had an associated intra-abdominal lesion.

Table 4. Management of the 78 testicular traumatisms							
		Testicular injuries (n=78)					
		Surgical management 35% (n=27)					Conservative management 65% (n=51)
Clinical presentation	Pain	100% (27)					100% (51)
	Scrotum swelling	74% (20)					75% (38)
	Hematoma	63% (17)					51% (26)
	Perineum extension of the hematoma	7% (2)					4% (2)
	Spermatic cord infiltration	19% (5)					2% (1)
	Testicular dislocation	7% (2)					2% (1)
Ultrasound (US) findings	Intra-testicular hematoma	**67% (18)** 66% (12)					**71% (36)** 36% (13)
	Peri-testicular hematoma	78% (14)					36% (13)
	Scrotal hematoma	17% (3)					19% (7)
	Parenchyma heterogeneity	72% (13)					44% (16)
	Albuginea rupture	72% (13)					8% (3)
	Doppler mode irregularity	56% (10)					11% (4)
Surgical findings	Albuginea rupture	51% (14)					
	Extra testicular hematoma	51% (14)					
	Intra testicular hematoma	37% (10)					
	Epididymis lesion	11% (3)					
	Spermatic cord lesion	22% (6)					
Surgical procedure			Orchiectomy (n=6)	Albuginea repair (n=7)	Hematoma draining (n=4)	Others (n=10)	
Short term follow-up			n=4	n=7	n=3	n=5	n=18
	Pain		0	43% (3)	0	20% (1)	22% (4)
	Hematoma		0	29% (2)	0	0	6% (1)
	Incomplete wound healing		25% (1)	29% (2)	66% (2)	40% (2)	0
US follow-up			n=0	n=6	n=2	n=0	n=5
	Atrophic testis		0	83% (5)	50% (1)	0	20% (1)
	Hematoma		0	17% (1)	0	0	40% (2)
Middle term follow-up			n=4	n=6	n=3	n=1	n=2
	Pain		0	33% (2)	0	0	50% (1)
	Atrophic testis		0	50% (3)	0	0	50% (1)
	Erectile dysfunction		25% (1)	17% (1)	33% (1)	100% (1)	0
	Infertility		25% (1)	0	0	0	0

The intraperitoneal ruptures represented 56% (5/9) of the perforations and were all managed surgically, with a mean length of postoperative catheterization of 10 days. Most of the perforations were located at the dome (60%). The extraperitoneal ruptures were all treated conservatively. No fistula was found during the cystography controls, and the mean length of catheterization was 6.3 days.

Discussion

To our knowledge, this is the largest report in the literature on LGUI following traffic accidents.

This is the only study on LGUI after traffic accidents, and it provides a detailed understanding of the presentation, management, and outcomes of these infrequent injuries.

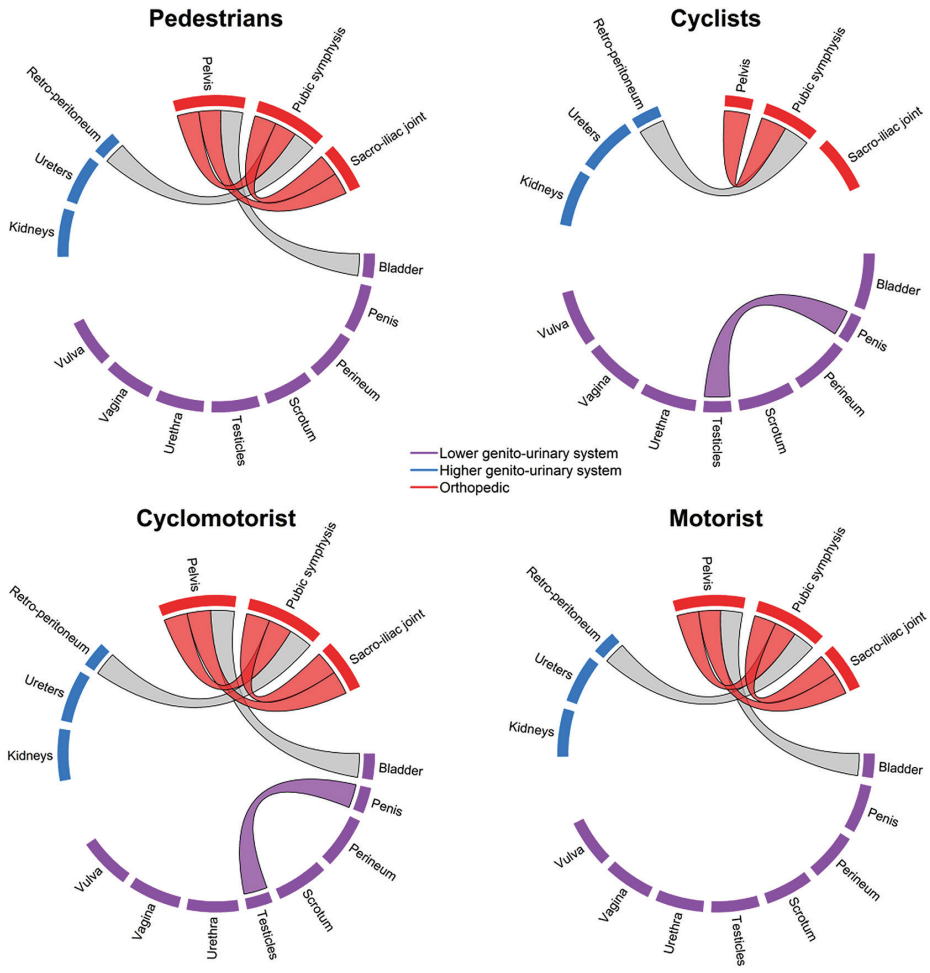

Figure 1. Injuries association by road user: application of the DataShared-SepLogit approach on the Rhone registry data. An association between two injured organ (odds ratio >1 and p<0.05) is represented by an edge (line between two organs). Grey color is for injuries associations between two different categories

This study may impact the daily management of LGUI after traffic accidents, given the higher morbidity compared to all causes of trauma combined. It may also change emergency clinical examination practices, considering the strong association between testicular and penile injuries in motorcyclists and cyclists.

We found a low rate of motorists (9%), compared with our previous study (22%) (4). This can be explained by the protection offered by the driver's compartment, which may limit LGUI (14).

More than 75% of LGUI victims were motorcyclists or cyclists, and 83% were men. This male predominance was also reported by Wessells et al. (6) and Hotaling et al. (7). This may be explained by a higher prevalence of at-risk road behaviors, such as speeding or alcohol abuse (15).

Conversely, for cyclists, being male was a protective factor. This can be explained by the fact that 72% of the vulva and vagina injuries in our study were recorded among bicycle users. Straddle-related injuries are well-known non-obstetric vulvovaginal injuries (16).

The finding that cyclists under the age of 15 years were at higher risk of presenting with LGUI, corroborates the finding of Tasian et al. (17) that children were nearly 10 times more likely to have a GUI after a bicycle accident compared to adults.

Injury Associations

Associations between urologic and orthopedic injuries have been described before. Symphyseal diastasis associated with bladder injuries has been well described by Aihara et al. (18) and Deibert and Spencer (19).

In this study, the large number of patients, the quality of the data collected in the registry, and the use of the DataShared-SepLogit approach, allowed new associations of injuries to be described. The most notable association found was the strong positive relationship between testicular and penile injuries in motorcyclists and cyclists.

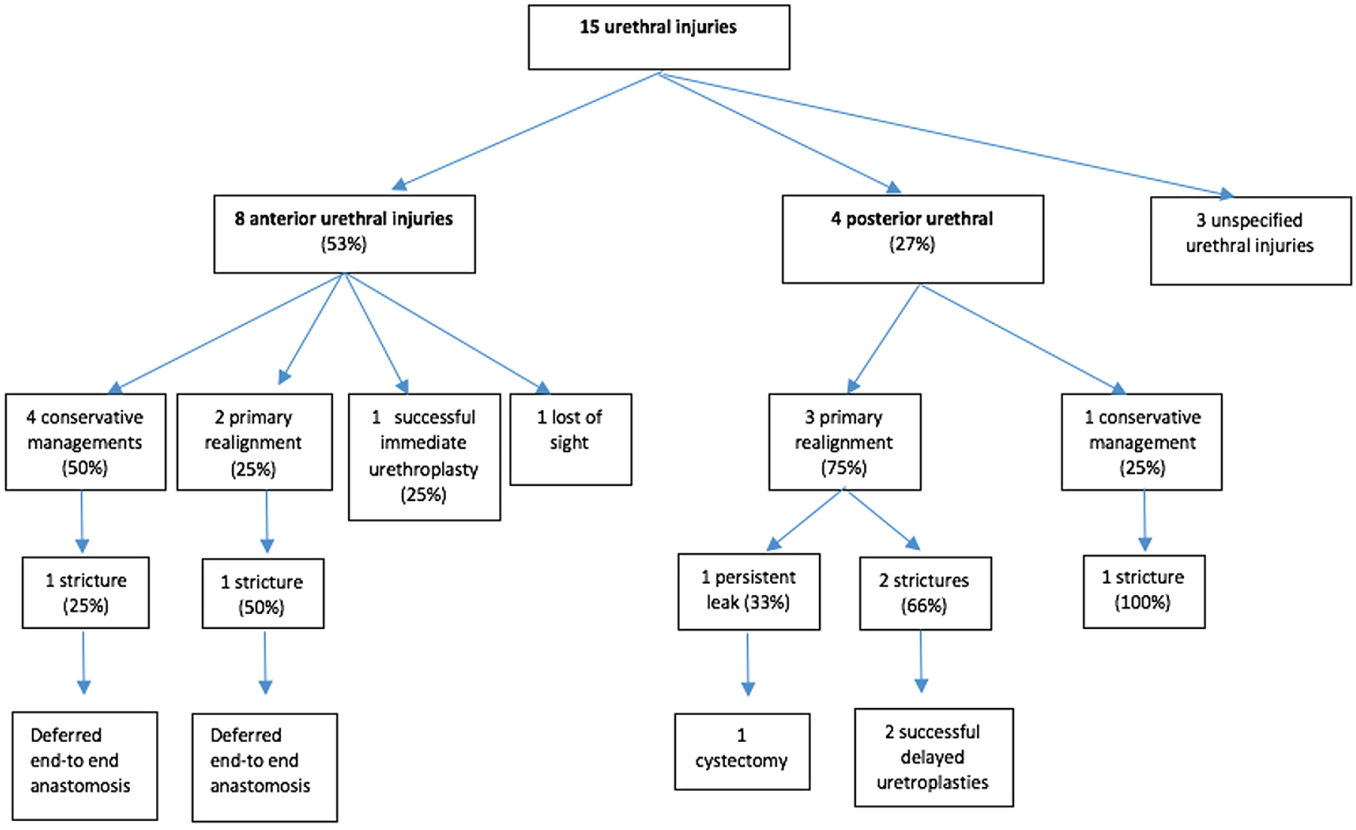

Figure 2. Management of the 15 urethral injuries

With this statistical tool, we can summarize the injury tables of road accident victims. We can also report injury associations based on age, user type, or antagonist use. Such a detailed description of injury associations could be useful for diagnosis and avoiding misdiagnoses, which can lead to severe morbidity.

Urethra

Rare in the trauma population, urethral injuries account for approximately 4% of GU trauma (2,20) and have the potential to incur substantial long-term morbidity, including intractable stricture disease and incontinence (2,21).

Our findings corroborate that approximately 65% of urethral injuries are complete disruptions, with the remaining 35% resulting in partial tears (22).

Meanwhile, posterior urethral injuries are reported to be four times more common than anterior ones in various studies (21). Conversely, in our study, most of the injuries were anterior injuries. This may be explained by the mechanism of trauma (straddle injuries or fuel tank injuries).

Eighty percent (12/15) of our patients with urethral injuries with available medical records had associated pelvic fractures. The management of pelvic fracture urethral injuries (PFUI) is a hotly debated and controversial topic because, currently, there is no level 1 evidence (23). The American Urological Association Guidelines leave it open to interpretation whether suprapubic tube (SPT) placement, with delayed repair or primary realignment (PER), is superior for PFUI (24).

In the only level 2 study to date, Hadjizacharia et al. (25) showed that PER resulted in a significantly shorter time to spontaneous voiding and a decreased risk of urethral stricture (14% in the PER group vs. 100% in the SPT group).

In our study, the stricture rate after PER of posterior urethral injury was higher than in the Hadjizacharia et al. (25) study (75% vs. 14%). The difference may be explained by the intensity and kinetic energy of the trauma.

Hypotheses were developed by Koraitim (26) suggesting that the posterior urethra may be initially stretched, and then partially or completely disrupted at the bulbomembranous junction, depending on the magnitude of trauma. These hypotheses were recently confirmed by computer-generated models for traffic accident modeling based on human imaging, which provided insight into the mechanics of posterior urethral injury (27,28).

Penis

Penile trauma is less common than testicular trauma but still comprises 10% to 16% of GUI according to several single-institution series (29). Most penile injuries in our studies were superficial open wounds treated non-surgically with excellent results. This confirms the findings of other large-scale studies. Krishna Reddy et al. (30), Phonsombat et al. (29), and Bjurlin et al. (10) also found that nonoperative management can be performed in well-selected patients with penile injuries superficial to Buck's fascia.

Bladder

Data from a 20-year prospectively maintained database (31) recently reported that road accidents are the most common cause of blunt bladder rupture (50.5%). Concomitant pelvic fractures are reported in approximately 70% (ranging from 35% to 87%) of bladder ruptures (31,19). Johnsen et al. (32) reported that the association with a PF resulted in both increased complications and increased hospital length of stay: 7.1 days vs. 2.8 days in the intensive care unit ($p<0.01$) and 13.5 days vs. 7.7 days in the hospital overall ($p=0.01$). The presence of pelvic fractures following blunt trauma serves as a marker of significant injury from high-energy force.

Extraperitoneal bladder ruptures, as seen in the present study, occur almost universally in the presence of pelvic fractures and are usually the result of shearing forces or laceration by bony spicules.

Intraperitoneal bladder ruptures, on the other hand, are most often due to blunt trauma to a distended bladder. Passengers wearing a seat belt without a shoulder attachment can sustain bladder injury from such a mechanism when the belt forcefully compresses the lower abdomen (33), resulting in elevated bladder pressures and, in most cases, a perforation through the dome of the bladder (34,35).

Testicular

While our blunt trauma salvage rate was low (64%), up to 82-86% of ruptured testicles after blunt trauma can be salvaged according to Buckley and McAninch (36), Altarac (37), and Lee (9) studies.

In the current literature, the salvage rate for open wounds ranges from 35-65% (28). In this study, we report a 33% salvage rate, which is higher than findings from studies on self-inflicted orchiectomies, which are less often salvageable.

Clinical examination of patients with polytrauma is often limited because of pain and coexisting life-threatening injuries, which may lead to the misdiagnosis of severe injuries, particularly testicular fractures. These misdiagnoses have been shown to increase orchiectomy rates (39).

Moreover, this difference in salvage rates can be explained by the high kinetic energy of the impact and the presence of a fuel tank.

Study Limitations

However, this study has several limitations. The primary limitation is the potential under diagnosis of penile and urethral injuries in the setting of polytrauma, where life-threatening conditions often take precedence. Urethral trauma may remain unrecognized in the absence of hallmark signs, such as acute urinary retention or urethrorrhagia, and injuries to the corpora cavernosa, particularly following blunt trauma, may similarly be overlooked. Such underdiagnosis is likely to result in mediumand long-term urogenital complications (as urethral stricture, penile curvature, and erectile dysfunction) which could not be assessed in the present study, as patients were not systematically referred for urological evaluation in these scenarios.

Conclusion

LGUI is an infrequent trauma after a traffic accident, with the testicles being the most commonly injured. Physicians must maintain a high awareness of testicular and penile injuries in motorcyclists and cyclists.

Ethics

Ethics Committee Approval: The registry covers the department and has been approved by health authorities (National Registry Committee and National Commission for Information Technology and Civil Liberties no 999211, date: 09.09.2016).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.K., Concept: A.N., N.K., Design: N.B., A.N., N.K., Data Collection or Processing: N.B., A.N., N.K., Analysis or Interpretation: P.N., N.B., N.K., Literature Search: N.K., Writing: P.N., N.K.

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

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

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ORIGINAL RESEARCH
Endourology

Doi: 10.4274/jus.galenos.2025.2025-9-5
J Urol Surg 2026;13(2):90-95

LLM-based Chatbots for Kidney Stones: A Readability and Quality Assessment

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What's known on the subject? and What does the study add?

Kidney stone disease is highly prevalent, and patients frequently use online resources to seek information. Artificial intelligence–driven chatbots, including large language models (LLMs), are increasingly used as digital health tools. Previous studies in urology have shown that chatbot outputs may align with guidelines in certain contexts but often lack accuracy, completeness, and readability. This study is the first systematic comparison of three widely used LLM-based chatbots (ChatGPT GPT-4o, Google Gemini 2.5 Pro, and DeepSeek R1) for kidney stone-related patient queries. It demonstrates that while quality scores were similar and generally limited to acceptable, readability significantly differed, with ChatGPT requiring higher health literacy than Gemini or DeepSeek. Findings highlight both the potential utility and the current limitations of chatbots in patient education, emphasizing the need for expert oversight and domain-specific refinement.

Abstract

Objective: Kidney stone disease is among the most common urological disorders worldwide. Patients frequently search online for information regarding etiology, management, and prevention; however, the quality and readability of available resources are variable. This study aimed to evaluate and compare the quality and readability of responses generated by three large language model (LLM)-based chatbots—OpenAI GPT-4, Google Gemini 2.5 Pro, and DeepSeek R1—for common patient-oriented kidney stone queries.

Materials and Methods: A set of 15 frequently asked questions was curated from online search trends and categorized into three domains: definitions and epidemiology, medical and surgical management, and lifestyle or behavioral aspects. Readability was assessed using Flesch Reading Ease Score (FRES) and Flesch-Kincaid Grade Level (FKGL). Response quality was evaluated with the Ensuring Quality Information for Patients (EQIP) tool and the modified DISCERN instrument. Statistical analyses were performed using the Kruskal-Wallis test with Dunn's post-hoc comparisons.

Results: Mean DISCERN and EQIP scores did not significantly differ among platforms, with overall ratings falling in the "limited to acceptable" range. FRES scores were comparable across groups, whereas FKGL revealed significant differences: Gemini responses required a lower educational level than those of ChatGPT ($p<0.016$) and DeepSeek (adjusted $p<0.02$). No differences were observed in word count, sentence count, or total text length.

Conclusion: Although all three LLMs generated structured, patient-centered outputs, quality remained modest and readability varied. Some ChatGPT responses demand higher health literacy, potentially limiting accessibility. These findings underscore the need for expert oversight and domain-specific refinement before widespread clinical adoption.

Keywords: Endourology, general urology, radiology

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Received: 09.09.2025 **Accepted:** 22.09.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Yılmaz AB, Bakır D. LLM-based chatbots for kidney stones: a readability and quality assessment. J Urol Surg. 2026;13(2):90-95.

Introduction

Kidney stone disease represents one of the most prevalent urological conditions, with a global lifetime risk ranging from 3% to 15% depending on geographic and demographic factors (1). Its recurrent nature and potential complications, including obstruction, infection, and renal impairment, make it a significant public health burden. Patients frequently search online for information about causes, treatment options, prevention strategies, and prognosis. However, online resources often vary in quality, reliability, and readability, raising concerns about misinformation and patient safety (2).

Artificial intelligence (AI)-powered chatbots, especially large language models (LLMs), have emerged as valuable tools for healthcare communication, delivering quick, tailored, and confidential responses to patient inquiries, which may enhance access to health information and alleviate barriers like stigma or embarrassment (3). In urology, studies have demonstrated that chatbot outputs may align with guideline-based recommendations in some contexts, such as urolithiasis, yet inconsistencies and inaccuracies remain (4,5).

Despite the growing interest in AI integration into clinical practice, few investigations have specifically evaluated chatbot performance on kidney stone–related patient queries. Existing evidence has focused on general urological conditions or cancer care, but a systematic analysis of chatbot-generated responses to kidney stone questions remains limited (6). Addressing this gap is clinically relevant given the high prevalence of stone disease and the reliance of patients on digital health platforms for guidance.

Materials and Methods

Study Purpose and Design

This cross-sectional, descriptive study was conducted to evaluate and compare the readability and quality of responses generated by three LLM-based chatbots—OpenAI GPT-4, Google Gemini 2.5 Pro, and DeepSeek R1—in addressing common patient-oriented questions about kidney stone disease. As the data consisted solely of machine-generated text with no human subjects, ethical approval or informed consent was not required.

Construction of Question Set

A curated set of patient-relevant questions was developed through a systematic review of online search behaviors. Search volume data for terms such as "kidney stone," "urolithiasis," and related synonyms were analyzed using Google Trends (Google LLC, USA) and keyword tools, including Semrush (Semrush Inc., USA) and Ahrefs (Ahrefs Pte. Ltd., Singapore), over a 10-year period. Redundant, ambiguous, or overly specific queries were excluded. The resulting set included 15 questions, grouped into three thematic areas:

- Definitions and epidemiology (5 questions)
- Medical and surgical management (5 questions)
- Lifestyle, behavioral, and psychological factors (5 questions)

Data Collection Process

Questions were submitted in English to the interfaces of the three chatbots (gpt-4o-2024-11-20, gemini-2.5-pro, deepseek-r1), using newly created accounts to eliminate potential bias from prior interactions. Full responses were collected and systematically stored in a standardized "Question-Model-Response" format as plain-text files for analysis.

Assessment of Readability

For each response, metrics including word count (WC), sentence count (SC), and syllable count (SYC) were calculated using custom Python scripts (Python Software Foundation) and verified in the R statistical environment (R Foundation for Statistical Computing). Two established readability metrics were applied. Flesch Reading Ease Score (FRES) is a 0-100 scale, where higher scores indicate greater ease of understanding. Flesch-Kincaid Grade Level (FKGL) reflects the U.S. educational grade level needed to comprehend the text. These metrics were computed using the formulae (7):

$$FRES = 206.835 - (1.015 \times WC/SC) - (84.6 \times SYC/WC)$$

$$FKGL = (0.39 \times WC/SC) + (11.8 \times SYC/WC) - 15.59$$

Evaluation of Response Quality

The reliability and accuracy of chatbot outputs were assessed using two validated tools: Ensuring Quality Information for Patients (EQIP): A 20-item scale, with items scored as yes (1), partly (0.5), or no (0). Four quality groups were defined: 0-25% = very poor, 26-50% = limited quality, 51-75% = acceptable but improvable, 76-100% = high quality. The percentage score was calculated as (8):

$$EQIP\ (\%) = [(yes \times 1) + (partly \times 0.5) + (no \times 0)] \div (20 - non\text{-}applicable\ items) \times 100.$$

Modified DISCERN (9,10): A 5-item binary scale (range 0-5), with higher scores denoting greater reliability. Lower scores (0-1) indicate poor or misleading information, 2 = incomplete, 3 = fair, 4 = good, 5 = excellent, and comprehensive.

Statistical Analysis

SPSS v20 was employed for statistical analysis. Normality was assessed via the Kolmogorov-Smirnov test. Group comparisons and subgroup analyses (Background & Epidemiology, Clinical Management, Lifestyle, & Patient Factors) were performed

using the Kruskal-Wallis test, and followed by Dunn's post-hoc pairwise comparisons with Bonferroni correction to adjust for multiple testing. Two researchers independently evaluated all responses. Inter-rater reliability was measured using weighted kappa statistics for ordinal data and intraclass correlation coefficients (ICC) for continuous data. A p-value <0.05 was considered statistically significant.

Results

A total of 45 AI-generated responses were evaluated across three platforms (Gemini, DeepSeek, and ChatGPT) for quality and readability metrics (Table 1).

Quality Metrics

The mean modified DISCERN score was comparable among the groups (Gemini: 1.93±0.8; DeepSeek: 2.0±0.65; ChatGPT: 2.1±0.8), with no statistically significant overall difference (p=0.85). Similarly, EQIP scores showed no significant variation (Gemini: 56±4.6; DeepSeek: 57.7±4.7; ChatGPT: 57.5±4.1), p=0.55. Inter-rater agreement was substantial for both the modified DISCERN score [weighted κ = 0.8, 95% confidence interval (CI): 0.750-0.852, p<0.001] and EQIP score (ICC: 0.870, 95% CI: 0.721-0.952, p<0.001).

Readability Metrics

The FRES indicated slightly easier readability for DeepSeek (42.1±6.4) compared to Gemini (42.2±9.3) and ChatGPT (40.9±8.4), though the overall difference was not significant (p=0.9). By contrast, the FKGL demonstrated significant variability across platforms. Gemini produced texts requiring the lowest educational level (18.2±1.6 grade level), while ChatGPT responses were significantly higher (20.8±1.1 grade level). Post-hoc pairwise analyses revealed a significant difference between Gemini and ChatGPT (p<0.016) and a significant difference between Gemini and DeepSeek (adjusted p<0.02), but there was not a significant difference between DeepSeek and ChatGPT (p=0.66).

Subgroup Analysis

Subgroup analyses stratified by clinical category revealed no statistically significant differences among the three LLMs for modified DISCERN, EQIP, FKGL, or FRES scores within any category. The relative performance of the models remained consistent across different types of patient-oriented questions, and no category-specific patterns of superiority or inferiority were observed.

Text Length Metrics

Regarding output length, no significant differences were observed among platforms. The total WCs were 343±101 (Gemini), 358±104 (DeepSeek), and 349±106 (ChatGPT) (p=0.93). Similarly, the total SC was consistent across groups (Gemini: 29±11; DeepSeek: 27±9; ChatGPT: 29±8; p=0.82). Finally, total SYC did not differ significantly (Gemini: 1007±305; DeepSeek: 991±259; ChatGPT: 980±242; p=0.93).

While overall quality scores (modified DISCERN and EQIP) and readability ease (FRES) did not vary significantly, the FKGL revealed that ChatGPT responses required a significantly higher educational level than those of Gemini. No differences were observed in the quantity of generated text across platforms. A comprehensive summary of all findings is presented in Table 2.

Table 1. List of questions on kidney stones by category

Category	Questions
General definitions and epidemiology	What is a kidney stone? How common are kidney stones in the general population? What are the main risk factors for kidney stone formation? Do kidney stones have a genetic basis? What is the natural course of kidney stones?
Medical and surgical treatments	Which medications are used to relieve pain in kidney stone disease? What is medical expulsive therapy? When is surgical treatment necessary for kidney stones? How effective is shock wave lithotripsy? What are the risks of ureteroscopy and percutaneous nephrolithotomy?
Behavioral, lifestyle, and psychological aspects	How much water should I drink to prevent kidney stones? Which foods increase the risk of kidney stones? How high is the risk of recurrence after a kidney stone episode? Do chronic diseases increase the risk of kidney stones? What lifestyle changes can help prevent kidney stones?

Table 2. Comparison of quality and readability metrics among AI-generated texts

	Gemini	DeepSeek	ChatGPT	p
Modified DISCERN score	1.93±0.8	2±0.65	2.1±0.8	0.850*
Ensuring quality information for patients (EQIP) score	56±4.6	57.7±4.7	57.5±4.1	0.550*
Flesch reading ease score (FRES)	42.2±9.3	42.1±6.4	40.9±8.4	0.900*
Flesch-Kincaid grade level (FKGL)	18.2±1.6	20.6±1.4	20.8±1.1	Gemini vs DeepSeek: <0.020* Gemini vs ChatGPT: <0.016* DeepSeek vs ChatGPT: 0.660*
Total word count	343±101	358±104	349±106	0.930*
Total sentence count	29±11	27±9	29±8	0.820*
Total syllable count	1007±305	991±259	980±242	0.930*

*: Kruskal-Wallis. Variables are presented as mean ± standard deviation. For non-parametric variables, overall group comparisons were performed using the Kruskal-Wallis test followed by Dunn's post-hoc tests with Bonferroni correction for pairwise contrasts. In the table, p-values are presented for both the overall group effect and the relevant pairwise contrasts (Gemini vs. DeepSeek, Gemini vs. ChatGPT, DeepSeek vs. ChatGPT). Bold p-values indicate statistical significance

Discussion

This study provides one of the first systematic comparisons of LLM-based chatbots in addressing patient-centered questions about kidney stone disease. By analyzing both readability and quality metrics across ChatGPT (GPT-4), Google Gemini 2.5 Pro, and DeepSeek R1, we aimed to evaluate the extent to which these emerging tools can provide accurate, accessible, and clinically useful information for patients.

Our findings demonstrated no significant difference among the three models in terms of quality, as assessed by the modified DISCERN and EQIP tools. Mean scores across platforms were in the "limited to acceptable" range, highlighting that while chatbots are capable of providing structured answers, they often lack the depth and reliability required for complex medical decision-making. This aligns with Cocci et al. (2), who reported that only 52% of ChatGPT's urology-related responses were deemed appropriate, with particularly poor performance in emergency scenarios. Similarly, McCarter et al. (6) found that while ChatGPT outperformed Perplexity and Bing in terms of overall quality and reduced misinformation, completeness of responses remained suboptimal. Collectively, these findings emphasize that although chatbot-generated responses can provide an initial framework of information, they require expert oversight to ensure accuracy and clinical safety.

In terms of readability, our analysis revealed that while FRES scores did not differ significantly, FKGL levels varied considerably, with ChatGPT responses requiring a higher educational level compared to Gemini. This finding is clinically relevant, as health literacy is a major determinant of patient adherence and outcomes. Although our analysis indicated relatively high FKGL scores, it should be emphasized that this index is calculated only from sentence length, WC, and SYC. Because of this formula-based structure, FKGL may sometimes overestimate the true difficulty of chatbot-generated texts. A higher score does not automatically mean that patients would be unable to understand the content; rather, it often reflects longer sentences or more complex word forms. Even so, adopting strategies such as plain-language principles, readability adaptation, and layered summarization could further improve the accessibility of these responses. Prior analyses similarly noted that ChatGPT responses in urology often correspond to a college-level reading difficulty, which may limit accessibility for the average patient (2). Huang and Scotland (11), in their evaluation of UroGPT™, reported that ease of use and patient satisfaction were high, suggesting that domain-specific tailoring of chatbots can help bridge this gap. Future developments should prioritize adaptive outputs that can adjust complexity according to user literacy.

Another important consideration is the degree of alignment with established clinical guidelines. Our study did not specifically assess guideline adherence, but previous literature provides insight. Talyshinskii et al. (4) demonstrated that while GPT-4's outputs often aligned with European Association of Urology guidelines in urolithiasis, critical omissions and inaccuracies were frequent, particularly in metaphylaxis and surgical planning. Likewise, Cil and Dogan (12) reported that although ChatGPT achieved high accuracy in straightforward kidney stone diagnostic scenarios, completeness of responses to more complex queries remained inadequate. These observations highlight the dual reality of LLMs: They can approximate guideline-based answers but are not yet robust enough for unsupervised use in clinical contexts.

From a patient perspective, LLM-driven chatbots offer anonymity, immediacy, and accessibility; features that may reduce stigma and enhance engagement. Studies have shown that patients with kidney stones are interested in interactive technologies, such as apps or chatbots, for improving dietary adherence and fluid intake (11). In fact, AI-based dietary counseling tools have already been piloted for oxalate management, with varying accuracy across platforms-Bard performing best, while GPT

models were less reliable (13). These findings suggest that condition-specific chatbot development may be more effective than relying solely on general-purpose LLMs.

Beyond performance metrics, ethical and practical concerns warrant attention. Chatbots may disseminate misinformation with confidence, potentially undermining patient trust or delaying medical care. Editorial commentary in Translational Andrology and Urology cautioned against over-reliance on LLMs, emphasizing their tendency to produce "confidently incorrect" outputs in urological oncology contexts (14). Moreover, issues of data privacy, informed consent, and medico-legal responsibility remain unresolved. As discussed by Ogbodo et al. (15), integrating AI into the consent process must be balanced with safeguards to ensure comprehension and mitigate liability.

Future Directions

While our findings highlight current limitations, the trajectory of LLM development is promising. Recent reviews indicate that LLMs are increasingly capable of assisting in diagnosis, patient counseling, and education in urolithiasis, but should currently be regarded as adjuncts rather than replacements for physician input (5). Domain-specific training, multimodal integration (e.g., combining chatbots with imaging or electronic health records), and iterative user feedback may improve performance. Additionally, stratified evaluation frameworks are needed to ensure outputs meet both clinical accuracy and readability thresholds. Another important direction for future research will be to systematically evaluate the concordance of chatbot outputs with established clinical guidelines, such as the European Association of Urology urolithiasis guidelines. Such an approach would provide stronger clinical relevance and allow a more comprehensive assessment of the accuracy and reliability of LLM-generated content.

Study Limitations

Our study is not without limitations. First, only three chatbots were evaluated, and future iterations of these models may yield different results. Second, we assessed responses in English only, whereas linguistic variability may influence performance. Third, the evaluation of quality and readability, though based on validated tools, cannot fully capture nuanced aspects such as empathy, cultural appropriateness, or dynamic adaptability in conversational settings.

Conclusion

In conclusion, this study highlights the potential and limitations of LLM-based chatbots in addressing patient-oriented kidney stone disease queries. While all three models produced responses of comparable quality and readability, with no significant differences in modified DISCERN, EQIP, or FRES metrics, ChatGPT required a higher educational level (FKGL) than Gemini, potentially limiting accessibility for patients with lower health literacy. The findings underscore that while these chatbots offer accessible, rapid responses, their outputs often lack the depth and reliability needed for complex clinical scenarios, necessitating expert oversight. Future advancements in domain-specific training, adaptive readability, and guideline alignment are essential to enhance their utility as reliable adjuncts in patient education and urological care.

Ethics

Ethics Committee Approval: Not necessary.

Informed Consent: Not necessary.

Footnotes

Authorship Contributions

Concept: A.B.Y., D.B., Design: A.B.Y., D.B., Data Collection or Processing: A.B.Y., D.B., Analysis or Interpretation: A.B.Y., D.B., Literature Search: A.B.Y., D.B., Writing: A.B.Y., D.B.

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

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

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ORIGINAL RESEARCH
General Urology

Doi: 10.4274/jus.galenos.2025.2025-6-1
J Urol Surg 2026;13(2):96-101

Bipolar RF Therapy as a Surgical Alternative for Symptomatic BPH: A Single-center Experience

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What's known on the subject? and What does the study add?

Benign prostatic hyperplasia (BPH) is a common condition in aging men and significantly affects quality of life through lower urinary tract symptoms. While transurethral resection of the prostate remains the gold standard surgical treatment, its applicability is limited in elderly patients or those with significant comorbidities due to the risk of perioperative complications. Bipolar radiofrequency (RF) ablation has emerged as a minimally invasive alternative with advantages such as shorter recovery time and a lower complication profile. This study evaluated the short-term outcomes of bipolar RF ablation therapy in patients with BPH who were unresponsive to medical treatment. Significant improvements were observed in both subjective and objective (Q_{max}, post-void residual) parameters following treatment, with no major complications reported. These findings suggest that bipolar RF ablation is a safe and effective therapeutic option, particularly suitable for patients who are poor candidates for conventional surgery.

Abstract

Objective: To evaluate the effect of bipolar radiofrequency (RF) ablation therapy on prostate volume, urinary flow rates, post-void residual urine volume (PVR), and symptom scores in benign prostatic hyperplasia (BPH) patients.

Materials and Methods: A retrospective analysis was conducted on 40 BPH patients who underwent bipolar RF ablation between November 2017 and June 2018 after failed medical treatment. Prostate volume, International Prostate Symptom Score (IPSS), Q_{max}, Q_{ave}, and PVR were assessed before treatment, and at 1, 3 months and 1 year post-treatment.

Results: The mean age was 72.8 years. Prostate volume decreased by 12.6% from 53.06±19.53 mL to 46.34±21.15 mL at 1 year, although this change was not statistically significant (p=0.105). PVR showed a significant reduction from 148.83±103.18 mL to 106.37±100.26 mL (p=0.0018). Maximum urinary flow rate (Q_{max}) increased by 48.3% from 11.03±6.62 to 16.36±6.70 mL/s at 3 months, and remained stable at 16.10±6.12 mL/s at 1 year. The IPSS improved significantly from 21.86±7.61 to 13.30±7.14 at 3 months, and further to 10.40±3.64 at 1 year (p<0.001). No major complications were observed throughout the follow-up period.

Conclusion: Bipolar RF ablation is a safe and effective minimally invasive treatment for BPH, especially in patients with high surgical risk. It significantly improves urinary parameters and symptom scores.

Keywords: Bipolar radiofrequency ablation, benign prostatic hyperplasia, minimally ınvasive surgery, symptomatic BPH treatment, prostate volume reduction

Introduction

Benign prostatic hyperplasia (BPH) is a common condition in men over the age of 40 and is characterized by lower urinary tract symptoms (LUTS). Histopathologically, it is observed in approximately 50% of men in their 60s and up to 80% in those over the age of 80 (1). BPH symptoms include weak urinary stream, increased urinary frequency, nocturia, and a sensation of incomplete bladder emptying, all of which significantly impacts quality of life (QoL) (2).

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Received: 10.06.2025 **Accepted:** 23.09.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Yunusov N, Bedir S, İlki FY, Ebiloğlu T. Bipolar RF therapy as a surgical alternative for symptomatic BPH: a single-center experience. J Urol Surg. 2026;13(2):96-101.

First-line treatment generally involves medical therapies: alpha-blockers and 5-alpha-reductase inhibitors are the most commonly used agents. However, in some patients, surgical intervention becomes necessary due to treatment resistance or complications (3). Transurethral resection of the prostate (TURP) has long been considered the "gold standard". However, due to TURP's perioperative risks and invasive nature, alternative methods are required, particularly for elderly and comorbid patients (4).

In recent years, bipolar radiofrequency (RF) ablation thermotherapy has emerged among minimally invasive techniques, attracting attention due to its feasibility under local anesthesia, short recovery time, and low complication rates (5,6). Although the efficacy of RF ablation in symptom control and improvement of urinary parameters has been demonstrated, clinical data from Türkiye remain limited.

This study aimed to evaluate the effects of bipolar RF ablation thermotherapy on prostate volume, voiding parameters, and the International Prostate Symptom Score (IPSS) in patients diagnosed with BPH who did not respond to medical treatment.

Materials and Methods

This single-center observational study retrospectively analyzed the data of 40 male patients, diagnosed with BPH and who did not respond to medical treatment between November 2017 and June 2018, at the Urology Clinic of Gülhane Training and Research Hospital, University of Health Sciences. The study was approved by the Health Sciences University Non-Interventional Research Ethics Committee (approval number: 18/175, date: 26.06.2018).

The inclusion criteria for the study were as follows: a confirmed diagnosis of BPH, persistent LUTS despite medical treatment, and the availability of complete follow-up data. Patients who were deemed poor candidates for surgery due to comorbidities [American Society of Anesthesiologists (ASA) 3 or higher], those who were receiving anticoagulant or antiplatelet therapy with a high-risk of complications upon discontinuation, and those who were unwilling to undergo general or spinal anesthesia were included. Exclusion criteria included patients with abnormal findings on digital rectal examination, patients previously diagnosed with prostate cancer, patients with a significant median lobe of the prostate, and patients with a prostatic urethral length either under 20 mm or over 70 mm. Patients who did not show improvement in IPSS scores and uroflowmetry parameters despite at least 6 months of dual drug therapy (alpha blocker + dutasteride) were considered non-responders to medical treatment. This criterion was used as part of the inclusion criteria to identify patients eligible for bipolar RF ablation therapy. The process of patient selection, including inclusion and exclusion criteria, and the final number of patients analyzed are summarized in Figure 1.

Some patients were managed with a urinary catheter prior to the procedure due to significant urinary retention. The reason for preoperative urinary catheterization was to protect the upper urinary tract in patients with markedly elevated post-void residual volumes (PVR). To minimize bias, PVR, Q_{max}, and IPSS values for these patients were recorded one week after catheter removal, allowing sufficient time for bladder function stabilization. This approach was applied consistently to ensure the accuracy and comparability of the preoperative measurements.

The patient was positioned in a supine position. A lubricant gel mixed with 2% lidocaine was applied through the penile urethra. The penis was clamped and held for 5 minutes. A specially designed 16 Fr (5.5 mm) applicator, equipped with 6 electrodes at its tip, was inserted into the bladder via the urethral route. The catheter balloon was inflated with 10 mL of saline to position it at the bladder neck. Subsequently, the other cable of the catheter was connected to the device, providing bipolar RF energy. Patient data were entered into the device system, and the electrode temperature was set to 55 °C. The procedure lasted for 1 hour. The procedure was well tolerated by all patients. After the procedure, the specially designed catheter was removed, and a standard 16 Fr 2-way Foley catheter was placed into the bladder.

Patients were followed up at 1, 3 months, and 1 year post-treatment, with evaluations including prostate volume (measured by a single urologist under transrectal ultrasound guidance), IPSS, and uroflowmetry parameters-specifically maximum urinary flow rate (Q_{max}), average flow rate (Q_{ave}), and PVR. In addition to the short-term follow-up, the study included 1-year post-operative data to evaluate the mid-term outcomes of the procedure. These long-term follow-up assessments included the same parameters (IPSS, Q_{max}, PVR, and prostate volume) as well as QoL scores derived from the IPSS questionnaire.

Statistical Analysis

The collected data were analyzed using SPSS version 22.0 software. The paired samples t-test was used for parametric data, while the Wilcoxon signed-rank test was applied for non-parametric data. A p-value of less than 0.05 was considered statistically significant.

Results

The mean age of the 40 patients included in the study was 72.8±7.4 years. These patients had LUTS, but were considered poor candidates for conventional surgery due to comorbidities (ASA 3 or higher), the risk of discontinuing anticoagulant or

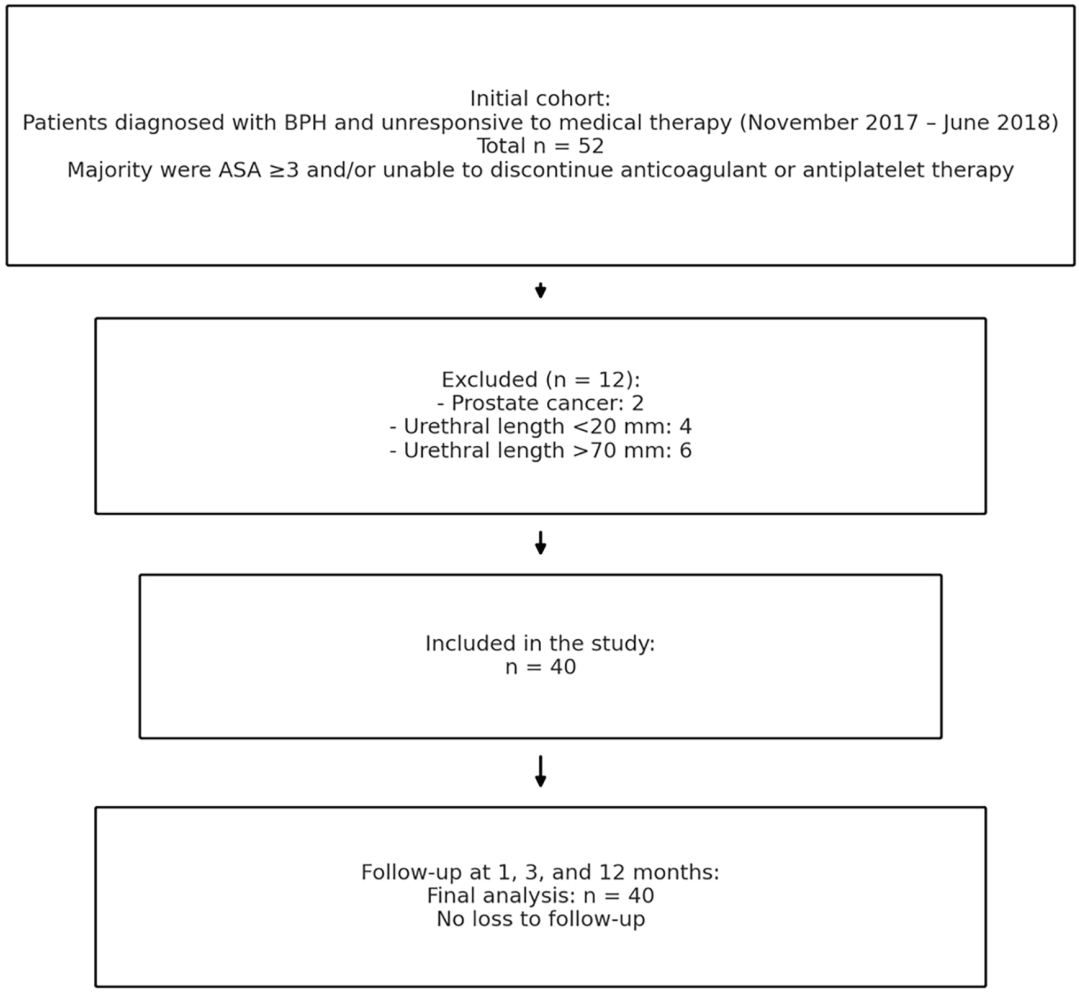

Figure 1. Flow diagram of patient selection and follow-up in the study. From the initial 52 patients diagnosed with BPH and unresponsive to medical therapy, 12 were excluded based on predefined criteria, resulting in 40 patients included in the final analysis with no loss to follow-up

BPH: Benign prostatic hyperplasia, ASA: American Society of Anesthesiologists

antiplatelet medications, or a preference against general or spinal anesthesia. Among the 40 patients, 32 were classified as ASA 3 or higher, indicating high surgical risk. Additionally, 28 patients were using acetylsalicylic acid, and 12 of these 28 patients were also using new-generation anti-aggregants. After consultations with cardiology and neurology, the discontinuation of medications was not allowed. This treatment protocol was implemented, considering the potential complications associated with conventional treatments and after discussing with the patients. Follow-up evaluations were conducted at the first, third months, and first year post-treatment.

The mean prostate volume was 53.06±11.9 mL before treatment, which decreased to 49.03±10.7 mL at the 1st month, and 47.53±10.2 mL at the 3rd month. Although the reduction in volume was 7.6% and 10.4%, respectively, this change was not statistically significant (p=0.53). Prostate volume decreased from 53.06±19.53 mL to 46.34±21.15 mL at 1 year; however, this reduction did not reach statistical significance (p=0.105) (Table 1).

The mean PVR was 148.8±41.6 mL preoperatively, 120.5±38.4 mL at the first month, and 118.4±37.9 mL at the third month. A significant reduction was observed between the preoperative and 3rd-month values (p=0.005). PVR decreased from a preoperative value of 148.83±103.18 mL to 106.37±100.26 mL at 1 year, and this change was also statistically significant (p=0.0018).

The maximum urinary flow rate (Q_{max}) increased from 11.03±3.1 mL/s pre-treatment to 14.76±3.8 mL/s at the 1st month and 16.36±3.9 mL/s at the third month. The increase in the third month was statistically significant (p=0.005). Q_{max} remained stable at 16.10±6.12 mL/s, reflecting maintained improvement in urinary flow at one year (p<0.001). The average urinary flow rate (Q_{ave}) was measured as 6.12±1.8 mL/s preoperatively, 7.43±2.1 mL/s in the 1st month, and 7.81±2.0 mL/s in the 3rd

Table 1. Clinical outcomes after RF ablation therapy				
Time	**Prostate volume (mL)**	**PVR (mL)**	**Q_{max} (mL/s)**	**IPSS**
Preoperative	53.06±19.53	148.83±103.18	11.03±6.62	21.86±7.61
1st month	49.03±20.27	120.54±103.56	14.76±8.05	15.60±6.71
3rd month	47.53±23.05	118.37±120.06	16.36±6.70	13.30±7.14
1st year	46.34±21.15	106.37±100.26	16.10±6.12	10.40±3.64
P-value (3 month vs. preoperative)	0.53	0.005	0.005	0.005
P-value (1 yr vs. preoperative)	0.105	0.0018	<0.001	<0.001

All values are expressed as mean ± standard deviation. Paired t-tests were used to compare 1-year values with preoperative values, n=40, RF: Radiofrequency, PVR: Post-void residual, IPSS: International Prostate Symptom Score

month. However, the increase in this parameter did not reach statistical significance (p=0.06).

There was a significant improvement in IPSS scores, decreasing from a preoperative mean of 21.86±7.61 to 13.30±7.14 at 3 months post-treatment (p=0.005). The mean IPSS decreased from 13.30±7.14 at 3 months to 10.40±3.64 at 1 year, and this difference was found to be statistically significant (p<0.001), indicating sustained symptomatic improvement.

The QoL score, as part of the IPSS questionnaire, was assessed both preoperatively and during post-treatment follow-up. In addition to the 3-month results, 1-year QoL scores have also been evaluated and added to the manuscript. These findings further support the sustained symptomatic relief and improved patient satisfaction achieved with bipolar RF ablation therapy.

The QoL score, assessed as part of the IPSS questionnaire, decreased from a preoperative mean of 4.7±1.2 to 2.6±1.1 at 3 months and 2.1±1.0 at 1 year post-treatment. This progressive improvement indicates a significant and sustained enhancement in patient-reported QoL (p<0.05).

The continued improvement in QoL scores observed at the 1-year follow-up suggests that bipolar RF ablation provides not only short-term but also mid-term symptomatic relief and contributes meaningfully to overall QoL.

Among the 14 patients with indwelling urethral catheters prior to the procedure, 5 (35.7%) were successfully transitioned to catheter-free follow-up after treatment. No serious complications were observed following the procedure. Temporary urinary retention occurred in 7 patients (17.5%) during the early postoperative period, all of whom were successfully managed with an additional one-week catheterization. Dysuria complaints were noted in 6 patients (15%) but resolved spontaneously within a few days. No cases of urinary tract infection, urethral stricture, incontinence, or hemorrhage were encountered. All patients discontinued medical treatment.

The incidence of retrograde ejaculation post-procedure was observed in 8 out of 40 patients. However, the use of alpha-blockers should not be overlooked, as it may influence the outcome prior to surgery. The difference between pre-operative and post-operative 3-month IIEF-5 scores was evaluated through comparative statistical analysis. The pre-operative IIEF-5 score was found to be 14.8±3.9, while the post-operative 3-month IIEF-5 score averaged 12.6±3.5. A paired t-test was performed, and the difference between the pre-operative and post-operative 3-month scores was not statistically significant (p=0.258).

Discussion

BPH is a condition that increases in prevalence with age and significantly affects QoL by causing LUTS. Although conventional surgical treatments are highly effective, they are associated with limitations in elderly or comorbid patients due to the risk of complications, hospitalization requirements, and postoperative recovery period (7).

In this study, we evaluated the short-term efficacy and safety of bipolar RF ablation thermotherapy in patients with BPH unresponsive to medical treatment. Our findings demonstrated significant improvements in clinical parameters such as Q_{max}, IPSS, and PVR following treatment, with no major complications observed postoperatively.

RF ablation is a technique that delivers controlled thermal energy to prostatic tissue to induce coagulative necrosis, thereby reducing obstructive symptoms. While long-term data remain limited, Cowan et al. (8) reported in a 5-year follow-up study that over 70% of patients maintained symptomatic improvement after RF therapy, with a low need for subsequent surgical intervention. Similarly, Gilling et al. (9) found a persistent decrease in IPSS and increased patient satisfaction following RF ablation.

In our study, we observed a 39% reduction in IPSS, a 48% increase in Q_{max}, and a significant decrease in PVR, indicating that RF ablation yields both subjective and objective benefits in the short-term. These findings are consistent with those reported in earlier clinical studies. The increase in Q_{max} suggests a substantial improvement in voiding dynamics by alleviating

the obstructive component of BPH. In fact, this degree of improvement is considered comparable to that achieved with TURP in the literature (10). The reduction in PVR indicates more effective bladder emptying and suggests that RF ablation can be safely used even in patients predisposed to urinary retention. Supporting bladder function is particularly important in elderly or comorbid patients and contributes critically to treatment success (11).

The reduction in IPSS confirms that patients experienced marked symptomatic relief, implying that RF ablation positively affects not only physiological parameters, but also overall QoL. Decreases in IPSS of similar magnitude have been reported following conventional surgical procedures (7). McNicholas et al. (12) emphasized that RF therapy is an effective symptomatic treatment for patients with moderate prostate volumes who may not tolerate invasive surgery.

RF ablation has also been considered a suitable option for patients on anticoagulant therapy or with contraindications to general anesthesia. Chughtai et al. (13) highlighted that minimally invasive therapies can be safely administered in this population, and that RF ablation has significantly lower rates of hematuria, infection, and retrograde ejaculation compared to TURP.

Although our study found an approximate 10% reduction in prostate volume, this difference did not reach statistical significance. This supports the notion that the primary therapeutic effect of RF ablation is not volume reduction per se, but rather the alleviation of obstruction and symptomatic relief. Furthermore, changes in prostate volume may become statistically significant over longer follow-up periods (14). Even though the reduction was not statistically significant, previous studies have suggested that a modest volume reduction may still contribute to meaningful symptom relief (15). The principal mechanism of RF ablation is likely the reduction of tissue resistance in the periurethral zone, rather than global prostate shrinkage.

Recent studies have further supported the clinical utility of RF ablation in patients with BPH, particularly in those with storage symptoms and high surgical risk. A 2024 comparative study demonstrated that bipolar RF thermotherapy led to significant reductions in overactive bladder symptom scores at both 3 and 6 months, outperforming TURP in terms of symptom relief and with comparable improvements in Q_{max} and PVR (16). Similarly, a 2023 randomized controlled trial reported that RF ablation was 2.35 times more effective than TURP in alleviating storage symptoms, while maintaining satisfactory urinary flow outcomes and symptom durability over 6 months (17).

Moreover, recent reviews have positioned RF ablation among the most promising minimally invasive surgical therapies, alongside modalities like Rezūm and Aquablation. These reviews emphasize RF ablation's suitability for patients on anticoagulants and those who are poor candidates for general or spinal anesthesia, highlighting its favorable safety profile and low complication rates (18).

These recent findings are consistent with our results and further support the use of bipolar RF ablation as an effective and safe therapeutic option in the modern management of BPH, particularly for patients with increased perioperative risk. RF ablation represents a clinically meaningful alternative to more invasive surgical procedures such as TURP, especially in elderly patients or those at high surgical risk (8,19,20).

Study Limitations

Despite the promising outcomes, this study has several limitations. The relatively small sample size and short follow-up period (1 year) may limit the generalizability of the findings and prevent robust conclusions regarding long-term efficacy and safety. Additionally, the absence of a control or comparison group (e.g., TURP or sham procedure) restricts direct comparisons with other treatment modalities. Future prospective, multicenter, randomized controlled trials with longer follow-up are necessary to better evaluate the durability of clinical benefits, recurrence rates, and the role of bipolar RF ablation relative to standard interventions.

Conclusion

This study demonstrated that bipolar RF ablation thermotherapy is a safe and effective minimally invasive treatment option for BPH patients who are unresponsive to medical therapy. Significant improvements were observed in IPSS, Q_{max}, and PVR following treatment, with no major complications reported. These findings support the potential integration of bipolar RF ablation into standard BPH treatment algorithms for appropriately selected patients.

Ethics

Ethics Committee Approval: The study was approved by the Health Sciences University Non-Interventional Research Ethics Committee (approval number: 18/175, date: 26.06.2018).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.B., T.E., Concept: N.Y., Design: N.Y., T.E., Data Collection or Processing: F.Y.İ., Analysis or Interpretation: F.Y.İ., Literature Search: F.Y.İ., Writing: F.Y.İ.

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

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

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ORIGINAL RESEARCH
Endourology

Doi: 10.4274/jus.galenos.2025.2025-6-7
J Urol Surg 2026;13(2):102-107

Evaluating Renal Stone Volume and Size as Predictors of Residual Fragments Post RIRS: A Prospective Study

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What's known on the subject? and What does the study add?

Renal stone size has traditionally been used as the primary predictor for residual fragments after retrograde intrarenal surgery (RIRS), and volume assessment is often overlooked in routine clinical practice. This prospective study highlights that stone volume may be a more accurate predictor of stone burden and residual fragments post-RIRS than stone size alone, suggesting the need for incorporating volumetric analysis into preoperative planning.

Abstract

Objective: To identify a better predictor of renal stone burden among stone volume and stone size, and their predictive efficacy on residual fragments post-retrograde intrarenal surgery (RIRS).

Materials and Methods: This single-center prospective observational study was conducted from July 2023 to December 2024, involving patients undergoing RIRS for renal calculi. Pre-operative renal stone parameters were analyzed on non-contrast computed tomography (NCCT) kidney, ureter, and bladder (KUB) scan. The residual fragments were determined by NCCT-KUB, on the 90th postoperative day. The relationships between possible predictors and the residual fragments were analyzed using a logistic regression model.

Results: According to multivariate analysis, the stone volume (p=0.038) was found to be the only significant independent predictor of residual fragments, while other factors such as stone size (p=0.627), age (p=0.251), location (p=0.506), and body mass index (p=0.69) did not have an impact on stone-free rates post RIRS. The area under curve generated cut-off was 889 mm^3 for stone volume.

Conclusion: Among the parameters of renal stone burden, the stone volume determined by NCCT-KUB was a statistically significant predictor of residual fragments, post-RIRS, compared to stone size.

Keywords: Stone burden, volume, residual fragment, predictor, stone-free rate

Introduction

The global prevalence of renal stone disease is around 12% (1). Non-contrast computed tomography (NCCT) kidney, ureter, and bladder (KUB) is considered the gold standard investigation for renal stone detection as well as further treatment planning (2). Major parameters to consider in NCCT-KUB are stone size, number of stones, location of stones, density of stones, volume of stones, and calyceal anatomy of the kidney. Different treatment options are available for symptomatic renal stone diseases such as percutaneous nephrolithotomy (PCNL), retrograde intrarenal surgery (RIRS), extracorporeal shock wave lithotripsy (ESWL), and laparoscopic interventions. Accurately evaluating a patient's stone burden is a key component in the effective management of urolithiasis. Despite its clinical importance, standardized guidelines for the preoperative assessment of renal stone burden remain lacking. Various parameters such as maximum stone diameter (stone size), cumulative diameter of stones, and stone volume have been utilized in prior studies to quantify and analyze stone burden (3). It is generally presumed that multiplanar measurements of renal stones provide a more comprehensive representation of stone burden, potentially

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Received: 18.06.2025 **Accepted:** 23.09.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Krushnadevsinh J, Thombare A, Rajeev C. Evaluating renal stone volume and size as predictors of residual fragments post RIRS: a prospective study. J Urol Surg. 2026;13(2):102-107.

offering superior predictive value for postoperative stone-free status. Nevertheless, evidence from existing studies has not consistently supported the superiority of multiplanar assessments over simpler metrics such as cumulative stone diameter (CSD), which remains one of the most frequently reported parameters. Currently, stone size is a major parameter in deciding among different treatment options. According to European Association of Urology and American Urological Association guidelines, RIRS is recommended for renal stones up to 2 cm in size (4).

The stone-free rate is one of the primary objectives for treatment of renal stone diseases. Reported stone-free rates for RIRS vary from 54% to 96% for renal stones smaller than 2 cm (5). Stone size is traditionally used to predict stone-free rates following RIRS, and residual fragments are known to increase morbidity and the likelihood of re-intervention. While linear measurements are commonly employed, volumetric assessment is emerging as a potentially more accurate method for evaluating stone burden. This prospective study compares the effectiveness of stone volume and size as predictors of residual fragments post the RIRS procedure and finds that stone volume more reliably predicts residual fragments. The findings support the integration of volumetric analysis into preoperative planning to enhance the prediction of surgical outcomes.

Materials and Methods

This prospective observational study was conducted over an 18-month period from July 2023 to December 2024, involving a total of 219 patients. Ethics and scientific clearance were obtained from the Institutional Review Board of Hall Clinic under registration no: RHC/BIOPMRFIEC/2022/443, date: 20.07.2023. After obtaining written informed consent, patients who were diagnosed with renal calculus and undergoing RIRS were included. Patients with anatomical anomalies such as cross-renal ectopy, duplicated collecting systems, or pelvic kidneys were excluded from the analysis.

Patients arriving at the urology department with clinical suspicion of renal stone disease were evaluated with a thorough history and detailed systemic examination. Demographic parameters were also considered, such as age, gender, and body mass index (BMI). NCCT-KUB was performed as a pre-operative workup in each patient. Pre-operative computed tomography (CT) scan parameters were considered, such as stone size, number of stones, total volume of stones, location of stone, density of stone (in Hounsfield unit), laterality of stone, number and anatomical details of calyces, and whether the patient was pre-stented. Stone size was assessed using the maximum linear diameter in cases of a single stone, while the CSD was used for multiple stones. Stone volume was calculated using the ellipsoid formula: (length × width × height × π × 1/6) (Figure 1). All measurements, including stone length, width, and height, were obtained from NCCT scans using digital calipers within the SYNAPSE-PACS software system.

During RIRS, standard operative procedures were followed, with all intraoperative parameters kept constant, including 35W TFL laser (IPG photonics), 200 µm laser fiber size, and standard UAS sheath of 9.5/11.5F. Securing the access sheath was straightforward for all the patients. After laser lithotripsy, each calyx was checked for complete dusting of stone. A Double-J (JJ) stent was placed in all patients after endoscopy, and the stent was removed 3 to 4 weeks postoperatively when we were certain that the bypass was no longer necessary. All major or minor intra-operative and post-operative complications were taken into consideration along with the total operation time. Postoperatively, the stone clearance rate was documented, using NCCT-KUB on the 90th postoperative day. For stone size, 4 mm was accepted as the cut-off level of significance (6).

Statistical Analysis

Data were recorded using a predesigned proforma and analyzed in Microsoft Excel and IBM SPSS Statistics for Windows, version 25. Descriptive statistics included mean ± standard deviation for quantitative variables and frequencies with percentages for categorical data. Normality was assessed using the Shapiro-

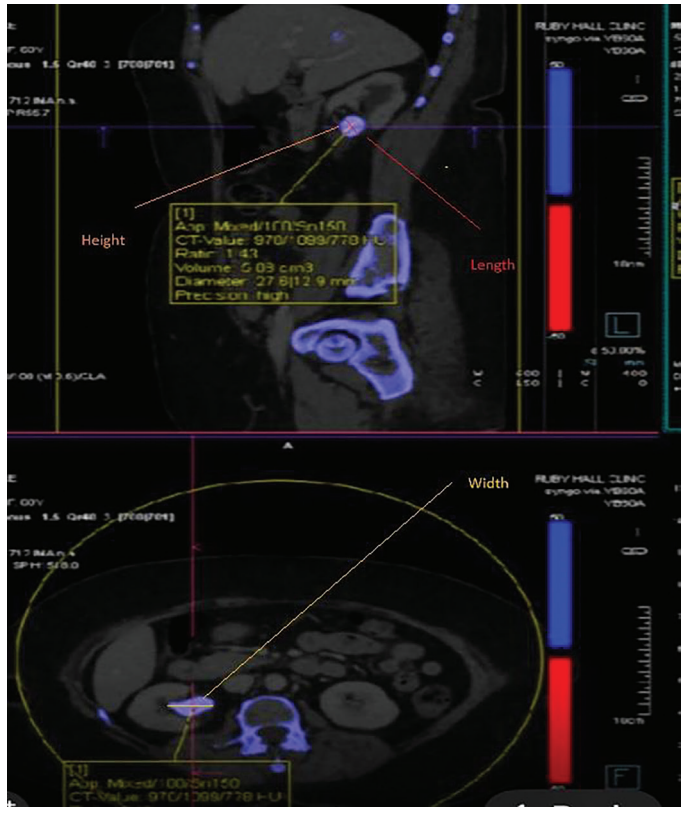


Figure 1. NCCT-KUB image of renal stone

NCCT: Non-contrast computed tomography, KUB: Kidney, ureter, and bladder

Wilk test. The chi-square test evaluated associations between qualitative variables, while the Mann-Whitney U test compared quantitative variables. Logistic regression was used for predictive analysis. A p-value <0.05 was considered statistically significant, with additional tests applied as appropriate.

Results

In our study, 219 patients were included, with a gender distribution of males (54.8%) and females (45.2%). The mean age was 37.19 years, with a range from 20 to 58 years, indicating a predominantly young adult cohort. The average BMI was 22.7 (±2.1). The most frequent presenting complaint was flank pain (50.7%), followed by dysuria (16.4%) and backache (11%). The duration of complaints varied widely from 0 to 90 days, with a mean duration of 15.63 days. Additionally, 16.4% of the patients had a JJ ureteral stent placed prior to the procedure; this was done in anticipation of the potential complexity of the procedure. This may come across as a possible selection bias.

A total of 219 patients underwent RIRS, out of which 201 (91.8%) were stone-free on post-operative day 90, while 18 (8.2%) had residual fragments. For analysis, patients were categorized into two groups: Those with residual fragments and those without residual fragments at postoperative day 90. Out of the 219 patients undergoing RIRS, only 12 (5.5%) patients had complications. All of them were Clavien-Dindo grade I (10 were post-operative fever and 2 were post-operative pain).

The multivariate logistic regression revealed that volume (mm^3) is statistically significantly independent predictor of residual fragments (p-value=0.038).

No statistically significant differences were observed in patient demographics such as age (p=0.226), BMI (p=0.069), and stone characteristics in NCCT-KUB such as laterality (p=0.455), pre-stenting status (p=0.107), number of stones (p=0.545), density (p=0.251), or location (p=0.506) between the two groups. As predictors of stone burden, two parameters were observed, which stone size has shown an insignificant impact (p=0.374), but stone volume has shown a significant impact (p=0.038) on residual fragments post RIRS (Tables 1-3, Graphs 1-3). The surgical duration was observed to be significantly higher among the residual fragments group.

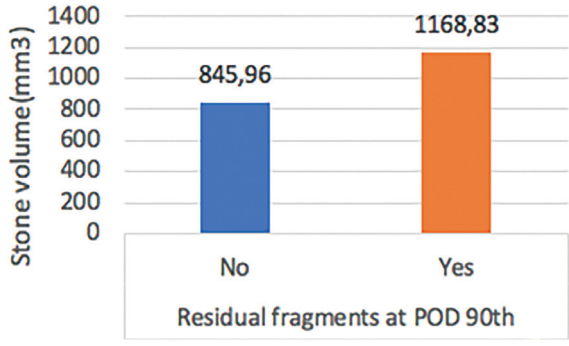
The ROC curve indicates that the "volume (mm^3)" variable is a statistically significant and a discriminator with fair to good performance for the condition being tested. The test has an AUC of 0.746, which suggests it has a reasonable ability to distinguish between the two groups.

Table 1. Impact of variables, including patient demographics and stone characteristics, on residual fragments post retrograde intrarenal surgery

Variables	Residual fragments at postoperative day 90th		p-value
	No	Yes	
Patients (n)	201	18	
Age	36.94±7.78	40±7.59	0.226
Gender			
Male	111	9	0.805
Female	90	9	
BMI	22.98±2.09	24.33±1.51	0.69
Laterality of stone			
Right	102	12	0.455
Left	99	6	
Pre-stented			
Yes	30	6	0.107
No	171	12	
Number of stones	1.67±0.64	1.83±0.41	0.545
Stone volume (mm^3)	845.96±385.51	1168.83±214.49	0.038
Stone size (mm)	14.58±3.8	16±2.28	0.374
Stone density (Hounsfield unit)	999.84±178.62	1086.33±114.1	0.251
Stone location			
Lower poler	39	3	0.506
Non-lower poler	162	15	
Surgical duration (minute)	79.70±18.83	98.33±16.02	0.022

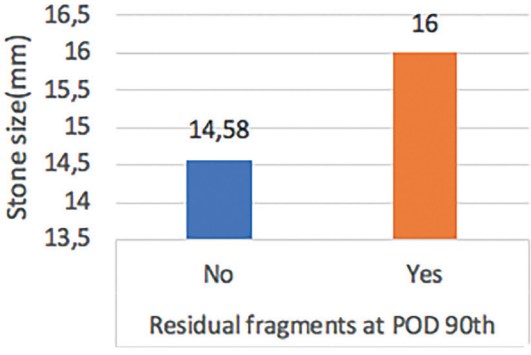
Table 2. Multivariate analysis of different parameters with residual stone fragments				
	B	S.E.	Sig.	Exp(B)
Age years	0.136	0.112	0.226	1.145
BMI	0.982	0.539	0.069	2.669
Pre-stented YN (1)	-3.178	1.971	0.107	0.042
Location (1)	-1.051	1.579	0.506	0.350
Duration	0.122	0.062	0.050	1.129
Size mm cumulative stone burden	0.123	0.254	0.627	1.131
Volume mm^3	0.005	0.002	0.038	1.005
Constant	-46.051	19.925	0.021	0.000
BMI: Body mass index				

Table 3. For Youden's index	
Youden index J	0.5224
Associated criterion	>889
Sensitivity	100
Specificity	52.24



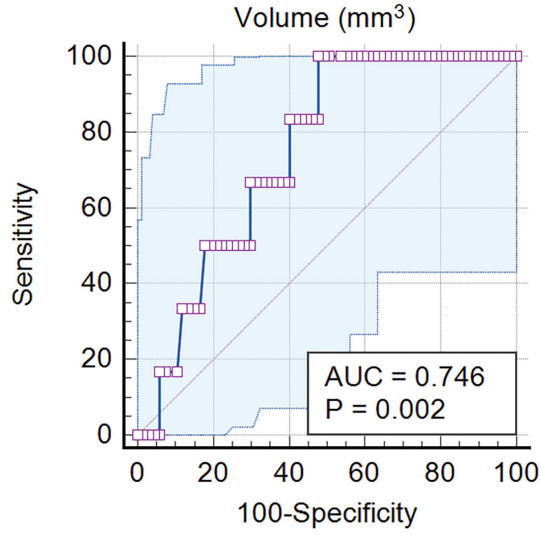
Graph 1. Stone volume as predictor of residual fragments post RIRS

RIRS: Retrograde intrarenal surgery, POD: Postoperative day



Graph 2. Stone size as predictor of residual fragments post RIRS

RIRS: Retrograde intrarenal surgery, POD: Postoperative day



Graph 3. ROC curve for stone volume

AUC: Area under curve, ROC: Receiver operating characteristic

Discussion

Stone burden remains one of the most critical factors influencing the choice of surgical intervention in the management of urolithiasis. Traditionally, it has been assessed using maximum stone diameter in case of single stone, or CSD in case of multiple stones, both of which are widely endorsed in current urological guidelines (4). This method is the simplest and most easily obtained among parameters used to assess stone burden; however, it does not account for stone width and depth. Additionally, these are linear measurements that fail to accurately represent the true stone burden, especially considering the irregular shape of most renal stones. Other factors that were conventionally used for predicting renal stone clearance are infundibulopelvic angle (IPA) and infundibular length. The reproducibility of IPA measurements has also been called into question. Rachid Filho et al. (7) examined the intra-observer and inter-observer variations of IPA measurements

using the Elbahnasy, Sampaio, and Gupta measurement method. They found significant inter-observer variations, with the Sampaio method producing the widest variations between observers. This suggests that routine use of IPA in daily clinical practice may be problematic, therefore, they have not been used in the present study. In contrast, stone volume, derived from the multiplanar reconstructions on NCCT, offers a more comprehensive and accurate representation of the actual stone mass (3). Despite this, it remains uncertain whether this more precise measurement leads to improved prediction of clinical outcomes and post-RIRS residual fragments.

In our cohort, patients with higher stone volumes (1168.83 $mm^3 \pm 214.49\ mm^3$) were more likely to retain residual fragments, even when stone diameters were within the traditionally acceptable range (≤20 mm). This suggests that stone volume may better represent procedural complexity, and potential for incomplete stone clearance. Furthermore, volume estimation can help guide clinical decision-making, such as anticipating the need for staged procedures, considering adjunctive therapies, or choosing alternative modalities like PCNL in selected cases with large-volume stones, despite a relatively small maximal diameter. Stone volume has emerged as a more reliable predictor of operative time in RIRS compared to other burden estimation methods. Larger stone volumes typically require longer fragmentation and retrieval times, which can extend surgical duration significantly. Prolonged operative times not only increase the risk of complications but may also contribute to surgeon fatigue, particularly in high-volume or complex cases. This fatigue can potentially impact surgical precision and efficiency, further influencing outcomes. Moreover, extended procedures may raise the likelihood of residual stone fragments, especially when complete clearance becomes difficult due to limited visibility in longer cases. Therefore, accurate preoperative assessment of stone volume is critical for surgical planning, better intraoperative decision-making, and minimizing residual stone rates in high-risk patients.

In our study, we calculated stone volume using the ellipsoid formula (length × width × height × π × 1/6). All measurements, including stone length, width, and height, were obtained from NCCT scans using digital calipers within the SYNAPSE-PACS software system. Automated or semi-automated volume calculation using widely available DICOM viewers can facilitate its use in clinical practice without significantly increasing interpretation time or cost.

However, to date, no studies have established a specific cut-off value for stone volume in the context of RIRS. In our study, we identified a single cut-off point, 890 mm^3 (as per the calculated Youden's index), as the most effective threshold for predicting RIRS outcomes and positively predicting residual fragments post-RIRS.

Our study supports prior literature that advocates for the integration of stone volume measurement into routine preoperative planning. In a prospective study by Merigot de Treigny et al. (8), suggested 3 formulas for stone burden estimation. They are the (1) CSD, (2) Ackermann's formula, and (3) the sphere formula. They suggested that if stones are below 20 mm, all three methods approximate stone burden correctly. However, for stones above 20 mm, the calculation of volume is recommended. However, no prospective study has compared the cumulative stone burden and stone volume on the prediction of residual fragments post-RIRS. There are different methods for estimating stone volume using CT images including 3D reconstruction of the stone to measure axis lengths and then applying an ellipsoid formula to estimate volume. Using stone volume instead of axial measurements may be a better predictor of treatment outcome, as small differences in manual axis measurements may lead to much larger volume changes. This may be more applicable with increasing stone size, as found by Finch et al. (9). As maximum stone diameter increases, stone volume estimation using ellipsoid volume equations becomes less accurate.

Yamashita et al. (10) reported that stone volume did not independently predict the stone-free rate in cases of ureteral stones, although it did serve as a predictor for renal stones. They suggested that this discrepancy might be due to the generally smaller size of ureteral stones.

In the above articles, it is implied that stone volume may not be a universally reliable predictor of outcomes across all stone sizes and anatomical locations.

Geraghty et al. (11) in their meta-analysis observed that in the case of PCNL, stone volume was not as reliable a predictive factor of residual stone prediction as it was in the case of RIRS and ESWL. This may be partly explained by the fact that more complex or irregularly shaped stones often have a lower volume than ellipsoid-shaped stones with the same maximum diameter, yet these complex stones are associated with a higher likelihood of residual fragments following the procedure.

Study Limitations

Our study has several strengths. The study is a prospective observational analysis evaluating predictors of residual fragments after RIRS, with 100% of assessments performed using NCCT-KUB. All scans were reviewed by a senior radiologist blinded to surgical outcomes, using optimized settings including magnification, bone window, and 3D reconstruction. To ensure procedural consistency, all surgeries were performed by experienced urologists using the same type of flexible nephroureteroscope and disposable instruments. The study, conducted in a high-volume reference center with high-quality imaging, reflects an ideal clinical setting. However, validation in

other centers with varying expertise, equipment, and surgical protocols is necessary to confirm its broader relevance.

Conclusion

Among the parameters of renal stone burden, the stone volume determined by NCCT-KUB was a statistically significant predictor of residual fragments post-RIRS compared to stone size. The shortcoming of the present study is that the stone volume correlation to the operative planning has not been evaluated. The current study indicates that, in future cases, stone volume estimation can be used to predict the possibility of residual fragments after RIRS and to explore possible alternatives.

Ethics

Ethics Committee Approval: Ethics and scientific clearance were obtained from the Institutional Review Board of Hall Clinic under registration no: RHC/BIOPMRFIEC/2022/443, date: 20.07.2023.

Informed Consent: Patient consent was obtained.

Footnotes

Authorship Contributions

Surgical and Medical Practices: J.K., A.T., C.R., Concept: J.K., A.T., C.R., Design: J.K., A.T., C.R., Data Collection or Processing: J.K., A.T., C.R., Analysis or Interpretation: J.K., A.T., C.R., Literature Search: J.K., A.T., C.R., Writing: J.K., A.T., C.R.

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

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

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ORIGINAL RESEARCH
Endourology

Doi: 10.4274/jus.galenos.2025.2025-8-1
J Urol Surg 2026;13(2):108-113

Is the Prognostic Nutritional Index a Predictor of Urolithiasis?

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What's known on the subject? and What does the study add?

The prognostic nutritional index (PNI) is calculated using serum albumin and lymphocyte counts and is thought to provide information about nutritional status, inflammation, and immunity. PNI has been frequently studied in malignancies. Studies examining the relationship between PNI and many malignancies are available in the literature. However, studies examining the relationship between PNI and urolithiasis are limited. Considering the relationship between albumin and stone disease and the effect of lymphocytes on inflammation and immunity, PNI may be a marker of urolithiasis. In our study, a low PNI value was associated with urolithiasis. PNI, given that it does not require additional testing, and can be calculated using routine blood tests, and is associated with urolithiasis, can give clinicians a preliminary understanding of patients with urolithiasis.

Abstract

Objective: Prognostic nutritional index (PNI) is a parameter that reflects nutritional status and inflammation. It is calculated from serum albumin and lymphocyte count. Our study investigated whether PNI has a predictive value in urolithiasis.

Materials and Methods: Data of patients who applied to Ağrı Training and Research Hospital with renal colic between January 2017 and December 2024 were retrospectively examined. Three hundred forty-eight patients were included in the stone group and 627 patients were included in the control group. Patients' age, gender, smoking, hypertension, and diabetes history, body mass index, hemoglobin level, glomerular filtration rate (GFR), blood urea nitrogen, uric acid levels, sodium, potassium, calcium, white blood cell count (WBC), neutrophil count, lymphocyte count, albumin, neutrophil/lymphocyte ratio (NLR), and PNI levels were compared.

Results: No statistically significant difference existed between the demographic data and the patients' comorbidities. In the stone patients group and the control group, mean GFR was 88.04 [standard deviation (SD): 13.21], 93.90 (SD: 13.17); mean WBC was 8910 (SD: 1629), 8268 (SD: 1562); mean neutrophil count was 6040 (SD: 1416), 4933 (SD: 1283); mean lymphocyte count was 2070 (SD: 879), 2535 (SD: 944); mean NLR was 3.62 (SD: 2.1), 2.34 (SD: 1.41); PNI was 30.73 (SD: 6.85), 53.66 (SD: 6.94) ($p<0.001$, all).

Conclusion: PNI value was lower in stone patients than in the control group. PNI may be a parameter predicting stone formation. Additionally, the predictive value can be strengthened with the NLR value.

Keywords: Prognostic nutritional index, urolithiasis, kidney stone

Introduction

Urinary system stone disease is prevalent, seen in 1-20% of people worldwide (1). Stone disease attracts attention with the high recurrence rates. However, there are studies with different recurrence rates. Old studies that dominate the literature report a recurrence risk of approximately 50% in 5 years (2). Being one of the most common diseases in the world, this condition, with its high prevalence and high recurrence rates, leads to increased treatment costs and complications (3).

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Received: 02.08.2025 **Accepted:** 26.09.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Coşkun Ç, Aydın U, Tarım K, Dereköylü E. Is the prognostic nutritional index a predictor of urolithiasis? J Urol Surg. 2026;13(2):108-113.

Prognostic nutritional index (PNI) is a score that includes serum albumin and lymphocyte levels, which was first used to evaluate nutritional status and surgical risk in gastrointestinal surgery patients (4). It is calculated using the albumin level, which reflects nutritional status, and the lymphocyte count, which can indicate inflammation (5). Various formulas calculated based on platelet, neutrophil, lymphocyte, and C-reactive protein levels are used as both nutritional and inflammation parameters. One of these, PNI, has generally been studied in cancers (6). The ratios of these parameters have been frequently shown to be prognostic factors in various diseases (7).

Our study examined patients who presented to our clinic with renal colic complaints. These patients were divided into two groups according to their computed tomography results: patients with and without urinary system stones. We aimed to compare the PNI values of these two groups. We aimed to investigate whether PNI is a predictor of urolithiasis.

Materials and Methods

The data of patients who applied to the Urology Department of Ağrı Training and Research Hospital, a tertiary hospital in Türkiye, with renal colic between January 2017 and December 2022, were retrospectively examined. The ethics committee approval for the study was received from Ağrı İbrahim Çeçen University Clinical Research Ethics Committee (approval number: 109, date: 27.03.2025). Patients who were younger than 18 years of age, had a previous diagnosis of cancer, had a history of major surgery such as gastrointestinal system surgery, had a history of trauma, had a history of chronic inflammatory disease, had end-stage liver or kidney disease, were receiving systemic steroid therapy, did not undergo computed tomography, and had incomplete data were excluded from the study. After screening, two groups were formed: patients with and without stones. As a result, 975 patients were included: 348 patients in the group with urolithiasis (group 1) and 627 patients in the control group (group 2). Age, gender, hemoglobin levels, white blood cell count (WBC), neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio (NLR), glomerular filtration rate (GFR), uric acid, blood urea nitrogen, sodium, potassium, calcium, and albumin levels, body mass index, hypertension history, smoking history, and diabetes history of patients in both groups were recorded. PNI was calculated using the formula determined by Onodera et al. (5) in 1984. This formula is calculated using the serum albumin level and the total lymphocyte count in the blood and is formulated as "10 x albumin (g/dL) + 0.005 x total lymphocyte count/mm³". All these data were recorded, and the PNI levels were examined to determine whether they differed between the stone patients and the control group. Thus, whether PNI has a predictive value for stone formation was investigated.

Statistical Analysis

SPSS Version 28.0.0.0 (IBM, Chicago) was used for statistical analysis. The Student's t-test was used for parametric distribution values when comparing two group means. The chi-square test was used to compare categorical parameters. The normality of continuous variables was assessed using analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data and median (interquartile range) for non-normally distributed data. To calculate the cut-off value of the PNI, receiver operating characteristic (ROC) curve analysis was performed (Figure 1). A cut-off value of 53.275 was found [area under curve (AUC): 0.62, 95% confidence interval (CI): 0.583-0.656]. For practical purposes, 53.3 will be used as a cut-off value. Patients whose PNI <53.3 and PNI ≥53.3 were compared based on the presence or absence of a stone by using the chi-square test. The significance level (α) was set at 0.05 for all analyses. The minimum number of samples required for the study was calculated by performing power analysis at an 80% power value.

Results

There was no statistically significant difference in the patients' age, gender, smoking history, hypertension history, diabetes history, body mass index, hemoglobin levels, blood urea nitrogen, uric acid, sodium, potassium, calcium, and albumin values between the two groups (Table 1).

While the mean GFR value was 88.04 (SD: 13.21)/mm³mL/min/1.73 m² in group 1, the mean GFR value was 93.90 (SD: 13.17) mL/min/1.73 m² in group 2 (p<0.001). The mean WBC value was 8910 (SD: 1629)/mm³ in group 1 and 8268 (SD: 1562)/mm³ in group 2 (p<0.001). The mean neutrophil count was 6040 (SD: 1416)/mm³ in group 1 and 4933 (SD: 1283)/mm³ in group 2 (p<0.001). Mean lymphocyte count was found to be 2070 (SD: 879)/mm³ in group 1 and 2535 (SD: 944)/mm³ in group 2 (p<0.001). Mean NLR values were found to be 3.62 (SD: 2.1) in group 1 and 2.34 (SD: 1.41) in group 2 (p<0.001). When PNI values were compared, mean PNI value was found to be 50.73 (SD: 6.85) in group 1 and 53.66 (SD: 6.94) in group 2 (p<0.001).

ROC curve analysis was performed to calculate the cut-off value of the PNI level (Figure 1). 53.275 was found to be a cut-off value (AUC: 0.62, 95% CI: 0.583-0.656). For practical purposes and with the knowledge that it does not affect the results, the value 53.3 will be used from this stage of the article onwards. Patients whose PNI <53.3 and PNI ≥53.3 were compared using the chi-square test, based on their stone presence. 43.6% of patients who had PNI <53.3 had a urinary stone, while 26% of the PNI ≥53.3 group had a stone (OR: 2.2, 95% CI: 1.67-2.88) (Table 2).

Table 1. Patient characteristics, laboratory values, prognostic nutritional index, and neutrophil-lymphocyte ratios of stone formers and control groups

Parameters	Group 1 (n=348)	Group 2 (n=627)	p-value
Age, mean (SD)	39.54 (8.47)	39.82 (8.61)	0.623
Gender, n (%)			
Male	193 (55.5)	358 (57.1)	0.621
Female	155 (44.5)	269 (42.9)	
Smoking history, n (%)	113 (33.4)	190 (33.2)	0.947
Missing data	10 (2.9)	55 (8.8)	-
Hypertension, n (%)	47 (14.0)	74 (12.3)	0.447
Missing data	13 (3.8)	25 (4.0)	-
Diabetes mellitus, n (%)	36 (10.8)	61 (10.3)	0.808
Missing data	14 (4.0)	33 (5.3)	-
Body mass index (kg/m^2), mean (SD)	22.95 (4.43)	22.67 (4.07)	0.340
Hemoglobin (gr/dL), mean (SD)	13.63 (1.25)	13.76 (1.13)	0.111
Glomerular filtration rate (mL/min/1.73m^2), mean (SD)	88.04 (13.21)	93.90 (13.17)	**<0.001***
Blood urea nitrogen (mg/dL), mean (SD)	17.68 (4.14)	17.36 (4.18)	0.245
Uric acid (mg/dL), mean (SD)	4.72 (0.81)	4.68 (0.82)	0.574
Sodium (mEq/L), mean (SD)	139.72 (3.03)	139.37 (3.24)	0.092
Potassium (mEq/L), mean (SD)	4.51 (0.42)	4.50 (0.41)	0.612
Calcium (mg/dL), mean (SD)	9.48 (0.82)	9.53 (0.86)	0.375
White blood count (/mm^3), mean (SD)	8910 (1629)	8268 (1562)	**<0.001***
Neutrophil (/mm^3), mean (SD)	6040 (1416)	4933 (1283)	**<0.001***
Lymphocyte (/mm^3), mean (SD)	2070 (879)	2535 (944)	**<0.001***
Albumin (g/dL), mean (SD)	4.04 (0.53)	4.1 (0.55)	0.097
Neutrophil/lymphocyte ratio, mean (SD)	3.62 (2.1)	2.34 (1.41)	**<0.001***
Prognostic nutritional index, mean (SD)	50.73 (6.85)	53.66 (6.94)	**<0.001***

*: Clinically significant, SD: Standard deviation

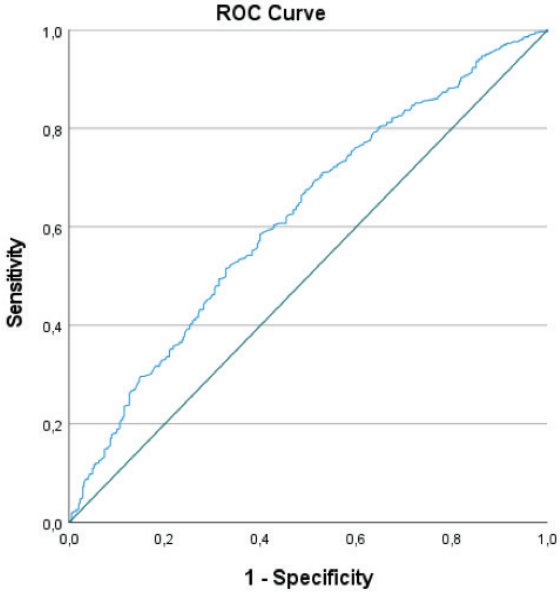

Figure 1. ROC curve analysis of groups according to PNI values
PNI: Prognostic nutritional index, ROC: Receiver operating characteristic

Table 2. Comparative analysis of having stone or not, acording to prognostic nutritional index cut-off values

	PNI <53.3 (n=537)	PNI ≥53.3 (n=438)	p-value
Patient with urinary stones, n (%)	234 (43.6)	114 (26)	**<0.001***
Patient without urinary stones, n (%)	303 (56.4)	324 (74)	

Odds ratio: 2.2; 95% confidence interval: 1.67-2.88, *: Clinically significant, PNI: Prognostic nutritional index

Discussion

Our study showed that patients with stones had lower PNI values than the control group. In addition, the cut-off value of PNI in terms of stone formation risk was found to be 53.3. These results indicate that it can provide insight to the physician without additional cost and intervention, since it is obtained from routinely checked blood parameters, and it is cheap and easily accessible.

The PNI was first used by Buzby et al. (4) in 1980 to predict surgical risk. Onodera et al. (5) used the formula more straightforwardly and focused only on serum albumin and lymphocyte levels. It was studied to predict the prognosis of many cancers, especially gastrointestinal system malignancies (8). Lymphocytes can indicate inflammation levels as well as immune status (9). Serum albumin is related to nutritional status and, as it is a negative acute phase reactant, to inflammation (10). For all these reasons, PNI can serve as an important marker reflecting nutritional status, immunity, and inflammation. A recent study by Wang et al. (11) found that higher PNI levels were associated with a reduced prevalence of urolithiasis. The results of this study support our findings. Lee et al. (12) used the controlling nutritional status score to assess the recurrence rate of urolithiasis and demonstrated that patients with poorer nutritional status experienced faster recurrence. They also found a significant negative correlation between nutritional status and stone recurrence. Both studies reflect the relationship between nutritional status and urinary system stones. Our study found that lower PNI levels are associated with a higher prevalence of urinary stones. PNI is considered to be affected by albumin and lymphocytes. Albumin may reflect protein-energy malnutrition, while lymphocytes may be associated with impaired immunity due to malnutrition. As a result, malnutrition may affect stone formation.

One component in the PNI formula is albumin. Albumin is the most common protein in plasma and is an indicator of nutritional status (10). Albumin is a molecule that can support stone formation by participating in the matrix structure of urinary system stones. At the same time, it acts as an inhibitor of stone formation in urine (13). There are many studies examining the relationship between protein and albumin and stones. Reddy et al.'s (14) study shows that high protein intake increases the formation of urinary system stones. One study showed that patients with normal calcium levels were fed a diet with lower animal protein, which reduced the risk of stone formation (15). Another two randomized controlled studies concluded that a low-protein diet did not positively affect stone recurrence (16,17). Another study stated that the risk of urolithiasis formation depends on the type of protein taken (18). A study evaluating the risk factors for urolithiasis after exogenous albumin intake concluded that there was no change in urine parameters (19). Another study comparing stone patients with controls showed that serum albumin levels of both groups were similar (20). Recent systematic reviews have demonstrated inconsistent evidence on the relationship between protein intake and the risk of stone formation (21). In our study, the two groups had no difference in albumin levels. We think the inconsistent findings in the literature regarding the association between albumin and urolithiasis make the use of a combined marker, such as PNI, more important.

In a study conducted by Mao et al. (22), NLR level was found to be related to stone prevalence. Another recently published case-control study concluded that NLR levels were higher and lymphocyte levels were lower in stone patients (23). In another study, it was concluded that neutrophil and NLR levels in stone patients were similar to those in the control group (24). Another notable study concluded that a decreased lymphocyte percentage plays a significant role in stone formation (20). In our study, neutrophil count and NLR were higher, while lymphocyte count was lower in the urolithiasis group. It has been shown that inflammation plays an important role in stone disease. Considering this situation, we think that the inflammatory profile in patients with stones is also related to the increase in neutrophils. In addition, our results are similar to studies showing a decrease in lymphocyte count in patients with urolithiasis (22,23). This supports the increase in NLR and the reduction in PNI.

In our study, WBC levels were higher in patients with stones. We believe this is due to the inflammation parameters and the high neutrophil count. In our study, the neutrophil count was higher in the urolithiasis group, but the lymphocyte count was lower. Considering that the neutrophil count was dominant in the leukocyte distribution, the lower WBC count in the urolithiasis group is an expected result. In addition, GFR was found to be lower in the stone group in our study. This is an expected result because there may be pathologies such as stone-related obstruction and impaired oral intake.

In our research, PNI values were lower in patients with stones. We think, using a combined marker that is affected by nutritional status, immunity, and inflammation may be important in diagnosing urolithiasis. We also think it is important to obtain it from a routinely applied test, which is cheap, easily accessible, and does not require additional examination. In addition, our study concluded that NLR is higher in stone patients. Combining parameters can provide important information regarding diagnosing patients with stones, advanced tests, and predicting recurrence. Since none of these require additional tests, we believe this combined use will significantly benefit physicians.

In our study, the PNI cut-off value for determining the urolithiasis risk was 53.3. Our study concluded that urinary system stone disease risk increases below this value. This value can be used practically by clinicians. Different cut-off values have been used in the literature-especially in cancer patients (6,25). The fact that PNI is an index mostly studied on malignancy makes direct comparison difficult. Multiple studies should support this value, and statistical analyses should determine this support. However, we still believe it can be a catalyst for other studies in the literature.

Study Limitations

Our study had some significant limitations. First, the retrospective nature of our study was the most important limitation. Second, the small number of patients was also a limitation. Another limitation is that genetic predisposition, occupational exposure, and environmental factors cannot be thoroughly examined. Additionally, patients' smoking, diabetes, and hypertension histories were retrieved from the hospital system. We consider this a limitation due to the potential for errors by physicians or healthcare professionals entering this information. In addition, these patients could not be followed for a long time was another limitation.

Conclusion

PNI is a score that reflects nutritional status and immune status. Our study found that the PNI value was low in patients with stones, suggesting that it is a parameter that predicts stone formation. In addition, NLR levels were higher in patients with stones. PNI is very important because it can be obtained from routine tests, is cheap and easily accessible, and predicts the risk of stone formation. Using it together with NLR can strengthen its predictive value. Nevertheless, more prospective and extensive studies with a larger number of patients are needed.

Ethics

Ethics Committee Approval: The ethics committee approval for the study was received from Ağrı İbrahim Çeçen University Clinical Research Ethics Committee (approval number: 109, date: 27.03.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ç.C., U.A., K.T., E.D., Concept: Ç.C., K.T., E.D., Design: Ç.C., Data Collection or Processing: K.T., E.D., Analysis or Interpretation: U.A., E.D., Literature Search: Ç.C., K.T., Writing: Ç.C., U.A., K.T., E.D.

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

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

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ORIGINAL RESEARCH
Pediatric Urology

Doi: 10.4274/jus.galenos.2025.2025-6-11
J Urol Surg 2026;13(2):114-120

Long-term Outcomes of Two Dextranomer-based Bulking Agents (Dexell vs. Deflux) in the Endoscopic Treatment of Vesicoureteral Reflux

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What's known on the subject? and What does the study add?

Vesicoureteral reflux (VUR) is a common urological condition observed in approximately 30-40% of pediatric patients presenting with urinary tract infections (UTIs). The primary objective in the management of VUR is to prevent febrile infections and subsequent renal damage, thereby reducing the morbidity associated with both the condition and its treatment. Endoscopic treatment of VUR is typically employed prior to major surgical interventions such as ureteroneocystostomy in patients who continue to experience febrile UTIs despite observation or antibiotic prophylaxis. Although a variety of bulking agents have been utilized in this procedure, the most commonly used substance is the dextranomer/hyaluronic acid (Dx/HA) copolymer. Deflux consists of dextranomer microspheres with a mean diameter of 80-250 µm, suspended in a sodium hyaluronic acid solution. In a recent study, a positively charged dextranomer product, Dexell-which comprises positively charged dextranomer microspheres with a smaller average diameter of 80-120 µm-was compared with Deflux. Previous studies have evaluated and published data on different Dx/HA copolymers in an effort to determine whether variations in microsphere size impact complication rates or success rates. However, these studies have predominantly focused on short-term outcomes. Therefore, the aim of the present study was to compare the long-term outcomes of Dexell (Istem Medical, Türkiye) and Deflux (Valeant Pharmaceuticals North America, LLC). In conclusion, no significant differences were observed between the two materials in terms of complication rates or treatment success, despite the variations in microsphere diameter.

Abstract

Objective: This study aimed to compare the clinical and radiographic success rates of endoscopic treatment for vesicoureteral reflux (VUR) using two different formulations of dextranomer microspheres.

Materials and Methods: This retrospective study included 119 children treated endoscopically for VUR between 2015 and 2020 at a single tertiary center. Subureteric injections were performed using either Dexell (n=61) or Deflux (n=58) by a single surgeon applying the hydrodistention implantation technique. Clinical data, including demographics, VUR grade, voiding status, injection volume, and complications, were collected from medical records. Treatment success was defined as the resolution of reflux on voiding cystourethrogram at 3 months, and the absence of febrile urinary tract infections during the 2- and 5-year follow-ups. Statistical analyses included chi-square and Mann-Whitney U tests, and logistic regression was used to identify predictors of treatment failure.

Results: The mean follow-up durations were 75.9 months in the Dexell group and 78.2 months in the Deflux group, with comparable baseline demographic and clinical characteristics between groups. The short-term success rates at 3 months were 83.6% for Dexell and 84.5% for Deflux (p=0.896). Long-term success rates remained similar at both 2 years (80.3% vs. 81.0%, p=0.922) and 5 years (72.1% vs. 74.1%, p=0.805). Postoperative obstruction occurred in 3 patients in the Dexell group and 2 patients in the Deflux group, all of which resolved conservatively. Multivariable analysis revealed no independent predictors of treatment failure.

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Received: 01.07.2025 **Accepted:** 03.10.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Özsoy AF, Karaburun MC, Kubilay E, Akıncı A, Güler AD, Soygür YT, Burgu B. Long-term outcomes of two dextranomer-based bulking agents (Dexell vs. Deflux) in the endoscopic treatment of vesicoureteral reflux. J Urol Surg. 2026;13(2):114-120.

Conclusion: Our analysis showed that the diameter of dextranomer microspheres, frequently utilized for the endoscopic treatment of pediatric VUR, did not affect the short-term or long-term success rates of the procedure. Therefore, Dexell may be considered a cost-effective alternative to Deflux in clinical practice. However, multicentric, randomized, prospective trials with long follow-up durations are necessary.

Keywords: Dextranomer/hyaluronic acid, vesicoureteral reflux, subureteric injection, michrospheres

Introduction

Vesicoureteral reflux (VUR) is a prevalent urologic anomaly (1). It is observed in 1%-2% of the pediatric population and in 30-40% of children with urinary tract infections (UTIs) (1,2). Reflux nephropathy is a common etiology of hypertension in children, potentially resulting in growth retardation and renal insufficiency (3). The objective of managing reflux is to prevent febrile infections and kidney damage, thereby reducing the morbidity associated with both the disease and its treatment. Conservative treatment is often the preferred option in patients diagnosed with VUR. Nonetheless, a subset of the population with recurrent febrile UTI despite antibiotic prophylaxis, who are unlikely to experience spontaneous resolution and possess renal scarring, necessitates interventional treatment options (4). Previously, the primary treatment included medical therapy and open surgical correction of reflux. However, in 1981, Matouschek (5) described the subureteral implantation of Teflon as a bulking agent for the treatment of vesicoureteral reflux. Subsequently, O'Donnell and Puri (6) published the initial clinical series in 1984. Despite the use of many injection materials, including Teflon, bovine collagen, and macroplastique, questions regarding their efficacy and safety have emerged; thus, Vantris and dextranomer/hyaluronic acid (Dx/HA) copolymer are being used for endoscopic treatment (7-10).

Dx/HA copolymer, approved by the Food and Drug Administration in 2001, is among the most widely used materials globally. Deflux consists of dextranomer microspheres averaging 80-250 µm, suspended in a sodium hyaluronic acid solution. The positively charged dextranomer (Dexell), employed for comparison with Deflux in the recent study, consists of dextranomer microspheres averaging 80-120 µm in diameter (11). Previous studies have compared and published findings on two Dx/HA copolymers to see whether there are differences in complication rates and success rates related to varying microsphere diameters. These studies indicated that similar results were observed in the context of the employed diagnostic or treatment methods (Dx/HA); however, they only included short-term outcomes. Therefore, we aimed to compare the long-term effects of Dexell (Istem Medical, Türkiye) and Deflux (Valeant Pharmaceuticals North America, LLC).

Materials and Methods

This study was conducted as a retrospective comparative analysis of two dextranomer-based bulking agents, Dexell (Istem Medical, Türkiye) and Deflux (Valeant Pharmaceuticals North America, LLC), used in the endoscopic treatment of VUR. The availability of these materials in our clinic depended on institutional purchasing policies, local supply conditions, and periodic procurement schedules, which might vary over time and are not under the direct control of the surgical team.

One hundred nineteen patients who were included in the study were treated at our clinic between 2015 and 2020. In our series, 61 patients underwent subureteral injection with Dexell, and 58 patients were treated with Deflux. The numbers of renal units with VUR were 82 and 76 in the Dexell and the Deflux groups, respectively. Patients with grade V reflux, duplex systems, paraureteral diverticula, or refractory lower urinary tract symptoms (LUTS) and patients who do not attend regular follow-up were excluded. The main goal was to evaluate whether one agent had a clear advantage over the other in terms of treatment success, safety, and associated clinical outcomes. Data were collected from patients' medical records, which included demographic information, clinical presentation, treatment details, and follow-up data. This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Demographic characteristics such as age, gender, and VUR grade were documented. Treatment details included the volume of injection material used, the presence of any intraoperative or postoperative complications, and the duration of follow-up. The primary outcomes were treatment success (defined as the absence of reflux on follow-up imaging) and postoperative complications, particularly the development of obstruction.

The resolution rate was determined by voiding cystourethrogram (VCUG) at the third postoperative month. We stated that the long-term success rate is defined by the absence of UTIs with fever in patients after two and five years. In cases where patients presented with a UTI accompanied by fever, an additional VCUG was performed.

All surgeries were performed by a single surgeon using a Karl Storz pediatric cystoscope with a 5 Fr working channel, and the

hydrodistention implantation technique (HIT), approach was applied using a metal injection needle.

Statistical Analysis

The statistical analysis included both categorical and continuous variables. Categorical variables were analyzed using chi-square tests to determine any significant differences between groups, while continuous variables were analyzed using either the t-test or Mann-Whitney U test, depending on the normality of the data distribution. Correlations between the volume of injection material and postoperative obstruction were analyzed using point-biserial correlation. This study was approved by the Ankara University Human Research Ethics Committee (approval no.: 2022000257-3, date: 27.04.2022).

Results

A total of 119 children were assessed, including 61 in the Dexell group and 58 in the Deflux group (Table 1). No statistically significant difference was observed between the two groups regarding the male-to-female ratio. The mean follow-up duration (75.90 and 78.21 months, respectively) and the mean age of the children (66 and 67 months, respectively) also showed no statistically significant differences between the Dexell and Deflux groups. Additionally, 14 children in the Dexell group and 13 children in the Deflux group were not toilet-trained at the time of treatment.

In the Dexell and Deflux groups, right-sided reflux was observed in 21 and 22 patients, left-sided reflux in 19 and 18 patients, and bilateral reflux in 21 and 18 patients, respectively. The differences between the two groups were not statistically significant. Additionally, multiple injection sessions were required in 11 patients (11.48%) in the Dexell group and 7 patients (15.52%) in the Deflux group. VUR grades were categorized into three groups: Grades 1-2, grade 3, and grade 4. In the Dexell and Deflux groups, the distribution of grades was as follows: Grades 1-2 in 14 and 13 patients, grade 3 in 33 and 34 patients, and grade 4 in 14 and 11 patients, respectively. Among patients with bilateral VUR who received injections on both sides, the contralateral reflux grades were as follows: Grade 1-2 in 9 patients in the Dexell group and 10 patients in the Deflux group, grade 3 in 10 patients in the Dexell group and 7 patients in the Deflux group, and grade 4 in 2 patients in the Dexell group and 1 patient in the Deflux group. No statistically significant difference was seen between the two groups regarding the presence of voiding

Table 1. Preoperative and perioperative clinical features

	Dexell (80-120 µm)	Deflux (80-250 µm)	p-value
Age, months, mean ± SD	66.11±29.79	67.05±30.45	0.81[b]
Follow-up duration, months	75.90±11.70	78.21±11.62	0.28
Gender			>0.906[a]
Male	28	26	
Female	33	32	
Reflux side			0.902[a]
Right	21	22	
Left	19	18	
Bilateral	21	18	
Grade of the main injection side			0.845[a]
Grade 1-2	14	13	
Grade 3	33	34	
Grade 4	14	11	
Grade of the other injection side			>0.709[a]
Grade 1-2	9	10	
Grade 3	10	7	
Grade 4	2	1	
Voiding dysfunction presence	18	16	0.977[a]
Circumsized boys, n	25	24	0.702[a]
Success rate of 3 months	83.6%	84.5%	0.896[a]
Success rate after 2 years	80.33%	81.03%	0.922[a]
Success rate after 5 years	72.13%	74.14%	0.805[a]
Postoperative obstruction, n	3	2	0.690[a]

[a]: Chi-square test, [b]: Mann-Whitney U test, SD: Standard deviation

dysfunction. The number of circumcised boys does not differ between the two groups. VCUG was obtained at postoperative 3 month. The success rates after subureteral injection at the third month (83.6% and 84.5%) were not statistically different.

We introduced success criteria indicating the absence of a UTI with fever as well as the absence of reflux. We established equivalent criteria for success rates in the second and fifth years. If patients experienced a UTI accompanied by fever, a new VCUG was conducted. The success rates over a two-year period following subureteral injection were 80.33% and 81.03%, with no significant difference seen. The differences in the success rates after subureteral injection over a five-year period (72.13% and 74.14%) were statistically insignificant.

When obstruction rates post-surgery were compared based on the volume of injected material between the two groups, point-biserial correlation analysis showed no substantial differences (n=3 for Dexell group, n=2 for Deflux group) (p=0.94). The correlation coefficient between the 2-year success rate and the presence of voiding dysfunction was found to be r=0.074, with a p-value of 0.42. Similarly, the correlation coefficient between the 5-year success rate and voiding dysfunction was r=0.089, with a p-value of 0.33. In both cases, the correlation is very low and not statistically significant (p>0.05), indicating that there is no meaningful relationship between voiding dysfunction and success rates at both time points.

In addition, a multivariable logistic regression analysis was performed to identify predictors of unsuccessful cases. In the univariate analysis, age [p=0.007, odds ratio (OR): 0.97, 95% confidence interval (CI): 0.96-0.99], a history of prior endoscopic treatment (p<0.001, OR: 6.13, 95% CI: 2.0-18.7), and grade 4 reflux on the dominant side (p<0.001, OR: 14.22, 95% CI: 3.33-60.0) were found to be significant predictors. However, none of these variables remained statistically significant in the multivariate analysis (Table 2).

Discussion

While several studies on dextranomer microspheres exist in the literature, they have predominantly focused on short-term outcomes. Although short-term success rates and postoperative complication outcomes appear similar among these materials, the long-term differences in success rates, recurrence risk, and complication profiles have not been well established. In the present study, no differences were observed between the two materials in terms of long-term success rates or complication outcomes, which makes our findings noteworthy. Although Dexell and Deflux are theoretically and legally considered equivalent dextranomer-based bulking agents, minor differences in microsphere diameter and manufacturing processes may influence their clinical behavior. Deflux is produced by a global manufacturer and is used worldwide, whereas Dexell is currently manufactured and distributed locally in Türkiye. Demonstrating comparable outcomes between these two agents is therefore valuable, as it supports the use of Dexell as a locally available and potentially more cost-effective alternative.

In the management of VUR in pediatric patients, three principal treatment modalities are available: antibiotic prophylaxis, subureteric injection, and open surgery, which is considered the gold standard (12). In addition, patients may be kept under observation without any treatment. According to the results of the Swedish reflux trial, a randomized prospective controlled study on VUR, the 2-year success rates were reported as 71% in the endoscopic treatment group, 39% in the prophylaxis group,

Table 2. Multivariable logistic regression model for predictors of unsuccessful cases

	Univariate			Multivariate
	p-value	Odds ratio	95% confidence interval	p-value
Type of dextranomer materials	0.805	0.979	0.96-0.99	0.368
Age	0.007	0.979	0.96-0.99	0.205
Gender	0.540	0.776	0.34-1.74	
Reflux side of dominant side Right Left Bilateral	 Ref 0.861 0.212	 0.910 1.848	 0.31-2.61 0.70-4.84	
Reflux grade of dominant side Grade 1-2 Grade 3 Grade 4	 Ref 0.339 <0.001	 1.926 14.22	 0.50-7.38 3.33-60	 0.584
Voiding dysfunction	0.329	0.622	0.24-1.61	
Prior endoscopic treatment history	<0.001	6.136	2.00-18.74	0.99
Circumcision history	0.141	4.154	0.62-27.72	

and 48% in the follow-up group (13). Similarly, Capozza et al. (14) reported a 69% success rate for endoscopic treatment and a 38% success rate for the antibiotic prophylaxis group. Although endoscopic treatment demonstrates increased success rates, prolonged use of prophylactic antibiotics may result in bacterial resistance, treatment non-compliance, and an enhanced risk of breakthrough UTIs. Open surgery presents a success rate of 92-98%, however, its disadvantages encompass invasiveness, prolonged hospitalization, and heightened anxiety for both the patient and their parents (15).

A meta-analysis of endoscopic treatment, encompassing 5,527 patients and 8,101 renal units, indicated that the reflux clearance rate (by ureter) after a single treatment was 78.5% for grades I and II, 72% for grade III, 63% for grade IV, and 51% for grade V (16). Capozza et al. (14) discovered that 80% of parents favored endoscopic treatment over antibiotic prophylaxis and open surgery after being provided with comprehensive information regarding all treatment alternatives. Endoscopic treatment is regarded as safe and minimally invasive, with a brief operating duration and short hospitalization, rendering it an attractive alternative to open surgical repair of reflux. Three procedures have been developed for subureteric injection: STING, HIT and double HIT. In a study conducted by Kirsch and Arlen (17), the overall success rates for patients and ureters were 89% and 92% for the HIT group, in contrast to 71% and 79% for the STING group, showing statistically significant differences.

Additionally, a 93% success rate was recorded in the double HIT cohort. To avoid heterogeneity and ensure a standardized approach, only the HIT technique was administered to all participants, and patients who had undergone STING or Double-HIT were not included in this study.

Many substances have been employed for subureteric injection; however, several have been discontinued due to specific complications and disadvantages (18). Currently, Dx/HA copolymer, launched in 1993, is the predominant injectable material owing to its non-immunogenic, biocompatible, non-allergenic, biodegradable, non-migratory, and durable characteristics (19). Dx/HA possesses many commercial designations based on the dimensions of the microspheres. Deflux comprises dextranomer microspheres of 80-250 µm, whereas Dexell's microspheres range from 80-120 µm. The price of Dexell (€180/cc) is lower to than that of Deflux (€400/cc) (Table 3) (11). A prior retrospective analysis conducted at our clinic revealed no significant difference in success and postoperative complication rates between the two Dx/HA formulations. Likewise, two more studies that evaluated these formulations also revealed no disparities in surgical success rates (7,20). Nevertheless, the duration of follow-up in both our study and the other two trials was short-term. The current study monitored patients over an extended period to assess both short- and long-term success rates and complication rates associated with variations in microsphere size.

In a study by Tekgül et al. (3), patients were divided into two groups: those younger than 54 months and those older than 54 months; with higher success rates observed in the older group. However, when we divided our patients into two groups, under 5 years of age and over 5 years of age, the Pearson correlation analysis showed no clinically significant difference in neither short- or long-term success rates between the two age groups.

Despite patients with voiding dysfunction typically exhibiting reduced success rates following subureteric injections, our study revealed low and statistically insignificant correlation coefficients between voiding dysfunction and 2-year success rates (r=0.074, p=0.42) as well as between voiding dysfunction and 5-year success rates (r=0.089, p=0.33). According to contemporary series and current guidelines, the success rates of subureteric injection are generally thought to be affected by voiding dysfunction. However, the lack of correlation observed in this study may be partially explained by the correction of voiding dysfunction both before and after the subureteric intervention. In addition, to minimize potential misinterpretations due to terminological overlap, it is important to distinguish between refractory LUTS and voiding dysfunction, as these entities may partially overlap although they have different clinical implications. Refractory LUTS refers to persistent LUTS despite appropriate medical and behavioral therapy, whereas voiding dysfunction represents functional abnormalities in the voiding phase that can often be corrected with targeted management. In our cohort, patients with refractory LUTS were excluded to avoid confounding effects on treatment outcomes, while

Table 3. Properties of Dexell and Deflux

	Dexell	Deflux
Dextranomer (mg/mL)	50	50
Hyaluronic acid (mg/mL)	15	17
Osmolality (mOsmol/L)	400	341
pH value	6.2	7.1
Diameter of dextranomer microspheres (µm)	80-120	80-250
Cost (€/cc) in Türkiye	180	400

patients with voiding dysfunction who had been appropriately treated prior to the endoscopic intervention were included. This approach allowed for a more homogeneous study population while reflecting real-life clinical practice.

A meta-analysis has shown that grade 4 reflux is associated with lower success rates compared to grades 1-3. Additionally, it has been reported that the success rates of repeated injections are lower than those of initial injections (16). In our study, younger age, a history of prior endoscopic treatment, and the presence of grade 4 reflux were identified as predictors of unsuccessful outcomes in the univariate analysis; however, none of these variables remained statistically significant in the multivariate analysis. This finding may be attributable to the limited sample size or to our definition of treatment success. If the criteria for defining unsuccessful outcomes had been broadened or if control VCUG had been performed in all patients during follow-up, the results of this analysis might have been different. Additionally, after 5 years of follow-up, 17 patients in the Dexell group and 16 patients in the Deflux group met the criteria for unsuccessful outcomes. In the Dexell group, 12 patients (70.6%) underwent open surgical repair and 5 patients underwent a repeat subureteric injection. In the Deflux group, 10 patients (62.5%) underwent open surgical repair and 6 patients underwent repeat subureteric injection.

Mazzone et al. (21) reported a 5% obstruction rate following subureteric injection. In our study, all patients underwent urinary ultrasound at 1 month postoperatively. In addition to routine ultrasound follow-up, patients presenting with worsening creatinine levels or flank pain underwent additional ultrasound imaging. During follow-up, obstruction was observed in 3 patients in the Dexell group and 2 patients in the Deflux group. However, all cases resolved conservatively without the need for further intervention. Point biserial correlation analysis was used to assess the relationship between injection material and postoperative obstruction, revealing no clinically significant difference (correlation coefficient =0.0069, p=0.94).

The success rate of subureteric injection could have been increased if the double-hit technique had been applied, but the application of the same technique may not have resulted in any discrimination between the two groups.

Study Limitations

This study has certain limitations that should be acknowledged. The first limitation is its retrospective design. Another limitation of this study is that the primary success criterion was defined as the absence of febrile UTIs during follow-up. Although this parameter is widely accepted as a reliable indicator of clinical resolution in current practice, additional factors such as recurrent afebrile UTIs, new scar formation on scintigraphy, decline in renal function, iatrogenic ureterovesical junction stricture, increased hydronephrosis on ultrasound, proteinuria, and hypertension were not systematically assessed due to the retrospective design of the study. In addition, control VCUG was not performed in all patients during follow-up, which could have provided a more objective comparison of anatomical resolution. Although performing VCUG at both baseline and follow-up would be ideal, it is not part of routine clinical practice and would be more feasible within the design of a randomized prospective study. Furthermore, the exclusion of patients with grade 5 VUR might have influenced the overall success rates. However, as these cases are generally associated with lower success rates after endoscopic treatment and are more likely to require surgical correction, we usually prefer open surgical repair for such patients in our daily practice. Their exclusion, therefore, may have reduced heterogeneity and prevented potential confounding in the interpretation of treatment outcomes. Moreover, a notable strength of this study is its provision of long-term outcome data for both Dx/HA materials, thereby addressing an existing gap in the current literature.

Conclusion

Our analysis shown that the diameter of dextranomer microspheres, frequently utilized for the endoscopic treatment of pediatric VUR, did not affect the short-term or long-term success rates of the procedure. Therefore, Dexell may be considered a cost-effective alternative to Deflux in clinical practice. Yet multicentric, randomized, prospective trials with long follow-up durations are necessary.

Ethics

Ethics Committee Approval: This study was approved by the Ankara University Human Research Ethics Committee (approval no.: 2022000257-3, date: 27.04.2022).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.T.S., B.B., Concept: M.C.K., Design: M.C.K., E.K., Data Collection or Processing: A.F.Ö., E.K., A.D.G., Analysis or Interpretation: A.F.Ö., A.A., Y.T.S., B.B., Literature Search: A.F.Ö., A.A., Writing: A.F.Ö.

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

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

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ORIGINAL RESEARCH
Endourology

Doi: 10.4274/jus.galenos.2025.2025-8-19
J Urol Surg 2026;13(2):121-128

Defining Myths and Facts of Supracostal Tubeless Mini-percutaneous Nephrolithotomy Performed Under Spinal Anesthesia: Single Center Experience

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What's known on the subject? and What does the study add?

Mini-percutaneous nephrolithotomy (PCNL) is taking over standard PCNL for the management of kidney stones because of fewer associated complications and better stone clearance. Supracostal PCNL is not very popular among urologists because of the associated thoracic complications, and there are only small case series reported in the literature exploring its safety. We highlight the safety of supracostal mini-PCNL performed under spinal anesthesia in terms of fewer thoracic and non-thoracic complications. It is the largest series of supracostal Mini-PCNL procedures performed under spinal anesthesia, which explores the versatility of upper calyces in clearing kidney stones.

Abstract

Objective: Percutaneous nephrolithotomy (PCNL) is considered the gold standard for the treatment of kidney stones >2 cm in size and those who fail other treatment modalities. Standard PCNL is associated with a significant number of complications mostly attributed to the larger tract circumference. Mini-PCNL, which utilizes a small tract size of less than 22 Fr, is associated with significantly fewer complications while maintaining a clearance rate comparable to that of standard PCNL. Prone position leads to upward migration of the kidney under the rib cage, making supracostal puncture necessary in a significant number of cases. Mini-PCNL, when performed under spinal anesthesia, is safe and reduces operative time without compromising stone clearance rate. This study was carried out to establish the safety and efficacy of supracostal tubeless mini-PCNL done under spinal anesthesia.

Materials and Methods: This is a retrospective study carried over a period of 5 years. It includes all the patients who underwent supracostal mini-PCNL under spinal anesthesia. The procedure was carried out in the prone position, employing 18 Fr Amplatz sheath with 12 Fr nephroscope. The outcome and perioperative complications were recorded and stored via Microsoft Excel and analyzed using SPSS Software, version 20.0.

Results: This study included 1135 patients with an average age of 40.6±13.8 years. The average stone size was 2.87±0.98 cm, and stones had predominantly calyceal distribution in 42.37% of cases. The 11th and 10th intercostal spaces were entered in 89.16% and 10.83% of cases, respectively, to gain access to superior (35.85%) and middle (64.14%) calyces. A single tract was usually required (78.32%) and the average operative time was 52.72±11.42 minutes. The rate of blood transfusion was 0.61%, and angioembolization was required to seal pseudoaneurysm/AVF in 0.52% of patients. The rate of hydrothorax/pneumothorax associated with 11th and 10th intercostal space entry was 0.49% and 7.3%, respectively. Only 1.23% of patients required intracostal tube drainage for pneumothorax/hydrothorax. The average rates of stone clearance and hospital stay were 97.53% and 1.8±0.45 days, respectively.

Conclusion: Supracostal tubeless mini-PCNL done under spinal anesthesia is safe and has high stone clearance rate. The associated thoracic and non-thoracic complications are minimal and the procedure can be safely performed when indicated, provided proper technique is employed.

Keywords: Hemothorax, hydrothorax, mini percutaneous nephrolithotomy, supracostal PCNL

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Received: 04.09.2025 **Accepted:** 11.10.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Para SA, Mushtaq Y, Khawaja AR, Beigh FA, Khan TA, Kannan G, Raina AB. Defining myths and facts of supracostal tubeless mini-percutaneous nephrolithotomy performed under spinal anesthesia: single center experience. J Urol Surg. 2026;13(2):121-128.

Introduction

Nephrolithiasis has affected humans since antiquity, and the incidence reaches up to 15% in the northern renal stone belt of the Indian subcontinent (1). Treatment of renal stone diseases has evolved from invasive open operations to minimally invasive endourologic procedures offering rapid recovery and significantly higher stone clearance. Percutaneous nephrolithotomy (PCNL) remains the gold standard for the management of large and complex renal stones. Both American Urological Association and European Association of Urology recommend PCNL as first line treatment for large size renal stones because it offers high stone free rate and effectiveness of the procedure is not limited by stone burden and composition. Utilization of small size nephroscope and tracts is associated with fewer complications and bleeding, with stone free rates comparable to standard PCNL (2,3). With advancements in optics and lithotripters, nephroscopes have become slimmer, reducing the tract size for PCNL. Mini-PCNL, defined as tract size less than 22 Fr, has proved to be effective in managing renal stones of all sizes with fewer complications and a clearance rate comparable to standard PCNL (4). Mini-PCNL permits better maneuverability in a less dilated pelvicalyceal system (PCS) resulting in better clearance, less bleeding, and a reduced number of tracts required to achieve complete clearance (5). PCNL, when performed under general anesthesia (GA), allows better control of hemodynamics, controlled ventilation to fix the target calyx for perfect entry, and permits the surgeon to prolong the procedure when required. On the other hand, spinal anesthesia (SA) is safe in patients with pulmonary comorbidities, reduces the procedure time, cost, and hospital stay. Although each method of anesthesia has advantages and disadvantages, final choice of anesthesia is dictated by patient condition and preference of surgical team (6).

An ideal calyx for PCNL is the one which provides the shortest path to the majority of the stone burden, while providing good access to the upper ureter. It is generally dictated by stone burden, distribution of stone, PCS anatomy, and surgeon preference. Middle and superior calyceal access in PCNL has been reported to provide better stone clearance, less need of additional punctures, and easy access to the upper ureter for stone clearance as well as deployment of a Double J stent (7). In the prone position, middle and superior calyces often stay above the 12th rib, making supracostal puncture a necessity for optimal clearance. Most urologists use deep breathing maneuvers to position the kidney below the 12th rib for renal puncture. With these maneuvers, descent of the lung is greater than kidney movements, making the lung and pleura susceptible to injury (8). In our retrospective study, we analyze the safety and efficacy of supracostal punctures in mini-PCNL performed under SA.

Materials and Methods

This is a retrospective study conducted over a period of 5 years from June 2015 to June 2020 at a tertiary care center. Patients with renal stones with a size greater than 1 cm who were planned for mini-PCNL and required supracostal puncture were included in this study. Pediatric patients with supracostal punctures were excluded from the study as all these patients were operated on under GA. Patients were evaluated by dedicated contrast computed tomography (CT) with urography. Informed consent was taken from all the patients and risks of the procedure were explained. The study was approved by the Sher-i-Kashmir Institute of Medical Sciences Institutional Ethical Committee (date: 03.06.2025, approval number: SIMS 131/IEC-SKIMS/2024-129). The procedure was carried out under SA in the prone position. Desired calyx for access was selected after retrograde contrast injection, and the entry point was marked on the intercostal space. An 18 G initial puncture needle was used for puncturing the calyx, and advanced with the fluoroscope in 0°, and depth was assessed by changing the fluoroscopy angle to 30° in the cranio-caudal direction. All punctures were made through the summit of the calyx on papillary impression, and the position was confirmed with a free flow of contrast. A 0.032 hydrophilic guidewire was passed through the needle, and the first dilatation was done with a 10 Fr Teflon dilator. Subsequent dilatation was carried out with a single 18 Fr Amplatz dilator over a guide rod. An 18 Fr Amplatz sheath was deployed for nephroscopy. A 12 Fr nephroscope was used with a pneumatic lithotripter for the fragmentation of renal stones. Fragments were mainly flushed out with saline, and larger fragments required forceps for retrieval. Small fragments in the non-accessible calyces were flushed out with a puncture needle under fluoroscopic guidance. Need for additional dilatations was determined by stone distribution, and no more than 4 dilatations were used in any given case. A 4.5 Fr stent was left inside at the end of the procedure, and no nephrostomy was used in any case. An X-ray abdomen was taken the next morning to assess clearance of stone, and any radiopaque shadow more than 2 mm or multiple radiopaque shadows were considered as incomplete clearance. Patients with chest pain and breathing difficulty were evaluated by chest X-ray (Figure 1) or chest CT (Figure 2) for any hydro or pneumothorax. Any complications in the perioperative period were recorded and graded as per the modified Clavien Dindo classification. Intercostal tube drainage (ICTD) was done for symptomatic pneumo/hydrothorax.

Statistical Analysis

The perioperative data were collected and stored via Microsoft Excel program and analyzed using SPSS Software, version 20.0. Categorical data were expressed as frequencies and percentages. Continuous variables were expressed as mean ± standard deviation. The chi-square test was used to compare the differences in proportions between the two groups. Student's t-test was used to compare continuous variables in two independent groups. The odds ratio (95% confidence interval) of the unrelated clinical parameters was calculated using univariate regression models to predict the outcome variable or complications. All p values less than 0.05 were considered statistically significant.

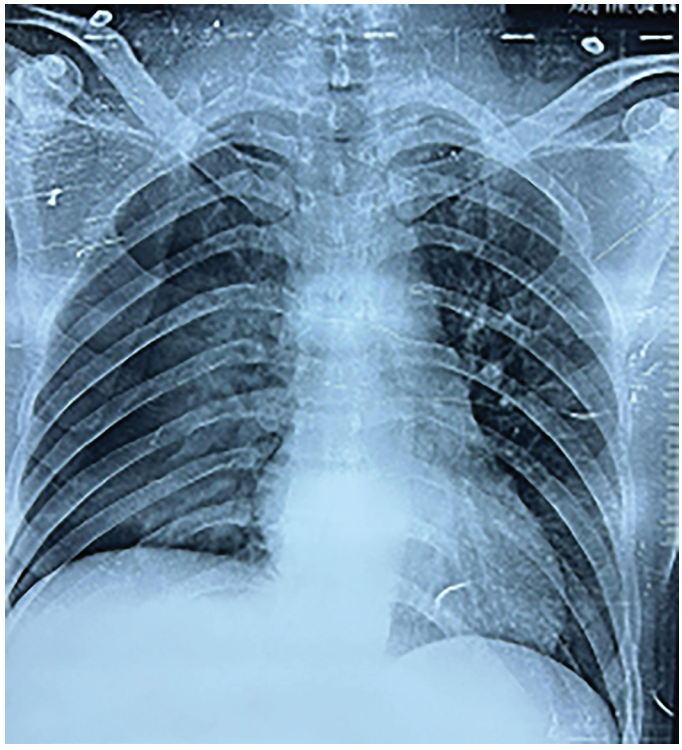

Figure 1. X-ray showing right sided pneumothorax

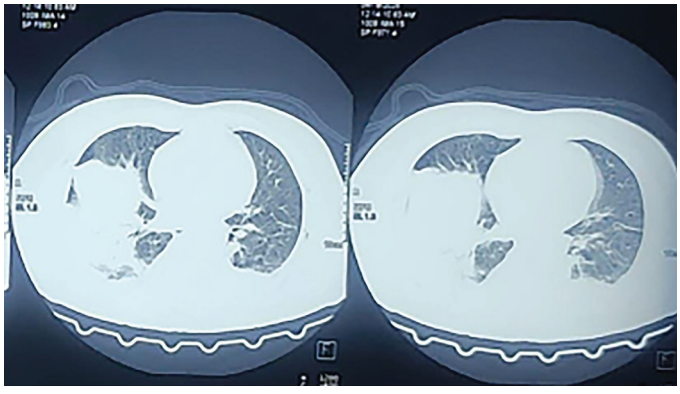

Figure 2. Computed tomography chest showing right sided hemothorax

Results

The demographic profile of patients is displayed in Table 1. Analysis of the data from patients with nephrolithiasis who underwent mini-PCNL at our center showed that 1135 patients underwent supracostal puncture to remove stones. All these procedures were performed on adults under SA. The percentage of male and female patients in our study was 63.5% and 36.5%, respectively. The mean age and body mass index of patients in the study were 40.6±13.8 years and 23.7±2.7 kg/m², respectively. 44.4% of patients had the procedure done on the right side and 51.71% of patients had the procedure done on the left side. Only 3.87% of patients had bilateral mini-PCNL performed concurrently. The distribution of stones was predominantly calyceal (42.37%) followed by pelvic (35.06%). 11.92% of patients had staghorn calculi while upper ureteric calculi were present in 10.66% of patients. 75.59% of

Table 1. Demographic profile of patients undergoing supracostal mini-PCNL under spinal anesthesia

Variables	Values
Number of patients	1135
Male/female (%)	721/414 (63.5/36.5)
Mean age in years ± SD (range)	40.6±13.8 (17-88)
Mean BMI ± SD (kg/m²)	23.7±2.7
Charlson comorbidity index n (%)	
0-1	812 (71.54)
2-4	209 (18.41)
5 or higher	114 (10.04)
Laterality n (%)	
Right	504 (44.4)
Left	587 (51.71)
Bilateral	44 (3.87)
Stone location n (%)	
Staghorn	135 (11.92)
Pelvis	398 (35.06)
Calyceal	481 (42.37)
Upper ureter	121 (10.66)
Previous stone procedure n (%)	
Pyelolithotomy	86 (7.57)
PCNL	102 (8.98)
ESWL	89 (7.85)
Nil	858 (75.59)
Renal anomalies	
Malrorated kidney	15 (1.32%)
Horseshoe kidney	11 (0.96%)
Ectopic kidney	1 (0.08%)
Average stone size (cm ± SD)	2.87±0.98

SD: Standard deviation, BMI: Body mass index, PCNL: Percutaneous nephrolithotomy, ESWL: Extracorporeal shock wave lithotripsy

patients were naive, while 8.98% and 7.57% of patients had previous history of PCNL and pyelolithotomy, respectively. The average size of stone operated on in this study was 2.87±0.98 cm.

The perioperative data of patients are assembled in Table 2. The primary entry was made through the middle calyx in 64.14% of cases and the superior calyx in 35.85% of cases. The supracostal punctures were made in the 11th intercostal space in 89.16% of patients, and the 10th intercostal space in 10.83% of patients. The majority of patients required single tract (78.32%) dilatation whereas two and three tracts were required in 17.18% and 3.87% of patients, respectively. Only 0.61% of patients required four tracts for complete clearance of stones. The average operative time in our study was 52.72±11.42 minutes, and included the time from the start of puncture to the closure of the tract. Perioperative complications, graded as per modified Clavien Dindo classification, were predominantly Grade I with transient fever, and transient rise in creatinine reported in 3.78 and 0.79% respectively. 0.26% of patients had a transient urine leak via the tract site, while significant bleeding requiring blood transfusion was recorded in 0.61% of patients. Bleeding resulting from pseudoaneurysm and arteriovenous fistula (AVF) requiring angioembolization was reported in 0.52% of patients. 1.23% of patients required ICTD for hemothorax/pneumothorax. One patient (0.08%) had pelviureteric junction stricture requiring subsequent pyeloplasty. Sepsis was reported in 1.32% of patients, however there was no mortality related to the procedure. Entry made through the 11th intercostal space resulted in hemothorax/pneumothorax in 0.49% of patients, while the same complication was reported in 7.3% of patients when the 10th intercostal space was chosen for entry. Complete clearance of stone was achieved in 97.53% of patients. The average hospital stay was 1.8±0.45 days in our study.

We performed a univariate analysis of demographic and operative variables according to the complications (Table 3). On analysis of the 123 complications observed in our series, it was found that high mean body mass index (p=0.018), non-pelvic location of stones (p=0.043), presence of renal anomalies (p=0.014), larger average stone size (p=0.0001), superior calyceal entry (p=0.049), 10th intercostal entry (p=0.0005), more than one tract dilatation (p=0.002) and longer operative time (p=0.0001) were independent risk factors for overall complications.

Discussion

Nephrolithiasis is prevalent worldwide, with high incidence in northern India. According to the international guidelines, PCNL should be preferred for renal stones >2 cm (9). Standard PCNL, which employs the tract size of 24 to 30 Fr, produces excellent stone clearance but with a relatively higher complication rate

Table 2. Perioperative parameters of operated patients undergoing mini-PCNL under spinal anesthesia

Variables	Values
Primary entry calyx, n (%)	
Superior	407 (35.85%)
Middle	728 (64.14%)
Supra 12th rib/11th intercostal entry	1012 (89.16%)
Supra 11th rib/10th intercostal entry	123 (10.83%)
Number of tracts dilated, n (%)	
Single	889 (78.32%)
Two	195 (17.18%)
Three	44 (3.87%)
Four	7 (0.61%)
Average operative time (minutes ± SD)	52.72±11.42
Complications classified by the modified Clavien grading system, n (%)	
Grade I	
-Postoperative pain on VAS scale	
*No pain	312 (27.49%)
*Mild pain	487 (42.90%)
*Moderate pain	315 (27.75%)
*Severe pain	15 (1.32)
*Very severe pain	6 (0.52%)
*Worst pain possible	0
-Transient fever	43 (3.78%)
-Transient rise of creatinine	9 (0.79%)
Grade II	
-Tract site urine leak	3 (0.26%)
-Bleeding requiring transfusion	7 (0.61%)
Grade IIIa	
-Bleeding requiring angioembolization	6 (0.52%)
*Normal renal anatomy	5 (0.44%)
*Horse shoe kidney	1 (9.09%)
-Hemothorax/pneumothorax requiring chest tube drainage	14 (1.23%)
*Normal kidney anatomy	13 (1.15%)
*Horse shoe kidney	1 (9.09%)
-Retenrion due to clots	3 (0.26%)
Grade IIIb	1 (0.08%)
-PUJ stricture	
Grade IVa	1 (0.08%)
-Acute kidney injury requiring hemodialysis	
Grade IVb	15 (1.32%)
-Sepsis	
Grade V	0
Pneumothorax/hydrothorax related to entry level (number of hydro or pneumothorax/no. of supracostal entries)	
Supra 12th rib/11th intercostal space	5/1012 (0.49%)
Supra 11th rib/10th intercostal space	9/123 (7.3%)
Complete clearance on fluoroscopy and X-ray KUB, n (%)	1107 (97.53)
Average hospital stay (days ± SD)	1.8±0.45

SD: Standard deviation, KUB: Kidney, ureter, and bladder, PCNL: Percutaneous nephrolithotomy, VAS: Visual analog scale, PUJ: Pelviureteric junction

of 23.3% (10). As reported in the literature, larger tract size has been attributed to an increased risk of bleeding, and attempts have been made to minimize it. Mini-PCNL, described as the tract size of 14-20 Fr, was introduced to reduce complications and achieve excellent stone clearance. We prefer mini-PCNL with a tract size of 18 Fr at our center, and all of the patients in our study were operated by the same technique and equipment. Mini-PCNL, initially introduced for small sized stones, has been found to be very effective in managing medium and large sized stones as well with a reduced complication rate (5). All types of stones, including staghorn calculi, were managed by mini-PCNL in our study, with the average size of the stones being 2.87±0.98.

PCNL can be done under general or regional anesthesia or SA. GA is preferred by most urologists and anesthesiologists because it offers better control of hemodynamics, controlled ventilation to fix target calyx for easy entry, and the ability to prolong anesthesia required for clearing larger stones. On the other hand, GA is associated with lung atelectasis, prolonged operative time, and is contraindicated in a chronic respiratory illness. SA offers better postoperative pain control, shorter operative time, and early identification of lung complications, with overall results, including stone clearance, comparable to those of GA (11). Indra Rachman et al. (6), in their meta-analysis of spinal vs GA for PCNL, documented reduced operative time, faster recovery, reduced hospital stay, and less need for analgesics in the postoperative period in patients operated under SA, without compromising on stone-free rate. All the patients were operated under SA, and the average operative time was 52.72±11.42 minutes, which is less than most of the studies, including the one done by Khadgi et al. (12)

Table 3. Univariate analysis of demographic and perioperative factors predicting complication in supra-costal mini-PCNL

Parameters	Complications (123)	No complications (1012)	Odds ratio	p-value
Age (mean ± SD)	39.27±12.7	41.23±13.12	(95% CI: 0.4898-4.4098)	0.116
Gender				
Male	79 (64.2%)	642 (63.43%)		0.863
Female	44 (35.77%)	370 (36.56%)		
Mean BMI ± SD	23.89±2.7	23.4±2.1	(95% CI: 0.8970-0.0830)	0.0183
Laterality				
Right	55 (44.71%)	449 (44.36%)	1 (reference)	0.941
Left	64 (52.03%)	523 (51.67%)	0.999 (95% CI: 0.6819-1.463)	0.995
Bilateral	6 (4.87%)	38 (3.75%)	1.289 (95% CI: 0.5212-3.187)	0.582
Stone location				
Pelvic	33 (26.82%)	365 (36.06%)	1.5386 (95% CI: 1.0119-2.3393)	0.043
Non pelvic	90 (73.17%)	647 (63.93%)		
Previous procedure				
No previous procedure	93 (75.6%)	765 (75.59%)	0.9991 (95% CI: 0.6461-1.5448)	0.996
Previous procedure	30 (24.39%)	247 (24.40%)		
Renal anomalies				
Normal	116 (94.30%)	992 (98.02%)	2.9931 (95% CI: 1.2390-7.2303)	0.014
Anomalies	7 (6.69%)	20 (1.97%)		
Average stone size (cm ± SD)	2.91±0.93	2.1±0.74	(95% CI: 0.9529-0.6671)	<0.0001
Primary entry calyx				
Superior calyx	54 (43.9%)	353 (34.88%)	1.461 (95% CI: 1.0003-2.1340)	0.049
Middle calyx	69 (56.09%)	659 (65.11%)		
Level of entry				
11th intercostal	98 (82.11%)	914 (90.9%)	2.379 (95% CI: 1.4633-3.8684)	0.0005
10th intercostal	25 (17.88%)	98 (9.09%)		
No. of tracts dilated				
Single	80 (65.04%)	809 (79.94%)	2.142 (95% CI: 1.4340-3.1997)	0.0002
More than one tract	43 (34.95%)	203 (20.05%)		
Average operative time	58.56±12.56	46.2±10.12	(95% CI: 14.310-10.409)	<0.0001

PCNL: Percutaneous nephrolithotomy, SD: Standard deviation, CI: Confidence interval, BMI: Body mass index

The reduced operative time in our study is partly attributed to the skills of the surgeon performing a large volume of PCNLs, the use of SA, and the tubeless nature of the procedure. Success of PCNL is primarily determined by the establishment of a proper tract that provides safe access to the bulk of the stone. Singh et al. (13), advocated that supracostal access made through superior and middle calyx provided good access to staghorn calculi, pelvic calculi, and ureteric calculi, significantly reducing the number of tracts required to achieve complete clearance. We have a preference for superior and middle calyces for most kidney stones, which results in better outcomes, reduced operative time, and less need for additional tracts for complete clearance. In our study, middle and superior calyceal access was made in 64.1% and 35.85% of cases, respectively. This is reflected in the higher clearance rate of 97.53%, with the majority of the procedures (78.32%) requiring a single tract for clearance. Khadgi et al. (12) reported a stone clearance of 87.6% by mini-PCNL in their study. The stone clearance rate in our study is much higher than in most of the studies. Besides the above-mentioned factors, use of a puncture needle under fluoroscopy to flush fragments out of calyces into the accessible pelvis reduced the need for additional tracts and markedly increased the stone clearance rate. Maheshwari et al. (14) reported the use of percutaneous calyceal irrigation for stones in inaccessible calyces during PCNL to increase stone clearance and reduce the need for additional tracts. Goldberg et al. (15) concluded from their randomized study that tubeless supracostal PCNL is associated with less postoperative pain, minimal tract site urine leak, decreased incidence of hydrothorax, and shorter hospital stay. We performed all our supracostal mini-PCNL as tubeless to utilize the aforementioned advantages.

Mini-PCNL has a lower complication rate, which is primarily attributed to its small tract size. Eddula et al. (16) reported that patients undergoing PCNL under SA experienced lower VAS scores and reduced requirement for analgesics in the postoperative period compared to GA. In our study, most patients had either no pain or mild pain, and only severe pain was reported among those patients with thoracic complications. Ruhaye et al. (17), reported that small tract size is associated with less bleeding and reduced need for blood transfusion. Ferakis et al. (5) reported a transfusion rate of 1.4% in their series. Post PCNL renal pseudoaneurysm/AVF is the result of direct injury to segmental arteries and their branches. These fragile anomalies are exposed to the high-pressure renal arterial system, resulting in bouts of massive bleeding usually on the 7th-14th postoperative day. The incidence of post PCNL pseudoaneurysm/AVF, as reported by Seitz et al. (10), ranges from 0.6-2.5% with a transfusion rate of 1% to 11%. The rate of angioembolization and transfusion in our series is just 0.52% and 0.615, respectively, which is much less than that reported in the literature. Most of the studies agree on the opinion that hypertension, diabetes, renal anomalies, anticoagulants, stone size, tract size, number of tracts, and non-papillary punctures increase the risk of a post-PCNL pseudoaneurysm/AVF (18). Among 11 patients with horseshoe kidney in our series, one patient developed pseudoaneurysm requiring angioembolization. The presence of renal anomalies proved to be an independent risk factor for overall complications in our series. Lower rate of pseudoaneurysm/AVF in our series may be related to small tract size, precise papillary puncture, limited number of tracts required attributed to needle flushing, and the volume of cases performed by the surgeon.

Despite the high success rate, the primary concern for supracostal puncture remains the thorax complications associated with it. The reported incidence of thoracic complications after supracostal puncture has been quite variable in the literature. Sekar et al. (19), reported the incidence of 2.17% thoracic complications in their series of supracostal punctures. Yadav et al. (20), in their series of 762 patients with supracostal puncture, needed intracostal tube drainage of hydrothorax in 3.35% of cases. In our series, the incidence of symptomatic hydrothorax/pneumothorax requiring intracostal chest tube drainage was 1.23%, which is less than most of the series of supracostal PCNL. Prone position leads to cephalad migration of kidneys, in about 80% of patients, making supracostal puncture imperative to clear stones in a significant number of patients (21). The incidence of thoracic complications after supracostal PCNL depends on level of intercostal space entered, laterality of entry point from midline, real time level of lung during breathing cycle, and rotational anomalies of kidneys. Maheshwari et al. (22), in their study of supracostal PCNL, reported an incidence of 4.9% of hydrothorax in total, with the percentage of hydrothorax increasing with the level of intracostal entry. They reported the incidence of hydrothorax as 1.2%, 10.6% and 35.7% on entering through 11th, 10th and 9th intercostal space respectively. While reviewing the anatomy of pleura, it is worth to note that the costophrenic recess reaches up to 12th rib medial to the midscapular line and recedes up on crossing lateral to the midscapular line reaching to 10th rib in mid axillary line. So, the supracostal punctures made medial to the midscapular line are more likely to cause pleural injury compared to the punctures made lateral to it. Same anatomical factor makes superior calyceal puncture in malrorated kidney prone to thoracic injuries. In horseshoe and malrorated kidneys, pelvis faces anteriorly and calyces are directed posteriorly, medial to the midscapular line. In our series there were 11 patients with horseshoe kidney, and one of them developed hydrothorax upon entering the superior calyx. The movements of the lungs during the breathing cycle change their relation to the surface markings on the chest wall. Hopper et al analysed the chest CT imaging of patients during breathing and found that on full expiration, the possibility of a needle passing through the 11th

posterior intercostal space traversing the lung was 29% on the right side and 14% on the left side, respectively. However, the same point of entry in full inspiration would penetrate the lung in most cases. With the 10th posterior intercostal approach, the chances of lung injury were excessive regardless of the phase of breathing (23). The low incidence of thoracic complications in our study is attributed to lateral intercostal puncture, needle descending during expiration, and entry close to the upper border of the rib.

The drawback of our study is its retrospective design. There is always a possibility of selection and recall bias in such studies. Since it is a single-center study, a multicentric study is therefore needed to formulate adequate results.

Conclusion

Our findings suggest that supracostal puncture in mini-PCNL under SA may be considered safe and effective when indicated, provided that careful technique is employed._It is highly efficient in clearing stones with minimal non-thoracic complications. Puncturing during expiration, entering lateral to the midscapular line and above the superior border of the rib is key to avoid thoracic complications in supracostal mini-PCNL.

Ethics

Ethics Committee Approval: The study was approved by the Sher-i-Kashmir Institute of Medical Sciences Institutional Ethical Committee (date: 03.06.2025, approval number: SIMS 131/IEC-SKIMS/2024-129).

Informed Consent: Informed consent was taken from all the patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.A.P., Concept: S.A.P., Design: S.A.P., Data Collection or Processing: Y.M., Analysis or Interpretation: G.K., A.B.R., Literature Search: F.A.B., Writing: A.R.K., T.A.K.

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

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

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VIDEO ARTICLE
Andrology

Doi: 10.4274/jus.galenos.2025.2025-4-14
J Urol Surg 2026;13(2):129-131

Surgical Management of Ossified Plaques in Complex Peyronie's Disease: Technical Tips and Tricks from a Challenging Case

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Abstract

This case report presents the surgical management of a patient with complex Peyronie's disease involving a densely ossified plaque. The report highlights technical tips and tricks used to overcome intraoperative challenges, including dissection strategies and grafting techniques. Our experience emphasizes the importance of surgical expertise in achieving successful outcomes in such demanding cases.

Keywords: Andrology, general urology, reconstructive urology

Introduction

Peyronie's disease (PD) is a urological condition characterized by the formation of fibrotic plaques in the tunica albuginea, resulting in penile deformity. The prevalence of PD in the general population ranges from 0.6% to 11% (1). Surgical intervention remains the gold standard for treatment. Surgical approaches include tunical shortening and lengthening techniques. According to the guidelines of the European Association of Urology and the European Society for Sexual Medicine, tunical lengthening procedures are recommended for complex cases of PD. These include severe penile curvature (>60 degrees), hinge deformity, hourglass deformity, and cases where the erect penile length is less than 13 cm (2-4). Based on current studies, the prevalence of complex PD is estimated to be approximately 10% among all PD cases (5). Techniques utilized in these cases include tunical incision or excision and penile prosthesis implantation combined with grafting. In a recent study based on the declaration by sexual medicine associations', it was stated that autologous or xenograft are often preferred in PD surgery (6). While saphenous vein and buccal mucosa, are most commonly preferred as autologous grafts, whereas small intestinal submucosa and bovine pericardium are preferred as xenografts (7).

Materials and Methods

To accurately evaluate penile deformity, all patients underwent an intracavernosal injection of 10 µg alprostadil followed by dynamic penile color Doppler ultrasonography, due to the limitations of preoperative self-photography (8). This protocol enabled standardized and objective evaluation of both erectile functional capacity and the degree of penile curvature. The patient's stretched penile length and girth were measured as 12.7 cm and 8.9 cm, respectively. The preoperative International Index of Erectile Function-5 (IIEF-5) score was found to be 21.

After routine skin cleaning in the supine position, the surgical site was covered with sterile drapes under aseptic conditions. A 16 Fr Foley catheter was inserted to achieve urethral catheterization. A circumferential skin incision was made along the previous circumcision line, and complete penile degloving was subsequently performed. An artificial erection was then induced by injecting saline through an angiocatheter inserted into the tunica albuginea. A dorsal curvature of approximately 70 degrees was observed at the penile base during artificial erection. Buck's fascia was carefully incised lateral to the urethra, and dissection was continued dorsally up to the 12 o'clock position to mobilize the neurovascular bundle (NVB). The NVB was subsequently suspended using vessel loops to ensure optimal exposure of the

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Received: 28.04.2025 **Accepted:** 11.10.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Doğan Ç, Şahin MF, Yazıcı CM, Turunç T, Topkaç EC, Akyıldız O, Tuncer FB. Surgical management of ossified plaques in complex Peyronie's disease: technical tips and tricks from a challenging case. J Urol Surg. 2026;13(2):129-131.

underlying plaque. Initial attempts at Peyronie's plaque incision were made using a scalpel. However, all of these efforts were ineffective due to the dense calcification and firmness of the plaque. Further efforts, to incise the plaque using Adson-toothed forceps, were also ineffective. An additional attempt was made with monopolar cautery, but this, too, failed due to the plaque's extensive calcification. Subsequently, the anterior aspect of the calcified plaque was thinned using a scalpel, thereby allowing for a successful incision. Following the dorsal tunica albuginea incision, a 5×2 cm tunica albuginea defect was created using microsurgical scissors. The size of the tunica albuginea defect is calculated based on geometric principles. As described by Vicini et al. (9), the measurement is determined by assessing the length discrepancy between the convex and concave sides of the penile curvature. This defect extended dorsally from the midline toward both lateral aspects of the urethra. The bovine pericardium was preferred to fill the tunica albuginea defect. A graft approximately 20% larger than the actual defect size was employed to prevent postoperative graft contraction. The graft was sutured in the defect using a continuous 4-0 Vicryl suture technique. Due to the difficulty in re-establishing optimal rigidity following graft placement, a second artificial erection was not performed. The procedure was completed with anatomical closure of Buck's fascia, dartos fascia, and skin. A compressive dressing was applied and scheduled for removal after 48 hours (Video 1).

Results

No complications were observed during the perioperative and postoperative periods. The duration of postoperative follow-up was six months. In the first postoperative month, stretched penile length was recorded as 13.0 cm, penile girth as 9.1 cm, and the IIEF-5 score was 20.

Discussion

It may be preferable, particularly during mobilization of the NVB in the presence of a densely calcified plaque, to perform dissection not directly over the area of maximal calcification but rather from the distal or proximal penile segments where the plaque density is lower.

Conclusion

Surgical correction of complex PD involving ossified plaques can be particularly challenging due to dense calcification and limited plaque pliability. In such cases, a meticulous dissection strategy and individualized grafting technique are crucial for successful outcomes. These complex cases require considerable surgical experience and expertise and are best managed by surgeons with sufficient proficiency in advanced reconstructive techniques. Delaying such procedures until an appropriate level of surgical experience has been attained may contribute to improved outcomes and satisfaction for both the patient and the surgeon.

Video 1. https://youtu.be/_sk2jfQMEtE

Ethics

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ç.D., M.F.Ş., Concept: Ç.D., M.F.Ş., Design: Ç.D., C.M.Y., T.T., Data Collection or Processing: E.C.T., O.A., Analysis or Interpretation: M.F.Ş., F.B.T., Literature Search: C.M.Y., F.B.T., Writing: Ç.D., M.F.Ş., C.M.Y., T.T., E.C.T., O.A., F.B.T.

Conflict of Interest: Tahsin Tunç Prof. MD is Associate Editor in Journal of Urological Surgery. He had no involvement in the peer-review of this article and had no access to information regarding its peer-review. Mehmet Fatih Şahin MD is Review Board Member in Journal of Urological Surgery. He had no involvement in the peer-review of this article and had no access to information regarding its peer-review.

Financial Disclosure: The authors declare that they received no financial support for this study.

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LETTER TO THE EDITOR
Endourology

Doi: 10.4274/jus.galenos.2025.2025-7-2
J Urol Surg 2026;13(2):132-133

Not All Stones are the Same: Personalizing Post-ESWL Surgical Choices

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Dear Editor,

As a medical student with an interest in clinical urology, I commend Baba et al.'s (1) new paper, "Treatment Strategies for Kidney Stones Following ESWL Failure: A Prospective Comparative Study of Three Surgical Approaches". We are all aware that nephrolithiasis, or kidney stone disease, is a significant international public health problem. Given the significant lifetime risk of 10-15% and a recurrence rate of 50% within 10 years of the index event (2), a paper addressing these statistics is worth reading. The observations made by the authors speak to the challenges we face in clinics on a daily basis-patients disillusioned by failed treatments, asking what they should do next.

I praise the authors' transparent methodology, prospective design, and patient-centered outcomes such as hospital stays and standardized Clavien-Dindo complication reporting, but certain methodological flaws should be noted. All stones do not have the same composition, i.e., calcium oxalate, uric acid, cystine, and struvite stones; these variations and patient considerations mandate a personalized approach to post-extracorporeal shock wave lithotripsy (ESWL) surgical decision making, in an attempt to avoid unnecessary interventions, because a one-size-fits-all doesn't fit stones-or the patients.

The heterogeneity of stone distribution within the lower pole [percutaneous nephrolithotomy (PCNL): 37% vs. retrograde intrarenal surgery (RIRS): 14%] is of clinical importance. As Karkin et al. (3) and other authors (4) discussed, stones of this composition are notoriously hard to clear, which affects operative time and distorts operative time and success rates. Although the sample size in the current study was adequate to meet statistical needs, we cannot overlook the trend towards a threefold greater rate of residual stones with RIRS versus miniPCNL (27.6% vs. 9.7%). Clinically, differences may impact treatment planning, particularly in anxious patients who do not want to undergo multiple procedures.

I also wonder if small anatomical idiosyncrasies could have had any unrecognized contributions. Although the authors have elegantly balanced the pros and cons of the three surgery techniques, I am still wondering "how" individual technique adjustments (e.g., laser settings or sheath sizes) can optimize outcomes.

In addition, the cohort's high stone burden (mean HU: 1023±129), previously noted as an ESWL failure predictor (5), was not correlated with results. Subgroup analysis was probably underpowered due to sample size limitations; the trend noted towards greater residual stone burden with RIRS (27.6% compared with miniPCNL: 9.7%; p=0.156) is yet to be confirmed in larger series.

Also, cost-utility analyses should be performed to weigh the reduced hospital stay of RIRS against its higher equipment cost. For example, when choosing between two interventions, one will be less costly but require a longer hospital stay; while the other will be more costly but allow faster recovery.

Future studies must emphasize randomized controlled trials based on the different stone types and their density. By accounting for the equipment expenses of RIRS against reduced hospital stays, and documenting patients' quality of life with extended follow-ups for a year or more, we can compare post-ESWL decisions more accurately. If all these factors are made available, we can make better healthcare decisions and enhance patient-reported outcomes.

Yours sincerely,

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Received: 07.07.2025 **Accepted:** 06.08.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Khawar I. Not all stones are the same: personalizing post-ESWL surgical choices. J Urol Surg. 2026;13(2):132-133.

Footnotes

Financial Disclosure: The author declared that this study received no financial support.

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CASE REPORT
Functional Urology

Doi: 10.4274/jus.galenos.2026.2026-1-3
J Urol Surg 2026;13(2):134-137

First Ketamine-induced Ulcerative Cystitis Cases from Türkiye: Clinical Course, Histopathological and Radiological Findings in Young Female Patients

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Abstract

Ketamine-induced ulcerative cystitis (KIC) is an emerging urological disorder associated with recreational ketamine use, characterized by inflammation, bladder wall hypertrophy, and involvement of the upper urinary tract. We report two female patients with ketamine-related ulcerative cystitis. The first case represented advanced-stage KIC, with findings including hydronephrosis, bladder fibrosis, and impaired renal function. In contrast, the second case presented at an early stage with clinical and radiological findings that were reversible after complete cessation of ketamine use. Histopathological examination in both cases revealed ulceration, chronic inflammation, and fibrosis. Radiological and cystoscopic findings closely correlated with disease severity. Early recognition of KIC and strict cessation of ketamine use are crucial to prevent irreversible bladder damage and progressive renal deterioration.

Keywords: Ketamine-induced cystitis, ulcerative cystitis, recreational drug abuse

Introduction

Ketamine, introduced in the 1960s as an N-methyl-D-aspartate receptor antagonist, remains widely used as an anesthetic agent (1). However, because of its dissociative and euphoric effects, ketamine has also been used illicitly as a recreational drug (2).

Ketamine-induced ulcerative cystitis (KIC) was first described by Shahani et al. (3) in 2007 in patients presenting with hematuria, urgency, increased daytime frequency, dysuria, and reduced bladder capacity. In some cases, involvement of the upper urinary tract and progression to chronic kidney disease were also reported.

More than 25% of recreational ketamine users develop urinary symptoms, which correlate with both cumulative dose and duration of use (4). Although symptoms may improve following ketamine cessation, irreversible bladder and renal damage may occur in some patients (5,6). Wu et al. (7) proposed a staging system for KIC, classifying the disease into inflammatory, early fibrotic, and severe fibrotic stages.

After obtaining informed consent, we present two young female patients diagnosed with ulcerative cystitis secondary to recreational ketamine use, representing both early and advanced stages of the disease.

Case 1

A 32-year-old woman with a 4-year history of recreational ketamine abuse had discontinued ketamine use six months prior to presentation. Her medical history included cholecystectomy, dyspareunia, endometrioma, and pelvic inflammatory disease. The patient reported the onset of suprapubic pain in April 2022, followed by dysuria in May 2022.

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Received: 05.01.2026 **Accepted:** 16.01.2026 **Epub:** 02.04.2026 **Publication Date:** 01.06.2026

Cite this article as: Madendere S, Kılıç M, Köseoğlu E, İğdem A, Tarcan T. First ketamine-induced ulcerative cystitis cases from Türkiye: clinical course, histopathological and radiological findings in young female patients. J Urol Surg. 2026;13(2):134-137.

Her first urological evaluation was conducted in November 2022. At that time, she reported severe lower urinary tract symptoms (LUTS), including increased daytime frequency (approximately hourly), nocturia (approximately hourly at night), dysuria, and bladder pain. Laboratory investigations revealed elevated alkaline phosphatase (ALP) (262 IU/L), gamma-glutamyl transferase (319 IU/L), C-reactive protein (CRP) (36 mg/dL), and eosinophilia (7.3%). Urinalysis demonstrated leukocyturia and hematuria, while urine culture was sterile. Ultrasonography showed bladder wall thickening measuring 9 mm, with no other significant findings.

A cystoscopy performed in November 2022, following hydrodistension, revealed an ulcerative lesion with mucosal bleeding. The maximum bladder capacity under general anesthesia was 200 mL. Urine cytology and biopsies of the lesion were obtained, and fulguration was performed. Histopathological examination demonstrated inflammation, vascular congestion, and fibrosis (Figure 1). The pathological findings were not entirely consistent with interstitial cystitis (IC). Urine cytology revealed reactive urothelial cells, neutrophils, and erythrocytes.

Following cystoscopy and hydrodistension, the patient experienced a slight improvement in her symptoms. The patient was recommended an IC-friendly diet and treated with amitriptyline and pentosan polysulfate; however, her symptoms progressively worsened by September 2023. She subsequently developed gross hematuria, anemia, and renal impairment with a serum creatinine level of 1.42 mg/dL. Urodynamic evaluation revealed urinary incontinence with terminal detrusor overactivity, reaching a detrusor pressure of 59 cm H_2O at a bladder volume of 37 mL. Abdominal magnetic resonance imaging demonstrated diffuse bladder wall thickening, bilateral grade 2-3 hydroureteronephrosis, and perivesical inflammation (Figure 2). Intravesical botulinum toxin injection was recommended, but she refused. By March 2024, bladder capacity had further declined to 60 mL.

During psychiatric evaluation, the patient admitted to ongoing ketamine abuse. She was subsequently hospitalized and underwent electroconvulsive therapy. She did not receive any further urological treatment during this period. Six months after cessation of ketamine use, urinary urgency and bladder pain improved markedly. Follow-up urinary ultrasonography revealed a bladder capacity of 68 mL, bilateral grade 1 hydroureteronephrosis, and regression of diffuse bladder wall thickening. The serum creatinine level at follow-up was 1.56 mg/dL.

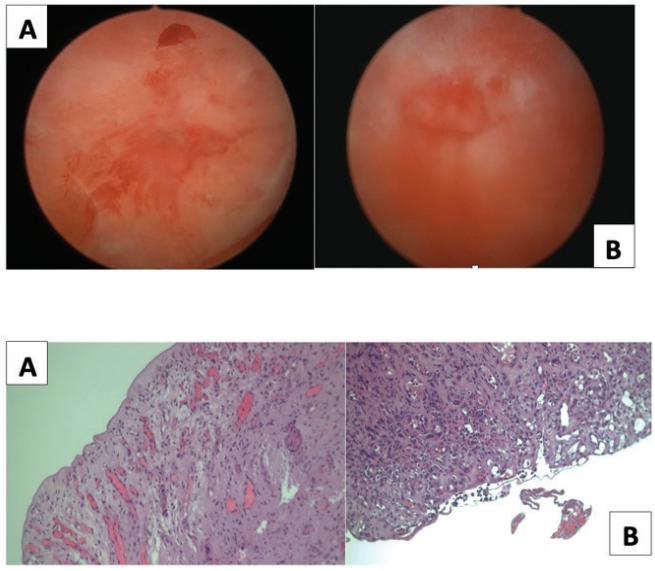

Figure 1. Cystoscopic and histopathological views of ketamine-induced ulcerative bladder lesions

A: Case 1, B: Case 2

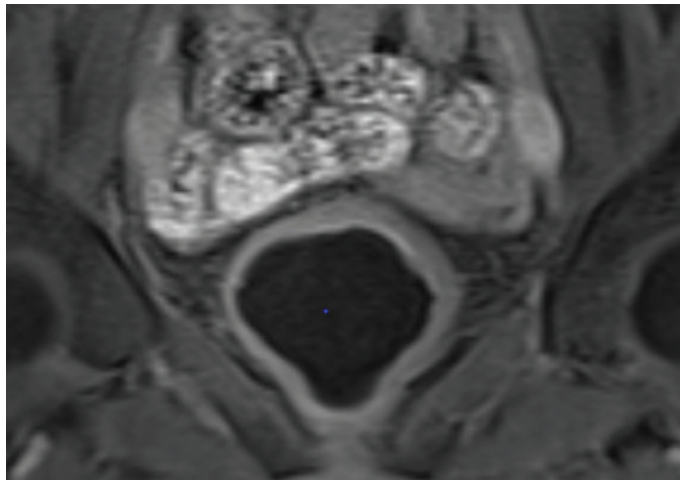

Figure 2. Magnetic resonance imaging of Case 1

Case 2

A 25-year-old woman reported a two-year history of recreational ketamine use via nasal insufflation. Her medical history included premenstrual syndrome and a prior uterine curettage. She presented with a one-week history of dysuria, hematuria, and increased daytime urinary frequency, occurring every 30-60 minutes. Urinalysis demonstrated pyuria, and a urine culture grew *Klebsiella pneumoniae*; oral cefuroxime 500 mg was administered. A cystoscopy performed in March 2024 revealed ulcerative lesions, glomerulations, and petechial

bleeding. The maximum bladder capacity under general anesthesia was 250 mL. Histopathological examination of bladder biopsies showed ulceration and chronic non-specific cystitis with eosinophilic infiltration; IC could not be excluded. Complete cessation of ketamine use and adoption of an IC-friendly diet were recommended. At the 3-month follow-up, the patient's symptoms had resolved and urinalysis findings were within normal limits. Subsequently, she experienced an uncomplicated pregnancy and delivery.

Discussion

We present two cases of KIC that represent different stages of the disease: one with an advanced-stage presentation and one with an early-stage presentation. Both cases involved young women. Although previous studies have reported that approximately 80% of patients with KIC are male, female patients tend to exhibit higher symptom severity scores (8). The clinical presentation of KIC can mimic carcinoma in situ, IC in women, and prostatitis in men, which may delay accurate diagnosis (9).

In our first case, laboratory evaluation revealed elevated CRP and eosinophil levels in the peripheral blood, along with abundant leukocytes and erythrocytes on urinalysis, despite a sterile urine culture. In contrast, the second case had a documented urinary infection, accompanied by pyuria and microscopic hematuria. Typical laboratory findings in KIC include sterile pyuria, microscopic hematuria, and, in some cases, elevated liver enzymes such as ALP (3,10). In the first case, peripheral eosinophilia and renal dysfunction suggested upper tract involvement, consistent with advanced-stage disease. Previous studies have demonstrated that elevated serum immunoglobulin E, eosinophilia, and eosinophilic infiltration of the bladder wall are associated with increased bladder pain severity (11).

The primary histopathological feature of KIC is inflammation, which underlies the development of LUTS. Persistent inflammation leads to collagen deposition and progressive fibrosis, ultimately resulting in a contracted bladder and, in advanced stages, involvement of the upper urinary tract (12,13). In both of our cases, histopathological examination of bladder biopsies demonstrated prominent inflammatory cell infiltration and fibrosis. It has been suggested that eosinophilic infiltration and detrusor muscle hypertrophy are distinguishing pathological features of KIC compared with other inflammatory bladder conditions such as IC (14). Nevertheless, clinical presentation and radiologic findings remain essential components of the differential diagnosis.

In our first case, the earliest radiological finding was increased bladder wall thickness. Following approximately one year of ketamine abuse, an magnetic resonance imaging scan revealed bilateral grade 2-3 hydronephrosis, perivesical inflammation, marked bladder wall thickening, and contracted bladder. Previous studies have shown that patients with IC typically exhibit bladder wall thinning, whereas patients with KIC exhibit bladder wall thickening (15). Recently, Betancur et al. (16) also reported a case of KIC that demonstrated significant bladder wall thickening on computed tomography. In addition, ureteral involvement and perivesical inflammation are features that more clearly distinguish KIC from other inflammatory bladder disorders (17). These findings support the notion that radiological changes correlate with both the intensity and duration of ketamine abuse.

Hydrodistension and an IC-friendly diet provided temporary symptomatic relief in both of our cases, consistent with previous reports (18,19). Nevertheless, absolute cessation of ketamine use remains the cornerstone of management (4). Although conservative management may alleviate symptoms in early stages, patients with advanced disease often require surgical interventions such as augmentation cystoplasty or urinary diversion (18-20). Recurrence is common following resumption of ketamine use (21).

To our knowledge, these cases represent the first reported instances of KIC from Türkiye. Although the short-term follow-up period limits our ability to draw conclusions regarding long-term renal outcomes, our findings illustrate the clinical and radiological progression of KIC and underscore the potential for partial recovery when the disease is recognized early and ketamine use is discontinued.

Conclusion

KIC should be considered in the differential diagnosis of ulcerative cystitis in young adults presenting with refractory LUTS. Radiological and cystoscopic findings are valuable in distinguishing KIC from other inflammatory bladder diseases. Early diagnosis and strict cessation of ketamine use, supported by a multidisciplinary approach, are essential to prevent irreversible bladder dysfunction and progressive renal damage.

Ethics

Informed Consent: Written informed consent was obtained from the patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.M., M.K., E.K., A.İ., T.T., Concept: S.M., M.K., E.K., T.T., Design: S.M., M.K., E.K., T.T., Data Collection or Processing: S.M., M.K., E.K., T.T., Analysis or Interpretation: S.M., M.K., E.K., T.T., Literature Search: S.M., M.K., E.K., T.T., Writing: S.M., M.K., E.K., T.T.

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

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

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CASE REPORT
Urooncology

Doi: 10.4274/jus.galenos.2025.2024-10-1
J Urol Surg 2026;13(2):138-140

Urethral Diverticulum with Malignant Histology - Two Case Reports

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Abstract

A female urethral diverticulum (UD) is a rare condition that poses significant diagnostic challenges due to its clinical presentation. Symptoms might be non-specific or absent, and in many patients, UD is incidentally discovered during a routine gynecological examination. The present case report describes two cases of UD, which were later diagnosed as adenocarcinoma with lymph node metastases. These cases underscore the seldom but inherent risk of malignant transformation of UD.

Keywords: Urethral diverticulum, adenocarcinoma, female lower urinary tract symptoms, urethral diverticulectomy, urogynecology

Introduction

Urethral diverticulum (UD) is a rare condition affecting 1-6% of adult women, where the urethral mucosa protrudes into the surrounding tissue (1). UD commonly presents as the classic triad of dysuria, dyspareunia and post-void dribbling (2). Additional symptoms may also include recurrent urinary tract infections, vaginal discharge, or the sensation of a vaginal mass (3). However, UD can also be asymptomatic, which is why the true incidence may be underestimated. Diagnosis is based on medical history, physical examination, and diagnostic imaging (4). The condition is frequently misdiagnosed or diagnosed late due to similarity with other urinary tract or pelvic disorders (5). UD may be congenital, but it is often acquired due to previous surgeries, repeated infections or traumatic vaginal deliveries (6).

To the best of our knowledge, fewer than 130 cases of malignant transformation of the UD have been reported in the literature (7). This case report explores two additional cases of malignant transformation within a UD, contributing valuable insights to the limited knowledge on this rare condition. Written informed consent was obtained from both patients for publishing this case report and magnetic resonance images (MRIs).

Case Presentation

Case 1

A 78-year-old woman was referred with three months of postmenopausal bleeding, recurrent urinary tract infection, and urge incontinence. Her medical history included breast cancer treated with bilateral mastectomy and tamoxifen, rheumatoid arthritis, and lichen sclerosus. Vaginal examination revealed discharge from the urethra upon compression of the anterior vaginal wall. Ultrasound identified a 19 mm cavity associated with the urethra, consistent with a UD. Urethrocystography revealed a 5.6 cm tumor both surrounding and extending into the urethra. Aspiration from the tumor showed *E. coli, Bacteroides fragilis*, and *Bifidobacterium*, suggesting an abscess or a chronic infection. Transurethral biopsies were inconclusive, but high-grade adenocarcinoma originating from the urethra was suspected. MRI confirmed a malignant tumor infiltrating the urethra, UD, and anterior vaginal wall (Figure 1). Fluorodeoxyglucose positron emission tomography/computed tomography showed no lymph node metastases. Based on multidisciplinary team recommendations, the patient underwent laparoscopic cystectomy, urethrectomy, removal of internal genitalia, and ileal conduit formation. Histopathology confirmed invasive adenocarcinoma (pT3) with lymph node metastases.

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Received: 08.10.2024 **Accepted:** 09.01.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Barslev-Jensen MG, Graugaard-Jensen C, Glavind-Kristensen M, Bor P. Urethral diverticulum with malignant histology - two case reports. J Urol Surg. 2026;13(2):138-140.

At the eight-month follow-up, hydronephrosis, hydroureter and enlarged lymph nodes were identified with a biopsy confirming recurrent adenocarcinoma. Immunotherapy was not an option due to ongoing methotrexate treatment. The patient was referred to palliative care and ultimately died due to the progression of her disease.

Case 2

A 46-year-old woman with no previous surgery presented with uterine prolapse. She had two vaginal deliveries. Physical examination revealed swelling near the urethra. Transvaginal ultrasound and MRI confirmed a 3.5 cm UD. As the patient was asymptomatic, no immediate intervention was performed. Two years later she returned with pain from the urethra. MRI showed no change in the size of the UD. A diverticulectomy was offered, but the patient declined the procedure. Four years later, she developed macroscopic hematuria, lower abdominal pain, urge incontinence and urethral discharge. Computed tomography imaging showed two small cysts in the left kidney and unchanged size of the UD. The hematuria was attributed to an infection in the UD. Three months later, the patient returned with vaginal bleeding and an MRI confirmed solid tumor growth within the UD (Figure 2). The patient underwent a successful transvaginal diverticulectomy. Histopathology confirmed clear cell adenocarcinoma (pT2), a very rare malignancy, with metastasis to the inguinal lymph nodes. The patient underwent radical cystectomy, removal of internal genitalia, inguinal lymph node dissection, and ileal conduit formation. Four months later, the patient developed a vaginal enterocele, which was successfully treated with Permacol mesh. At the 36-month follow-up, ureteral dilation was performed due to stenosis, but there was no evidence of recurrence.

Discussion

Urethral adenocarcinoma in UD is exceptionally rare and accounts for less than 0.02% of all cancer diagnoses in women (8). While adenocarcinoma is the most common histological subtype, squamous cell carcinoma and transitional cell carcinoma have also been reported (9). Prognosis depends on local tumor extent and lymph node involvement, but there is still no consensus on which histological subtypes are associated with the poorest prognosis (9).

Notably, the classic symptoms of UD dysuria, dyspareunia and post-void dribbling were absent in our cases. Instead, the patients presented with non-specific symptoms such as postmenopausal bleeding and vaginal mass, leading to initial diagnoses including abscess, vaginal cyst, or infection. A heterogenic structure, solid elements, or increasing growth of a UD may indicate a higher risk of malignancy (10). The diagnostic challenges associated with UD emphasize the need for detailed patient history, physical examination, and MRI should be considered for a comprehensive evaluation of the UD (5).

Numerous treatments of UD have been proposed in the literature and vary from no intervention to surgical intervention. The largest case series to date on UD in women included 228 cases, and 172 underwent transvaginal diverticulectomy (1).

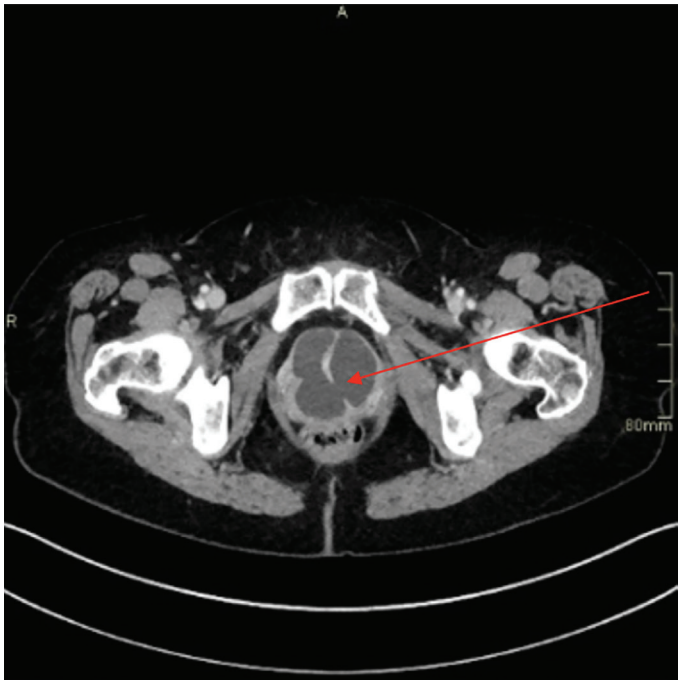

Figure 1. Axial cut of the urethral diverticula

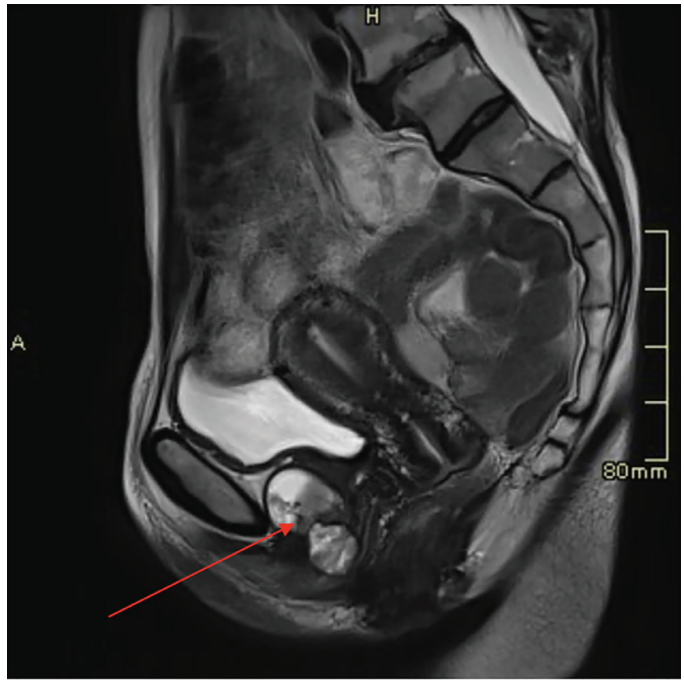

Figure 2. Sagittal plane of the urethral diverticula

Transvaginal diverticulectomy is the most described treatment modality in the literature and is performed in most cases with a cure rate up to 86% (11,12).

Complications of transvaginal diverticulectomy include infection, fistula formation, urethral stenosis, and de novo stress urinary incontinence (13). Recurrence rates of UD following surgery range from 1.4 to 23.4% and may arise due to inadequate removal of the UD sac or a subsequent infection (1,4,13). Successful surgical removal of the UD requires complete removal of the UD sac, urethral closure in a watertight manner, and multi-layered closure using absorbable sutures. Pathological evaluation of the excised tissue is essential to rule out malignancy. In cases of confirmed malignancy, more extensive surgical intervention is warranted, such as cystectomy combined with urethrectomy and ileal conduit formation, as demonstrated by our two cases. However, the rarity and histological variability of malignant UD make it challenging to develop standardized management guidelines, which are currently lacking.

Conclusion

These cases highlight the importance of considering UD in the differential diagnosis of women presenting with atypical urinary tract or pelvic disorders. Moreover, the potential risk of malignant transformation, although rare, emphasizes the need for comprehensive evaluation and early intervention. Advancing our understanding of this rare condition will be pivotal in refining management guidelines and improving patient outcomes.

Ethics

Informed Consent: Written informed consent was obtained from both patients for publishing this case report and magnetic resonance images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.G.B-J., C.G-J., M.G-K., P.B., Concept: M.G.B-J., C.G-J., M.G-K., P.B., Design: M.G.B-J., C.G-J., M.G-K., P.B., Data Collection or Processing: M.G.B-J., C.G-J., M.G-K., P.B., Literature Search: M.G.B-J., C.G-J., M.G-K., P.B., Writing: M.G.B-J., C.G-J., M.G-K., P.B.

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

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

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CASE REPORT
General Urology

Doi: 10.4274/jus.galenos.2025.2024-11-11
J Urol Surg 2026;13(2):141-143

Granulomatous Cystitis in an Adult Female: A Case Report

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Abstract

Granulomatous cystitis of the bladder is a rare urological pathology resulting from infection, Bacillus Calmette-Guerin treatment for bladder cancer, granulomatous disease, or idiopathic origins. We report a 63-year-old female with dysuria and abdominal pain. Computed tomography imaging revealed a thickening of the bladder wall, which raises concerns for malignancy. A transurethral resection of bladder tumor procedure was performed, and a biopsy revealed chronic granulomatous cystitis that was negative for malignancy. The patient experienced no complications post-operatively and was on continued oxybutynin and tamsulosin treatment. We discuss the etiologies of granulomatous cystitis and attempt to provide theories for this patient's uncommon disease.

Keywords: Functional urology, general urology, pathology, urooncology

Introduction

Granulomatous cystitis is a rare type of chronic inflammation in the bladder associated with *Mycobacterium tuberculosis* infection, Schistosoma haematobium infection, Bacillus Calmette-Guerin (BCG) intravesical instillation chemotherapy for the treatment of bladder cancer, and chronic granulomatous disease (1-5). Though most bladder lesions represent malignancy, benign conditions such as granulomatous cystitis must be considered in the differential diagnosis. In this report, we describe a 63-year-old woman presenting with dysuria, urinary urgency, and left-sided abdominal pain. Imaging revealed a diffuse, infiltrative-appearing bladder wall. A biopsy of the specimen revealed acute-on-chronic granulomatous inflammation consistent with granulomatous cystitis. There was no evidence of malignancy.

Case Presentation

A 63-year-old woman presented to the outpatient clinic with lower left abdominal pain, dysuria, and urinary urgency. Her past medical history includes previous breast cancer under remission, spinal stenosis, obesity, type II diabetes mellitus, hysteroscopy, dilation, and curettage for polyp removal, and recurrent nephrolithiasis. Urinalysis revealed cloudy urine with microscopic hematuria, glucosuria, proteinuria, and pyuria. Urine culture was negative for the growth of any organism. The patient was prescribed oxybutynin for her urinary urgency, and a computed tomography (CT) of the abdomen and pelvis with and without contrast was obtained due to her chronic abdominal pain, which revealed multiple non-obstructing stones within the left renal pelvis and evidence of splenic granulomatous disease. CT urogram identified a left proximal 2 mm ureteral stone and infiltrative multifocal thickening of the bladder wall, suggestive of malignancy (Figure 1). A review of a previous CT of the chest revealed a calcified granuloma in the right middle lobe of the lung.

A transurethral resection of bladder tumor (TURBT) was performed two weeks following the appointment. The patient was placed under general endotracheal anesthesia, and the operation began by intubating the urethral meatus with a 22-French Olympus cystoscope with a 30-degree lens and a digital camera. Diffuse, bullous edematous changes to the bladder trigone and a pedunculated lesion on the left lateral wall towards the anterior wall was noted, which was consistent with findings on imaging.

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Received: 26.11.2024 **Accepted:** 04.03.2025 **Epub:** 16.03.2026 **Publication Date:** 01.06.2026

Cite this article as: Finkelstein MJ, Hookim K, Zeffren M. Granulomatous cystitis in an adult female: a case report. J Urol Surg. 2026;13(2):141-143.

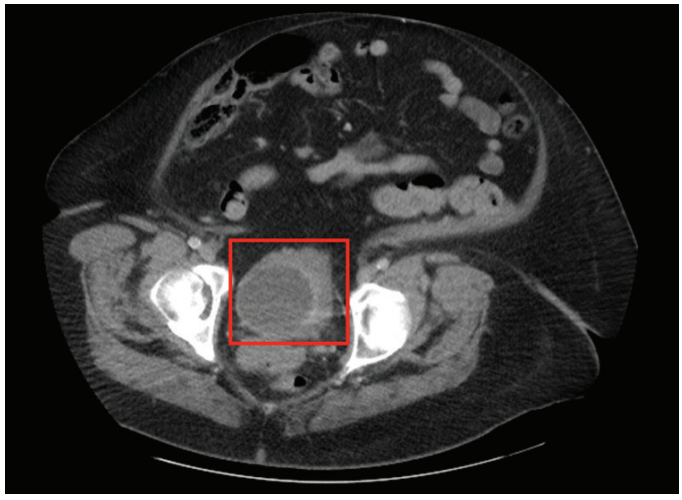

Figure 1. CT abdomen and pelvis imaging revealing granulomatous cystitis. Persistent soft tissue thickening and infiltration of the bladder anteriorly and along the left lateral wall with a mass-like component of this thickening measuring 3.8x2.6 cm along the anterior bladder floor

CT: Computed tomography

Complete resection of the bladder tumor to the muscular layer was achieved without complication. An end-loop electrode gyrus electrocautery set was used to accomplish hemostasis. A left-sided 4.7 French x 24 cm Double-J ureteral stent was placed due to the presence of left-sided collecting system dilatation, and proximal left ureteral stone. The bladder was then intubated with a 22-French Foley catheter, which drained clear urine into a drainage bag. The patient was subsequently awakened by the anesthesia team without any complications.

Biopsy revealed acute on chronic granulomatous cystitis with ulceration and granulation tissue; marked acute and chronic inflammation; and focal granulomata (Figure 2). The muscularis propria was present and negative for malignancy. Patient consent was obtained.

Discussion

Granulomatous cystitis is a rare inflammatory condition resulting from a variety of causes, including Mycobacteria or Schistosomal infections, chronic granulomatous disease, sarcoidosis, and surgical complications (1-6). The use of intravesical BCG instillation to treat intermediate or high-risk urothelial carcinoma is another common cause of granulomatous cystitis, with about 60% to 80% of patients experiencing this complication from the treatment (6,7). Due to the various causes of this condition and possible confusion with a neoplasm, it is necessary to complete a thorough patient history and to rule out infectious causes.

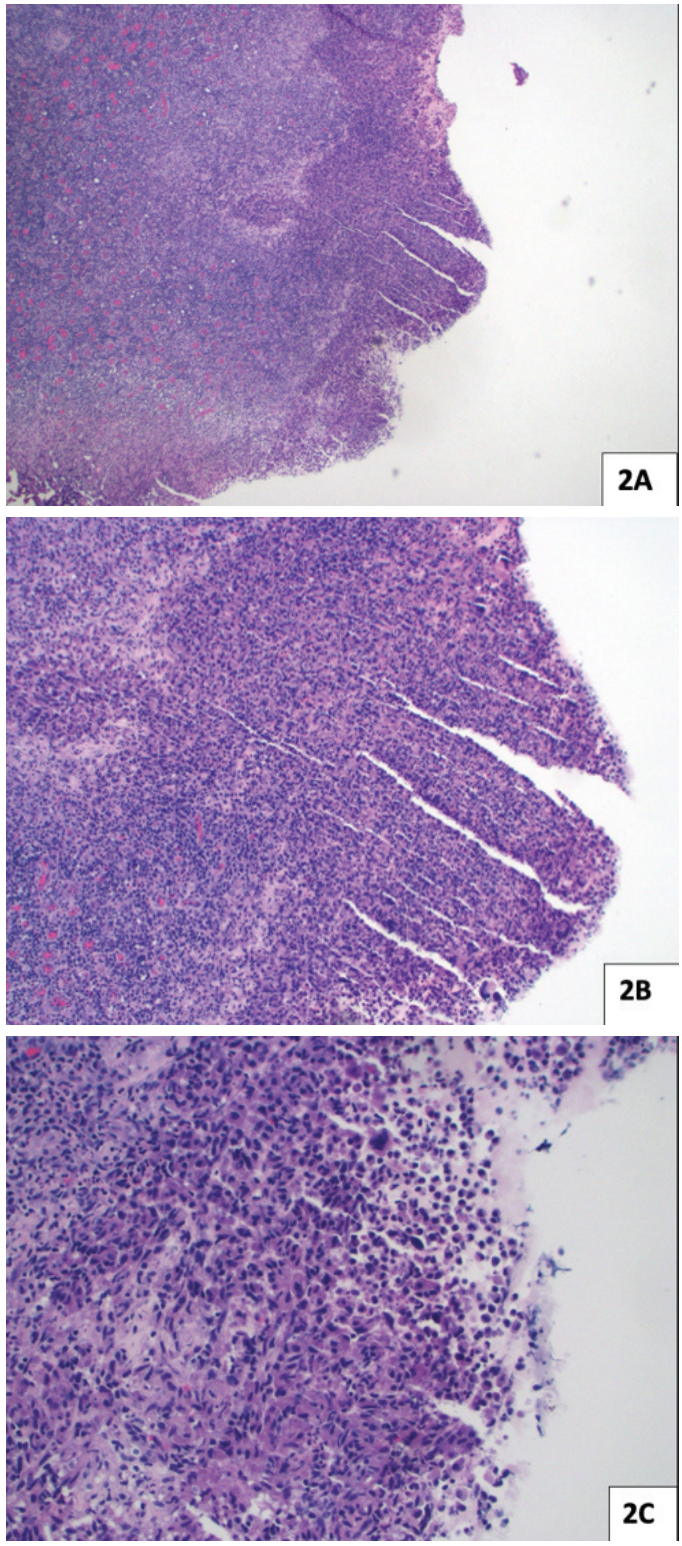

Figure 2. Histological appearance of granulomatous cystitis. Acute on chronic granulomatous cystitis with ulceration, granulation tissue with marked acute and chronic inflammation and focal granulomata; muscularis propria was present and negative for malignancy (A. H&E, 4x; B. H&E 10x, C. H&E, 20x)

H&E: Hematoxylin and eosin

The incidental CT findings of a granuloma in the right middle lobe of the lung and evidence of granulomatous disease in the spleen hint at the possible etiology of granulomatous cystitis in this patient. Genitourinary tuberculosis, which occurs in about 40% of patients following extrapulmonary tuberculosis infection, is a common complication with a latency period of up to 20 years (1). However, smear microscopy with a Ziehl-Neelsen stain and *Mycobacterium* culture was never completed, leaving this possibility open to speculation (1). Another possible cause of granulomatous cystitis in this patient could have been trauma-related, as the patient underwent hysteroscopy and dilation and curettage for polyp removal approximately a year prior to her urological symptoms. A multicenter study consisting of 21,676 hysteroscopies, in Germany, revealed an overall complication rate of 0.22%, with 0.02% of complications related to bladder or bowel injury caused by uterine perforation (8,9). Another cause of granulomatous cystitis is intravesical BCG therapy for superficial carcinoma of the bladder. Although not seen in our patient, it is important to take a proper medical history to rule this out as a possible cause of granulomatous cystitis. It is suggested that the internalization of BCG by bladder cancer cells induces an anti-tumor effect through direct cytotoxic mechanisms, with $CD4^+$ Th1 cells primarily mediating this reaction (10-12).

Treatment of granulomatous cystitis can involve both pharmacological and surgical management. In the case of the former, corticosteroid and antibiotic treatment improved the bladder-related symptoms of a child with a history of chronic granulomatous disease (13). Radical cystectomy was an effective surgical option for a patient diagnosed with granulomatous cystitis secondary to an intravesical BCG treatment for urothelial carcinoma (14). In the case of our patient, a TURBT was performed due to the concern for malignancy.

Conclusion

In conclusion, we present a 63-year-old woman with abdominal pain, dysuria, and urinary urgency who was found to have an infiltrative thickening of the anterior, left, and posterior bladder walls. The patient subsequently underwent TURBT, which revealed chronic granulomatous cystitis with ulceration and granulation tissue, marked by marked acute and chronic inflammation and focal granulomata. Due to its rare incidence, further studies will be needed to evaluate effective treatment options. A thorough review of a patient's medical history is also necessary to rule out infectious or traumatic etiology.

Ethics

Informed Consent: Patient consent was obtained.

Authorship Contributions

Surgical and Medical Practices: K.H., M.Z., Concept: M.J.F., M.Z., Design: M.J.F., M.Z., Data Collection or Processing: M.J.F., Analysis or Interpretation: M.J.F., K.H., M.Z., Literature Search: M.J.F., Writing: M.J.F., K.H., M.Z.

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

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

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