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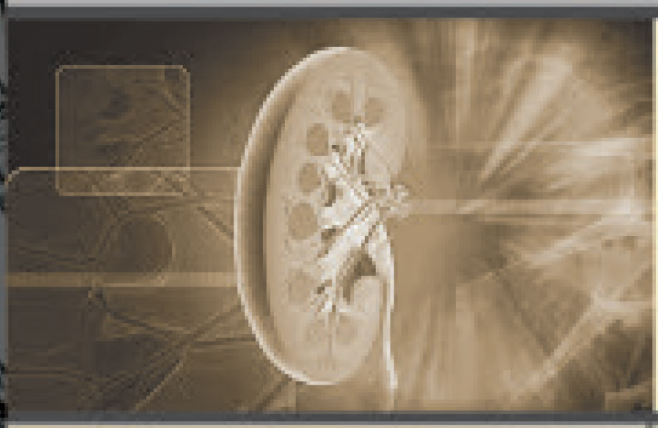

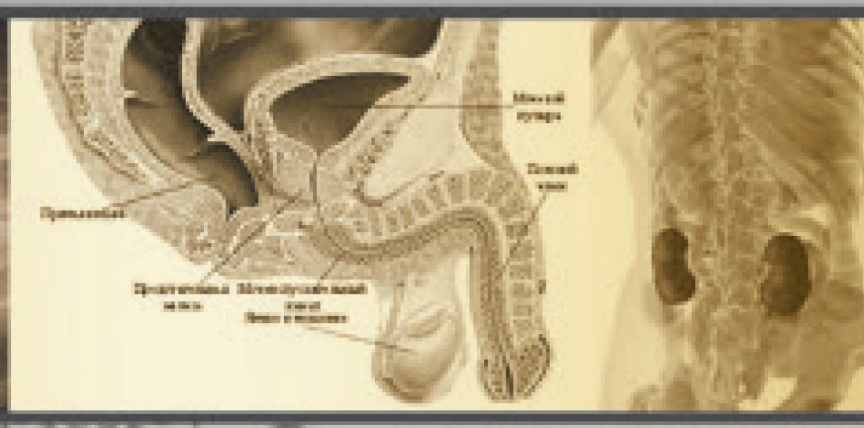

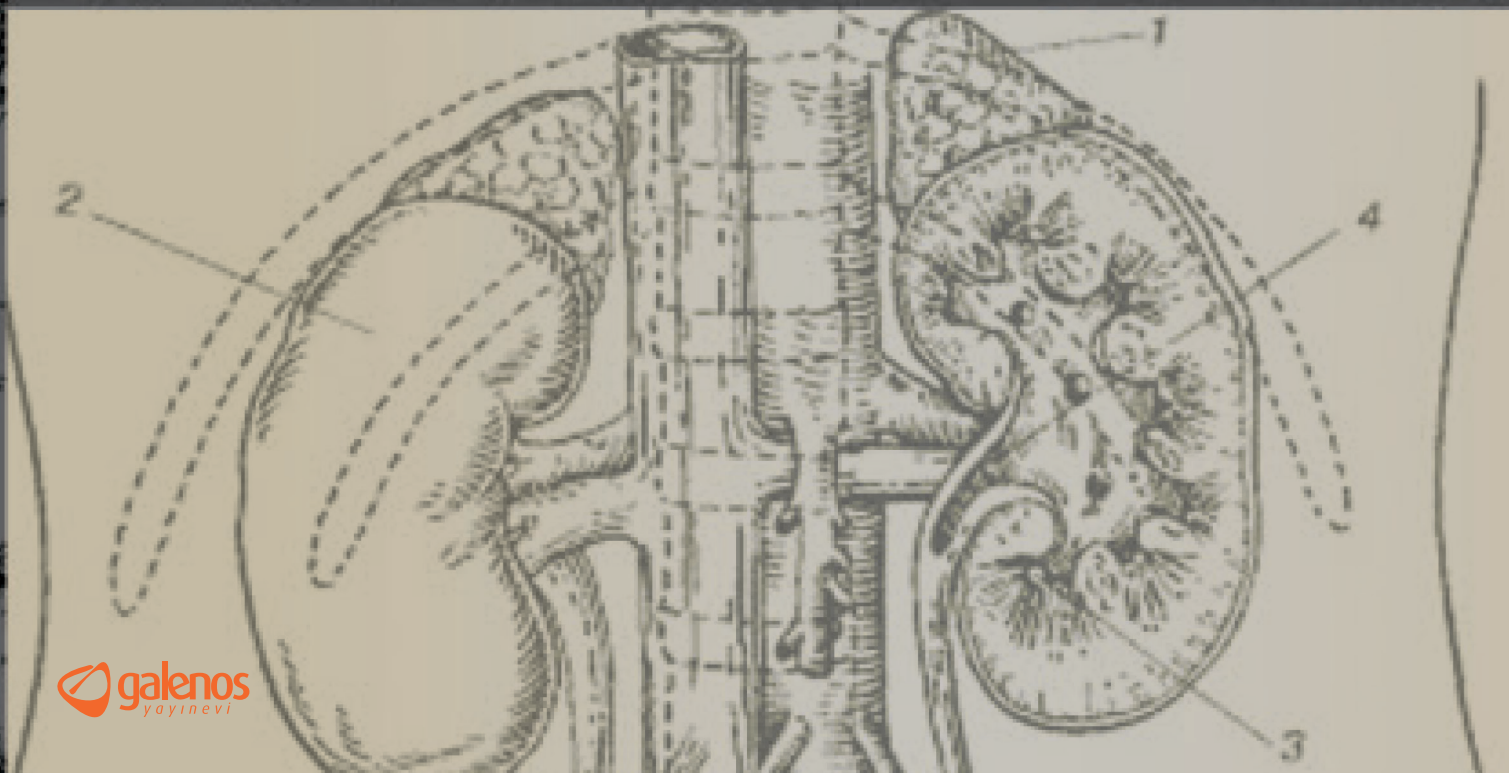

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CONTENTS

REVIEW
Urooncology

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Immunotherapy Applications in Urology

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Abstract

Immunotherapy has transformed the management of urological cancers, offering renewed optimism for individuals diagnosed with bladder, kidney, and, to a lesser degree, prostate tumors. Conventional therapies, such as chemotherapy and radiation, frequently demonstrate restricted efficacy. At the same time, immune checkpoint inhibitors (ICIs) have surfaced as promising alternatives, especially in urothelial and renal cell carcinoma (RCC). This review examines immunotherapy mechanisms, focusing on immune checkpoint pathways such as programmed cell death protein 1 and cytotoxic T lymphocyte-associated protein 4, and their contributions to improving immune recognition and eliminating tumor cells. Bacillus Calmette-Guérin immunotherapy is essential for non-muscle-invasive bladder cancer, whereas ICIs have transformed the management of muscle-invasive and metastatic forms of the disease. In RCC, ICIs have markedly enhanced survival outcomes, whether alone or in conjunction with tyrosine kinase inhibitors. Although advancements have been made, the role of immunotherapy in prostate cancer remains in development, with limited efficacy documented thus far. Current research focuses on optimizing combination therapies and identifying biomarkers to improve patient selection. The future of immunotherapy in urology involves its incorporation into earlier treatment stages and its combination with innovative agents, which may enhance outcomes for patients with urological cancers.

Keywords: Immunotherapy, urooncology, bladder cancer, prostate cancer, renal cancer

Introduction

Immunotherapy has transformed the treatment of numerous malignancies, and its use in urology has profoundly altered the management of urological tumors. Conventional therapies for urological malignancies, including chemotherapy and radiation, frequently provide suboptimal results, whereas immunotherapy presents a promising approach for enhancing outcomes, especially in bladder, kidney, and, to a lesser degree, prostate tumors.

In the field of urothelial carcinoma and renal cell carcinoma (RCC), immune checkpoint inhibitors (ICIs) have become crucial components, utilized either as standalone treatments or in conjunction with other therapies. Notwithstanding these developments, their effectiveness in prostate cancer remains limited. This study examines the basic mechanisms of immunotherapy, its present applications in various urological malignancies, and future prospects that may enhance patient outcomes.

Mechanisms of Immunotherapy in Urological Malignancies

Immunotherapy in urological malignancies improves the body's capacity by enhancing the immune system's ability to identify and eliminate malignant cells. The progression of cancer signifies a disruption in the equilibrium between immune surveillance and tumor evasion systems, permitting the unregulated proliferation of aberrant cells. Immunotherapy aims to restore this equilibrium by enhancing the immune system's ability to identify and eliminate tumor cells that have escaped recognition.

Mechanisms of Tumoral Immune Evasion

The microenvironment of the tumor contains several mechanisms that prevent the immune system from effectively combating the tumor, including T-cell exhaustion. Due to prolonged exposure to antigenic stimuli, exhausted T-cells exhibit a loss of normal T-cell functions, and their effector capacities (e.g., cytokine production and cell killing abilities) are reduced. These cells become resistant to reactivation and express high levels of multiple inhibitory surface molecules, such as cytotoxic T

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lymphocyte antigen-4 (CTLA-4), programmed death 1 (PD-1), lymphocyte activation gene-3, and T-cell immunoreceptor with Ig and Immunoreceptor Tyrosine-based Inhibitory Motif (ITIM) domains, T-cell immunoglobulin and ITIM domain. These molecules suppress T-cell activation and help tumor cells evade the immune system (1).

Cancer cells bypass immune detection through many strategies, such as diminished tumor antigen production and the secretion of inhibitory chemicals that provoke T-cell anergy or apoptosis (2). Immune checkpoint molecules, including programmed death ligand 1 (PD-L1), are pivotal in this process. The binding of PD-L1 on tumor cells to the PD-1 receptor on T lymphocytes initiates an inhibitory signal that diminishes T-cell activity, hence promoting immune evasion (3).

The CTLA-4/CD80-CD86 association similarly inhibits T-cell activation, facilitating immunological evasion. The introduction of ICIs, including anti-PD-1/PD-L1 and anti-CTLA-4 antibodies, marks a key advancement in the management of many urological cancers. By obstructing these inhibitory pathways, ICIs can rejuvenate T lymphocytes, enabling them to effectively target and eliminate tumor cells (Figure 1).

Advances in Immuno-Oncology

Recent advancements in immuno-oncology have led to medications that accurately target specific immune pathways, improving precision and reducing off-target effects. ICIs have demonstrated notable effectiveness in RCC and bladder cancer,

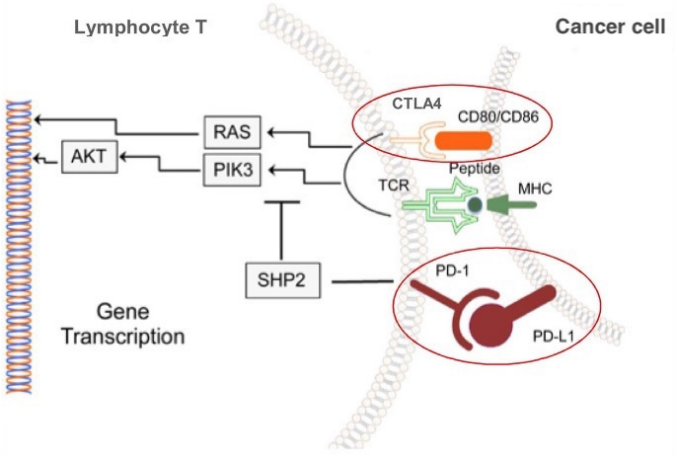

Figure 1. Major immune checkpoints involved in T-cell anergy (4)

CTLA-4, CD80/CD86: Membrane-bound glycoprotein that belongs to the B7 family of immunoglobulin superfamily proteins, PD-1: Programmed death 1 and its ligand (PD-L1), MHC: Major histocompatibility complex, a group of genes that code for proteins responsible for presenting antigens to T-cells, which is a critical step in the immune response, SHP2: Protein tyrosine phosphatase (PTP) encoded by the *PTPN11* gene in humans, RAS: Plays an important role in intracellular signaling. TCR: T-cell receptor, PIK3: Phosphoinositide 3-kinase, a family of enzymes involved in critical cellular processes such as growth, proliferation, survival, metabolism, and motility, AKT: Protein kinase B, is a serine/threonine-specific protein kinase that plays a central role in regulating various cellular processes, including metabolism, growth, survival, and proliferation

leading to their integration into treatment protocols. However, the benefits of immunotherapy for prostate cancer are still under investigation, producing mixed results so far.

The US Food and Drug Administration has approved ICIs for clinical use in certain genitourinary tumor patients (5). Biomarkers are pivotal in early tumor diagnosis, drug development, disease monitoring, and prognosis evaluation. Many methods exist to detect biomarkers, depending on the laboratory and the material to be analyzed (such as tissue or serum). Polymerase chain reaction is a common method for mRNA or DNA-based analysis. ELISA, Western Blot, or immunohistochemical examination may be preferred for a specific analysis at the protein level. Programmed death ligand-1 (PD-L1) expression is a widely used biomarker to predict response to immunotherapy and is evaluated according to expression levels in tumor cells or immune cells (6). Microsatellite instability (MSI) and high tumor mutational burden are other important biomarkers that indicate that immunotherapy may be effective (7). Additionally, the presence of intratumoral $CD8^+$ T-cells may indicate a strong immune response (8). Selecting patients with higher mutational burden, with specific markers, may increase the likelihood of response to immunotherapy.

Immunotherapy for Bladder Cancer

Non-muscle invasive bladder cancer (NMIBC) Bacillus Calmette-Guérin (BCG) immunotherapy has long been a fundamental treatment for NMIBC, demonstrating more efficacy than transurethral resection of the bladder alone or in conjunction with intravesical chemotherapy in minimizing recurrence (9,10). A Cochrane review demonstrated the advantage of BCG compared to mitomycin-C in decreasing NMIBC recurrence (11). Moreover, maintenance BCG therapy has been shown to be effective in reducing the risk of progression in high- and intermediate-risk NMIBC (12,13). Intracavitary treatment poses a potential risk for disseminated BCG infection (in less than 5% of patients) and may cause infusion reactions (14). The presence or absence of side effects does not seem to be a prognostic factor for the efficacy of BCG, and maintenance therapy is not associated with a significant increase in toxicity (15).

Recent data on BCG-unresponsive patients with carcinoma *in situ* (16), either alone or with concomitant papillary tumors, have shown promising results with new immunotherapies. Systemic pembrolizumab demonstrated a 40% complete response rate in a phase II prospective study, with 48% of responders maintaining their response for up to 12 months (17). Promising results from a phase III multicenter randomized controlled trial (RCT) demonstrated that intravesical nadofaragene firadenovec achieved a 53.4% complete response rate in patients with BCG-unresponsive carcinoma *in situ* (16). Forty-five percent of responders maintained their response at one year (18). Additional

ongoing studies are exploring the use of combination therapies involving intravesical or systemic immunotherapy to enhance treatment outcomes (19,20).

Muscle-invasive and Metastatic Bladder Carcinoma

In recent years, immunotherapy has emerged as a prominent option for treating muscle-invasive bladder cancer. Traditionally, chemotherapy has remained the first-line treatment for metastatic disease for an extended period; however, it is increasingly being supplanted by immunotherapy approaches. Preliminary studies indicate that the ICI pembrolizumab demonstrates an overall survival advantage of approximately three months compared to second-line chemotherapy. Nevertheless, the current data are insufficient to facilitate its immediate integration into routine clinical practice (21).

The phase III trial Alliance A031501 AMBASSADOR demonstrated that adjuvant pembrolizumab significantly improved disease-free survival (29.6 months *vs.* 14.2 months; hazard ratio: 0.73, p=0.003) compared to observation in patients with high-risk muscle-invasive urothelial carcinoma after radical surgery. These findings support pembrolizumab as an effective adjuvant therapy in this population. However, pembrolizumab was associated with a higher rate of grade 3 or higher adverse events (50.6% *vs.* 31.6%) (22).

Nivolumab, a PD-1/PD-L1 checkpoint inhibitor, is recommended as an adjuvant treatment for patients with tumor cell PD-L1 expression ≥1% who are at high risk of recurrence after surgery in non-metastatic pT3-4 urothelial carcinoma and cannot receive cisplatin-based chemotherapy. The CheckMate 274 trial, which indicated significant improvements in disease-free survival (23), supports this recommendation.

The EV-302/KEYNOTE A39 and Checkmate 901 RCTs have recently revised the first-line treatment algorithm in metastatic disease (24,25). The combination of enfortumab vedotin (EV) and pembrolizumab in metastatic urothelial carcinoma now establishes the new standard of care for patients who are considered eligible for combination therapies. The major eligibility criteria include an Eastern Cooperative Oncology Group performance status of 0-2, a glomerular filtration rate of ≥30 mL/min, and adequate organ function, as determined by the requirements for treatment with EV, and Pembrolizumab. This combination has significantly enhanced progression-free survival (PFS) and overall survival, irrespective of PD-L1 expression. PFS was significantly prolonged with EV+P *vs.* chemo, reducing the risk of progression or death by 55% (median PFS, 12.5 mo *vs.* 6.3 mo, respectively). Additionally, severe side effects were found to be lower than those associated with chemotherapy (24).

However, it should be noted that EV has not yet been included in the reimbursement scope of the social security institution in our country. Li et al. (27) evaluated the cost-effectiveness of EV plus pembrolizumab as a first-line treatment for metastatic urothelial carcinoma compared to chemotherapy. While EV plus pembrolizumab improved survival, providing an additional 2.10 life-years (26) and 1.72 quality-adjusted life-years (QALYs), the incremental cost-effectiveness ratio was $558,973 per QALY-well above the willingness-to-pay threshold of $150,000 per QALY. Subgroup analysis suggested that the combination was slightly more cost-effective in cisplatin-ineligible patients, but overall, the therapy is not considered cost-effective from the perspective of U.S. payers (27).

Numerous combinations are currently being studied in various clinical studies. The JAVELIN bladder 100 study evaluated the efficacy of ongoing treatment with the PD-L1 inhibitor avelumab following platinum-gemcitabine chemotherapy. After four to six cycles of platinum-gemcitabine chemotherapy, an increase in overall survival was noted among patients treated with avelumab, with respective survival rates of 21.4 and 14.3 months for those who received and did not receive avelumab (28).

Currently, phase I, II, and III studies indicate that ICIs, including pembrolizumab, nivolumab, atezolizumab, avelumab, and durvalumab, exhibit comparable efficacy and safety in patients who have progressed during or following platinum-based chemotherapy (21,29-32). Sacituzumab govitecan is a humanized monoclonal antibody that targets trophoblast cell surface antigen 2 (Trop-2). Research indicates that it enhances progression-free and overall survival prior to chemotherapy (33). As a result of new molecules or combinations, it is anticipated that standard treatment algorithms will undergo changes in the near future.

Adverse events can affect any organ in the body and range in severity from mild to severe. The most affected organs include the skin, gastrointestinal tract, liver, lungs, thyroid, adrenal glands, and pituitary gland. Other potentially impacted systems include the musculoskeletal, renal, nervous, hematologic, ocular, and cardiovascular systems. Any new symptoms or changes observed during immunotherapy should prompt consideration of a potential connection to the treatment (34).

Immunotherapy in Renal Carcinoma

The majority of immunotherapy studies in RCC focus on clear cell RCC (ccRCC), as it is the most prevalent subtype, accounting for approximately 70-80% of all RCC cases (35). As a result, there is limited knowledge regarding the optimal management of non-clear cell RCC (nccRCC) subtypes. Treatment options for nccRCC remain scarce due to the lack of specific studies focused on these variants. For these reasons, our review primarily focuses on clear cell RCC.

Before the introduction of ICIs, the primary treatments for metastatic RCC included tyrosine kinase inhibitors (TKIs), mTOR inhibitors, and vascular endothelial growth factor (VEGF) inhibitors. CheckMate trials 025 and 214 demonstrated that nivolumab, both alone and in combination with ipilimumab, enhanced overall survival in metastatic ccRCC, resulting in a significant shift in treatment approaches (36,37).

As a monotherapy, nivolumab has demonstrated superiority over everolimus in terms of overall survival for patients with VEGF-refractory ccRCC. However, no advantage in PFS has been observed in this patient population (38). Currently, no RCTs support the use of single-agent ICIs in metastatic kidney cancer.

To date, numerous combination treatments have been investigated in the context of kidney cancer. Combining immunotherapy with interventions explicitly targeting the VEGF pathway has demonstrated significant efficacy. First-line ICI combination trials for clear-cell RCC are presented in Table 1. The Keynote 426 phase III clinical trial indicates that the combination of pembrolizumab and axitinib outperforms first-line sunitinib in terms of overall survival among treatment-naïve patients, irrespective of PD-L1 expression (39).

A comprehensive five-year analysis of the Keynote 426 study revealed that combination therapy offers a PFS advantage. In the study, for pembrolizumab + axitinib *vs.* sunitinib, the 60-month overall survival rates were 41.9% *vs.* 37.1%, and the 60-month PFS rates were 18.3% *vs.* 7.3%. Furthermore, no significant differences were identified in treatment-related side effects compared to standard treatments (40).

Randomized controlled phase III trials evaluating the combinations of nivolumab with cabozantinib, as well as lenvatinib with pembrolizumab, demonstrated a PFS advantage, compared with sunitinib. These studies assessed efficacy without regard to risk group or PD-L1 status (41,42).

The COSMIC-313 study is the first RCT aimed at evaluating the efficacy of the cabozantinib-nivolumab-ipilimumab triple combination treatment against the nivolumab-ipilimumab standard treatment combination, with a cohort of 855 patients (22). Although the study has not yet yielded long-term results, initial findings suggest that the triple combination provides a significant advantage in PFS (43).

In light of these findings pertaining to the metastatic stage, new prospective studies are underway to assess the potential impact of immunotherapy, whether administered as neoadjuvant or adjuvant treatment, in patients with localized kidney cancer who are deemed to be at high risk of recurrence. Currently, evaluating PD-L1 expression status is not a standard procedure. Combination therapies, which include immunotherapy, have now been established as the standard treatment for metastatic kidney cancer. It is anticipated that modifications to the treatment algorithm may occur in the future due to numerous RCTs that are currently in progress.

The meta-analysis of 95 RCTs involving 40,552 participants evaluated the risk of renal adverse events (RAE) (11) associated with ICIs. The overall incidence of RAE and acute kidney injury was low, but anti-CTLA-4 monotherapy showed higher toxicity, particularly for grade 3-5 RAE, compared to other ICIs like anti-PD-1 and anti-PD-L1. Combination therapies, such as anti-CTLA-4 plus anti-PD-1 and ICI plus chemotherapy, were associated with higher risks of RAE and AKI compared to monotherapies or traditional therapies, with ICI plus chemotherapy being the most toxic regimen. These findings emphasize the need for careful monitoring of renal function in patients receiving ICI-based treatments (44).

There is certainly a need for studies reporting the cost-effectiveness of immunotherapy. The study evaluated the cost-effectiveness of seven treatment strategies for metastatic renal cell carcinoma, including immunotherapy-TKI combinations and sunitinib, using public-payer costs in the United States. Nivolumab + ipilimumab provided the highest QALYs at 3.6. Still, it was not cost-effective at a willingness-to-pay threshold of $150,000 USD/QALY because of its high incremental cost-effectiveness ratio of $297,465 to $348,516 USD compared to sunitinib. Sunitinib, as the least expensive option, emerged as the most cost-effective treatment, while cost reductions of 22-38% in NI could improve its cost-effectiveness (45).

Immunotherapy in Prostate Cancer

Unlike in bladder and kidney cancers, the use of immunotherapy has not yet gained widespread acceptance in prostate cancer due to limited efficacy.

In the context of castration-resistant prostate cancer (CRPC), sipuleucel-T immunotherapy has undergone extensive investigation. This therapeutic approach involves cultivating the patient's serum mononuclear cells with the PA2024 fusion protein, which comprises a prostate antigen linked to granulocyte-macrophage colony-stimulating factor. Sipuleucel-T, formulated using the patient's blood cells, has demonstrated an overall survival advantage of 4.1 months for CRPC patients exhibiting no or minimal symptoms. However, it has not shown an impact on disease progression (46). Many similar prostate cancer vaccine studies have been conducted (47,48).

Research indicates that ICIs exhibit minimal efficacy in the treatment of prostate cancer. While some studies demonstrate a response to immunotherapy, the treatment for prostate cancer may require a more tailored approach for each patient. This

necessity arises from the substantial variation in mutation burden and spectrum observed among patients with CRPC (49).

MSI arises from the insufficient functionality of DNA repair mechanisms. This deficiency within cancer cells can result in tumors being more readily identified by the immune system, thereby exhibiting an enhanced response to immunotherapy. Although individuals with high MSI in prostate cancer are infrequent, pembrolizumab has received FDA approval for patients with metastatic CRPC and may represent a beneficial supplementary treatment option (50,51).

Conclusion

Recent advancements in immunotherapy have notably enhanced its application in urology, especially concerning the treatment of bladder and kidney cancers. ICIs are critical elements in the treatment protocols for these malignancies, providing significant enhancements in survival rates. Despite these advancements, the application of immunotherapy in prostate cancer is still limited, necessitating additional research to identify predictive biomarkers and enhance combination strategies for optimal benefit.

Table 1. First line immune checkpoint inhibitor combination trials for clear-cell RCC (52)

Study	n	Experimental arm	Primary endpoint	Risk groups	PFS (22) median (95% CI) HR	OS (22) Median (95% CI) HR
KEYNOTE-426 NCT02853331 Median follow-up 67 months (39,40,53,54)	861	PEMBRO 200 mg. IV Q3W plus AXI 5 mg. PO BID vs. SUN 50 mg PO QD 4/2 wk.	PFS and OS in the ITT by BICR	IMDC FAV 31% IMD 56% POOR 13% **MSKCC** Not determined	(ITT) PEMBRO + AXI: 15.7 (13.6-20.2) SUN: 11.1 (8.9-12.5) HR: 0.69 (95% CI: 0.59-0.81) p<0.0001	(ITT) PEMBRO + AXI: 47.2. (43.6-54.8) SUN: 40.8 (34.3-47.5) HR: 0.84 (95% CI: 0.71[0.99) p=0.001
JAVELIN 101 NCT02684006 Median follow-up 34.1 months (16,55,56)	886	AVE 10 mg/kg IV Q2W plus AXI, 5 mg PO BID vs. SUN 50 mg PO QD 4/2 wk.	PFS in the PD-L1+ population and OS in the ITT by BICR	**IMDC** FAV 22% IMD 62% POOR 16% **MSKCC** FAV 23% IMD 66% POOR 12%	(PD-L1+) AVE + AXI: 13.9 (11.0-17.8) SUN: 8.2 (6.9-9.4) HR: 0.67 (95% CI: 0.57-0.79) p<0.0001	(PD-L1+) AVE + AXI: NR (40.0-NR) SUN: 36.2 (30.0-NE) HR, 0.81 (95% CI: 0.62-1.04) p=0.0498
IMmotion151 NCT02420821 Median follow-up 24 months (57,58)	915	ATEZO 1200 mg fixed dose IV plus BEV 15 mg/kg IV on days 1 and 22 of each 42-day cycle vs. SUN 50 mg PO QD 4/2 wk.	PFS in the PD-L1+ population and OS in the ITT by IR	**IMDC** Not determined **MSKCC** FAV 20% IMD 69% POOR 12%	(PD-L1+) ATEZO + BEV: 11.2 (8.9-15.0) SUN: 7.7 (6.8-9.7) HR: 0.74 (95% CI: 0.57-0.96) p=0.0217	(ITT) ATEZO + BEV: 36.1 (31.5-42.3) SUN: 35.3 (28.6-42.1NE) HR: 0.91 (95% CI: 0.76-1.08) p=0.27
CheckMate214 NCT02231749 Median follow-up of 60 months (37,59)	1096	NIVO 3 mg/kg plus ipilimumab 1 mg/kg IV Q3W for 4 doses then nivolumab 3 mg/ kg IV Q2W vs. SUN 50 mg PO QD 4/2 wk.	PFS and OS in the IMDC inter- mediate and poor risk population by BICR	**IMDC** FAV 23% IMD 61% POOR 17% **MSKCC** Not determined	(IMDC IMD/poor) NIVO + IPI: 11.6 (8.4-16.5) SUN: 8.3 (7.0-10.4) HR: 0.73 (95% CI: 0.61-0.87)	(IMDC IMD/poor) NIVO + IPI: 47.0 (35.4-57.4) SUN: 26.6 (22.1-33.5) HR: 0.68 (0.58-0.81) p≤0.0001
CheckMate9ER NCT03141177 Median follow-up of 44 months (26,41,60)	651	NIVO 240 mg. fixed dose IV every 2 wk. plus CABO 40 mg PO daily vs. SUN 50 mg PO QD 4/2 wk.	PFS in the ITT by BICR	**IMDC** FAV 22% IMD 58% POOR 20% **MSKCC** Not determined	(ITT) NIVO+CABO: 16.6 (12.8-19.5) SUN: 8.4 (7.0-9.7) HR: 0.59 (95% CI: 0.49-0.71) p<0.0001	(ITT) NIVO+CABO: 49.5 (40.3-NE) SUN: 35.5 (29.2- 42.3) HR: 0.70 (98.9% CI: 0.56-0.87) p=0.0034
CLEAR NCT02811861 Median follow-up of 49.8 months (42,61,62)	712	PEMBRO 200 mg IV Q3W plus LEN 20 mg PO QD vs. SUN 50 mg PO QD 4/2 wk.	PFS in the ITT by BIRC	**IMDC** FAV 31% IMD 59% POOR 9% NE 1% **MSKCC** FAV 27% IMD 64% POOR 9%	(ITT) PEMBRO+LEN: 23.9 (20.8-27.7) SUN: 9.2 (6.0-11.0) HR: 0.47 (95% CI: 0.38-0.57) p>0.001	(ITT) PEMBRO+LEN: 53.7 (48.7-NE) SUN: 54.3 (40.9-NE) HR: 0.79 (95% CI: 0.63-0.99) p=0.005

Table 1. Continued

Study	n	Experimental arm	Primary endpoint	Risk groups	PFS (22) median (95% CI) HR	OS (22) Median (95% CI) HR
COSMIC-313 Median follow-up of 20.2 months (43)	855	NIVO 3 mg/kg plus IPI 1 mg/ kg IV Q3W for 4 doses then NIVO 3 mg/kg IV Q2W + CABO 40mg PO QD vs. NIVO 3 mg/ kg plus IPI 1 mg/ kg IV Q3W for 4 doses then NIVO 3 mg/kg IV Q2W	PFS in the PITT population (first 550 pts. randomised)	**IMDC** IMD 75% POOR 25%	(PITT) NIVO+IPI+CABO: NR (14.0-NE) NIVO+IPI: 11.3 (7.7- 18.2) HR: 0.73 (95% CI: 0.57-0.94) p=0.013	NR

CI: Confidence interval, RCC: Renal cell carcinoma, PFS: Progression-free survival, HR: Hazard ratio, OS: Overall survival

Current clinical trials are investigating the application of immunotherapy in both neoadjuvant and adjuvant contexts, with potential outcomes that may broaden its utilization in early-stage cancers. The advancement of knowledge regarding tumor biology and immune interactions is expected to lead to the development of innovative agents and combination therapies, thereby significantly altering the treatment landscape for urological cancers and providing new hope for patients.

Footnotes

Authorship Contributions

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

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ORIGINAL RESEARCH
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Lower Urinary Tract Symptoms in Men Living with Human Immunodeficiency Virus: A Case-control Study

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

Human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) remains a global public health challenge, affecting populations worldwide. By the end of 2022, an estimated 39.0 million individuals were living with HIV, with approximately 1.3 million new infections reported that year. The widespread availability of contemporary antiretroviral therapy (ART) has significantly improved life expectancy among people living with HIV, leading to an increased prevalence of age-related comorbidities. Existing literature indicates that HIV-negative individuals have a lower risk of developing non-AIDS-related complications, including bone, cardiovascular, and renal diseases, compared to those living with HIV. While LUTS are prevalent in the general aging male population, research specifically examining their occurrence among males living with HIV (MLWH) is scarce. Addressing this gap is particularly important, as MLWH may be exposed to unique risk factors, such as chronic immune activation, systemic inflammation, and potential adverse effects of long-term ART, which could influence the development and progression of LUTS compared to HIV-negative individuals. The prevalence of all types of LUTS was higher among MLWH compared to HIV-negative controls. Statistically significant differences were noted for hesitancy, intermittency, reduced urinary flow rate, and sensation of post-void residual urine. The sensation of post-void residual urine was the most frequently reported LUTS among MLWH. The prevalence of moderate to severe LUTS was significantly higher in MLWH compared to HIV-negative controls. A significantly higher proportion of MLWH had OAB V8 scores of ≥11 compared to HIV-negative controls, indicating an increased likelihood of OAB in MLWH. All MLWH in our study were receiving ART, providing contemporary insights into the relationship between HIV and LUTS in the modern treatment era. Bictegravir-based ART was the most commonly used regimen among MLWH. No statistically significant differences were observed in LUTS prevalence across ART regimen subgroups.

Abstract

Objective: Human immunodeficiency virus (HIV)/acquired immune deficiency syndrome constitutes a global pandemic affecting populations worldwide. There's a gap in data regarding lower urinary tract symptoms (LUTS) among men living with HIV (MLWH) during the antiretroviral therapy era. The aim of this study is to evaluate the potential influence of HIV status on the presence of LUTS.

Materials and Methods: Infectious Diseases and Clinical Microbiology Clinic, referred MLWH and HIV-negative men (control group) to Urology Clinic after their initial assessment. In both groups, International Consultation on Incontinence Questionnaire-Male Lower Urinary Tract Symptoms (ICIQ-MLUTS), International Prostate Symptom Score (IPSS), King's Healthcare Questionnaire, 8-item Overactive Bladder Questionnaire (OAB-V8), ICIQ-Short Form, Urogenital Distress Inventory 6 and 7 were used. The presence or absence of each LUTS was individually assessed.

Results: A total of 95 males (51 MLWH and 44 HIV-negative controls) were included. Both groups exhibited similar perceptions of general health. Scores of ICIQ-MLUTS, (for both voiding and incontinence scores), IPSS, and OAB-V8 were higher in the MLWH group. There were statistically significant differences between ICIQ-MLUTS and IPSS scores. The MLWH group exhibited a higher frequency of all types of LUTS. Statistical significance was observed in hesitancy, intermittency, decrease in urine flow rate, and sensation of incomplete bladder emptying between the MLWH group and the control group.

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Conclusion: LUTS were more commonly observed among MLWH compared to HIV-negative individuals. MLWH had more symptoms related to the emptying phase, as evidenced by higher scores on the IPSS and ICIQ-LUTS. While the results did not achieve statistical significance, there was a trend indicating a higher likelihood of OAB among MLWH. Continuing to explore this correlation within larger prospective cohorts, including comprehensive information on sexual behaviors, sexually transmitted diseases, and urodynamic data, might offer insights into the pathophysiological basis of this correlation.

Keywords: Functional urology, general urology, pathology, radiology, reconstructive urology

Introduction

Human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) constitutes a global pandemic affecting populations worldwide. By the conclusion of 2022, there were an estimated 39.0 million individuals living with HIV, with approximately 1.3 million new HIV infections occurring worldwide during that year (1). As contemporary antiretroviral treatment (ART) options gained wide availability, people living with HIV started to live longer and confront age-associated illnesses (2). Data in the literature have already shown that HIV-negative controls were at lower risk for non-AIDS-related complications such as bone, heart, and renal diseases than patients living with HIV (3-6). There's insufficient data on lower urinary tract symptoms (LUTS) among men living with HIV (MLWH) during the ART era. Although LUTS are commonly observed in the general aging male population, there is a scarcity of studies specifically focusing on the prevalence of these symptoms among MLWH. This research gap is particularly important, as MLWH may face unique risk factors such as chronic immune activation, inflammation, and potential side effects of prolonged ART, all of which could exacerbate or modify the presentation of LUTS in comparison to HIV-negative men. The mechanisms by which HIV infection and ART influence the development and progression of LUTS remain largely unexplored. While ART is essential for extending life expectancy, it may carry side effects or long-term consequences for urinary health. Furthermore, limited research has examined the relationship between HIV-specific clinical markers such as CD4 count, viral load, and history of opportunistic infections and LUTS. Despite a general recognition that MLWH may have distinct healthcare needs, few studies have directly compared the prevalence, severity, and risk factors of LUTS between MLWH and matched HIV-negative controls. The aim of this study is to evaluate the potential influence of HIV status on the presence of LUTS.

Materials and Methods

The case-control study protocol was approved by the Institutional Review Board. Infectious Diseases and Clinical Microbiology Clinic (IDCMC) referred MLWH and HIV-negative men (control group) to Urology between August 2022 and June 2023. MLWH were under routine follow-up for HIV whereas the control group was composed of patients who presented to the IDCMC for long-term follow-up after completely recovering from non-genitourinary conditions such as upper respiratory tract infections or gastroenteritis, with no acute infectious symptoms.

Ages, laboratory test results (levels of CD4 T-lymphocytes and HIV RNA), types of ART and syphilis serology results (for MLWH group) were recorded. MLWH who defined themselves as "men who have sex with men (MSM)" were categorized and analyzed separately.

Exclusion criteria included non-native speakers, men receiving treatment and/or who underwent urological surgery due to LUTS, individuals with clinical or laboratory findings suggestive of urinary tract infection, those with uncontrolled diabetes mellitus, and those with a history of neurological disorder. Urinalysis and fasting serum glucose level measurements were conducted in the IDCMC for all patients. Patients with abnormal urinalysis findings (such as hematuria, pyuria, leukocyte esterase positivity, nitrite positivity) or abnormal fasting serum glucose levels were also excluded. Neurological disorders were screened during history taking or through measurable deficits, as outlined in International Continence Society (ICS) documents (7).

Table 1 was created based on the answers provided by the patients, regarding the presence or absence of a particular LUTS as defined by the Glossary of the ICS. These symptoms include hesitancy, intermittency, decrease in urine flow rate, sensation of post-void residual urine, urgency, urgency urinary incontinence, stress urinary incontinence, terminal dribbling, increased daytime urinary frequency, and nocturia.

MLWH and control groups were asked to complete the following native language-validated questionnaires: International Consultation on Incontinence Questionnaire-Male Lower Urinary Tract Symptoms (ICIQ-MLUTS), International Prostate Symptom Score (IPSS), King's Healthcare Questionnaire (KHQ), 8-item Overactive Bladder Questionnaire (OAB-V8), ICIQ-Short Form (ICIQ-SF), Urogenital Distress Inventory 6 and 7 (UDI 6 and UDI 7).

The ICIQ-SF score ranges indicating the severity of OAB were as follows: 1-5 (mild), 6-12 (moderate), and 13-21 (severe and very severe) (8). Responses to the initial item of the KHQ

were categorized into two groups for analysis: "very good" and "good" versus "fair", "poor", and "very poor". The threshold value denoting a high likelihood of OAB was set at 11 in the OAB V8 questionnaire (9). IPSS symptom severity was classified into three levels: mild (0-7), moderate (8-19), and severe (20-35) (10). Elevated scores on UDI 6 and UDI 7 indicated a higher level of disability associated with LUTS (11).

This study was conducted according to the principles of the Declaration of Helsinki and was approved by the Koç University Ethics Committee (approval number: 2023 127.IRB1.039, date: 03.04.2023). Written informed consent was obtained from all patients. Clinical Trial Registration ID NCT05964803.

Statistical Analysis

The sample size for each group has been calculated as 39 patients, with an approximate standard deviation of 3 units, a Type I error rate of α=0.05, and a study power of 1-β=0.80. Taking the dropout rate into consideration, 41 was the minimum number of patients to be included in each group (12). Sample size calculation was conducted using MedCalc Statistical Software version 19.1 (MedCalc Software bv, Ostend, Belgium; https://www.medcalc.org; 2019). Statistical analyses were conducted using either Student's t-test or the Mann-Whitney U test for continuous variables, and the chi-squared test or Fisher's exact test for categorical variables.

Table 1. Comparative analysis of LUTS distribution in MLWH and control groups including subgroup of ART regimens for MLWH

LUTS	MLWH group n=51 (%)	Control group n=44 (%)	p
Hesitancy	29/51 (56.8)	15 (34)	**0.02***
ART including Bictegravir	21/29		
Other ART regimens	8/29		
Intermittency	32/51 (62.7)	18 (41)	**0.03***
ART including Bictegravir	23/32		
Other ART regimens	9/32		
Decrease in urine flow rate	24/51 (47)	12 (27)	**0.04***
ART including Bictegravir	17/24		
Other ART regimens	7/24		
Sensation of post-void residual urine	37/51 (72.5)	21 (47.7)	**0.01***
ART including Bictegravir	27/37		
Other ART regimens	10/37		
Urgency	39/51 (76)	26 (59)	0.06
ART including Bictegravir	28/39		
Other ART regimens	11/39		
Urgency urinary incontinence	11/51 (21.5)	5 (11.3)	0.1
ART including Bictegravir	9/11		
Other ART regimens	2/11		
Stress urinary incontinence	5/51 (9.8)	2 (4.5)	0.3
ART including Bictegravir	4/5		
Other ART regimens	1/5		
Terminal dribbling	33/51 (64.7)	22 (50)	0.1
ART including Bictegravir	25/33		
Other ART regimens	8/33		
Increased daytime urinary frequency	28/51 (55)	17 (39)	0.1
ART including Bictegravir	22/28		
Other ART regimens	6/28		
Nocturia	25/51 (49)	13 (29.5)	0.06
ART including Bictegravir	19/25		
Other ART regimens	6/25		

LUTS: Lower urinary tract symptom, MLWH: Males living with HIV, ART: Antiretroviral treatment
*: Statistically significant value

Results

A total of 95 males (51 MLWH and 44 HIV-negative controls) were included. A total of 40 patients were excluded based on exclusion criteria during the study period.

The median patient age in MLWH and HIV-negative groups was 40 (22-62) and 39 (24-67) years, respectively (p>0.05). The median CD4 T lymphocyte count of MLWH was 665 cells/mm^3 [interquartile range (IQR) 404.5], and all MLWH had non-detectable HIV RNA levels. The number of MLWH receiving tenofovir alafenamide fumarate + emtricitabine + bictegravir, emtricitabine + tenofovir alafenamide elvitegravir + cobicistat, and medications including dolutegravir was 38, 7, and 6, respectively.

Table 1 presents the comparative prevalence of LUTS in both the MLWH and control groups. The MLWH group exhibited a higher frequency of all types of LUTS. Statistical significance was observed in hesitancy, intermittency, decrease in urine flow rate, and sensation of incomplete bladder emptying between the MLWH group and the control group (p<0.05). An additional subgroup analysis was performed regarding the effects of different ART regimens on LUTS within the MLWH group (Table 1). There were statistical differences between bictegravir-based ART and other regimens.

The comparison of questionnaire scores is outlined in Table 2. Both groups exhibited similar perceptions of general health, while scores of ICIQ-MLUTS (for both voiding and incontinence scores), IPSS, and OAB-V8 were higher in the MLWH group. Additionally, there were statistically significant differences between ICIQ-MLUTS and IPSS scores. Questionnaire scores recorded in the MSM group were analyzed separately and the results are presented in Table 2.

Table 2. Mean questionnaire scores recorded in MLWH and control groups

Questionnaire & score	MLWH group (n=51)	MSM subgroup (n=24)	Control group (n=44)	p
ICIQ-MLUTS (IQR; range)				
Voiding score	4.2 (4; 0-12)	3.9 (3; 0-11)	2.8 (4; 0-14)	**0.01***
Incontinence score	3 (3; 0-8)	3.5 (3.2; 0-8)	1.7 (1; 0-6)	**0.002***
ICIQ-SF				
Mean (IQR; range)	0.62 (0; 0-11)	0.7 (0; 0-11)	0.1 (0; 0-3)	0.3
None	46	21	41	
Slight (1-5), n	3	2	3	
Moderate (6-12), n	2	1	-	
Severe-very severe (13-21), n	-	-	-	
IPSS				
Mean (IQR; range)	7.9 (5.5; 0-26)	7.2 (5.2; 0-18)	4.1 (5; 0-19)	**0.01***
Mild (0-7), n	30	13	38	
Moderate (8-19), n	19	11	6	
Severe (20-35), n	2	-	-	
KHQ				
General health perception				
Mean total score %, (IQR; range)	23.5 (0; 0-50)	25 (0; 0-50)	16.1 (25; 0-50)	0.3
Very good & good, n (%)	43 (84.3)	19 (79.1)	38 (86.3)	
Fair, poor and very poor, n (%)	8 (15.7)	5 (20.9)	6 (13.7)	
OAB V8				
Mean total score (IQR, range)	10 (6; 3-32)	9.4 (6; 3-24)	5.8 (3; 2-15)	0.05
Scores ≥11, n (%)	14 (27.4)	7 (29.1)	5 (12.1)	
UDI-6 (IQR; range)	2.5 (4; 0-8)	2.8 (3.5; 0-8)	1.1 (2; 0-8)	NA**
UDI-7 (IQR; range)	0.8 (0; 0-9)	0.7 (0; 0-9)	0.1 (0; 0-4)	NA**

The scores recorded in the MSM subgroup of MLWH are shown as a separate column. P-value was calculated for the difference between MLWH and control groups. Mean scores were given on the table for each questionnaire scores, MLWH: Males living with HIV, MSM: Men having sex with men, ICIQ-MLUTS: International Consensus on Incontinence Male Lower Urinary Tract Symptoms, ICIQ-SF: International Consensus on Incontinence Short Form, IPSS: International Prostate Symptom Scale, KHQ: King's Healthcare Questionnaire, OAB V8: Overactive Bladder Version 8, UDI: Urogenital distress inventory, IQR: Interquartile range

*: Statistically significant value

**: Not calculated

Out of 51 MLWH, 20 individuals (39.2%) tested positive for treponemal chemiluminescent microparticle immunoassay (CMIA). The median age for MLWH with positive and negative CMIA results was 39 (28-62) and 40 (22-55) years, respectively (p>0.05). There were no statistically significant differences in the presence of any type of LUTS between the MLWH and CMIA results.

Twenty-four of 51 MLWH (47%) defined themselves as MSM; 2 patients identified as heterosexual. The remaining 49.1% preferred not to answer the question related to sexual orientation. The median age of MSM was 38 (IQR 35.5-49.5) years. The mean age of the MSM subgroup did not significantly differ from that of other MLWH subgroups or the control group. Seven (29.1%) MSM had positive treponemal CMIA results. Eighty percent of MSM were under bictegravir treatment. The median ICIQ-MLUTS (Voiding), ICIQ-MLUTS (Incontinence), and IPSS scores were 3.5 (IQR 2-5), 3 (IQR 2-5.5), and 6 (IQR 3.5-9), respectively. Ten (41.6%) had IPSS scores over 7. Seven (29.1%) had OAB-V8 scores above 10. One had ICIQ-SF score above 5. The distribution of LUTS in the MSM subgroup and its comparison with the larger group of MLWH and HIV-negative controls is provided in Figure 1.

Discussion

The role of HIV status as an independent risk factor related to the presence or severity of LUTS in men receiving ART remains uncertain. Life expectancy and quality of life for MLWH have improved with modern ART options. Concurrently, there is an increasing focus on studying the health outcomes of the aging population affected by HIV (13,14).

The relationship between HIV infection and LUTS was first assessed in a retrospective case series. In 1996, Kane et al. (15) documented that among 18 HIV-positive males with voiding dysfunction, the most prevalent urodynamic diagnoses were detrusor hyperreflexia (27.7%), detrusor-sphincter dyssynergia (27.7%), and detrusor areflexia (5.5%). Hermieu et al. (12) evaluated 39 HIV-positive patients (35 males, 4 females) with voiding symptoms. Only 5 (12.8%) of the patients had a normal urodynamic evaluation. The predominant urodynamic finding was the presence of uninhibited detrusor contractions (69.2%). Notably, among these patients, over 60% presented with coexistent neurological disorders (cerebral toxoplasmosis, HIV encephalitis, etc.) (12). The frequency of neurological disorders in these studies might have influenced urodynamic results. In our study, we excluded all males with neurological disorders to minimize confounding factors. We found a higher percentage of patients in the MLWH group scoring ≥11 on the OAB V8 (27.4% *vs.* 12.1%, p=0.05), which indicates a high likelihood of OAB. Moreover, to our knowledge, our study is the first to compare OAB symptoms between MLWH and an HIV-negative control group. Furthermore, we observed marginally elevated ICIQ-SF, UDI 6, and UDI 7 scores in MLWH. Total scores obtained from these questionnaires were quite low in both cohorts, suggesting that the differences remained minimal and possibly subclinical.

Our results revealed a higher prevalence of all types of LUTS in MLWH compared to the HIV-negative controls. The differences were statistically significant for hesitancy, intermittency, decrease in urine flow rate, and sensation of post-void residual urine. Sensation of post-void residual urine were the most common (72.5%) LUTS among MLWH in our study. Breyer et al. (3) surveyed 1507 HIV-negative and 323 HIV-positive

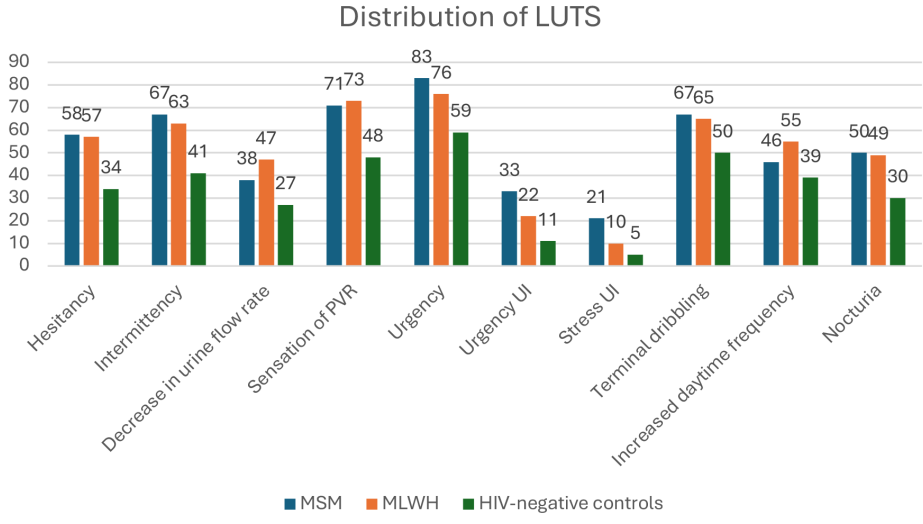

Figure 1. Distribution of LUTS among the MSM subgroup of MLWH, MLWH group in total, and HIV-negative controls. Percentages per symptom were given for all groups

LUTS: Lower urinary tract symptoms, PVR: Post-void residual urine, UI: Urinary incontinence, MSM: Men having sex with men, MLWH: Males living with HIV

MSM online using the IPSS in 2011. HIV status surfaced as an independent factor associated with the reporting of LUTS. In their study, HIV-positive males exhibited a higher prevalence of severe (11.4% *vs.* 4.2%) and moderate LUTS (33.2% *vs.* 29.2%) when compared to their HIV-negative counterparts (3). Similarly, our data showed the prevalence of moderate to severe LUTS was significantly more prevalent in MLWH (41.1% *vs.* 13.6%). Moreover, the ICIQ-MLUTS-Voiding scores corroborated the IPSS scores, revealing significantly higher prevalence of emptying phase-related symptoms among MLWH compared to the control group.

In our study, a relatively lower percentage of MLWH (47%, 24 out of 51 individuals) self-identified as MSM, while a smaller proportion (3.9%, 2 out of 51 individuals) self-identified as heterosexual. The sexual orientations of the remaining MLWH (25 out of 51 individuals) were unknown. Additionally, the individuals in the control group were not queried regarding their sexual behaviors or orientations. The predominant symptoms observed in our MSM subgroup were urgency (83.3%) and the sensation of post-void residual urine (70%). The questionnaire responses recorded in the MSM subgroup resembled those of MLWH. The small number of patients within the MSM subgroup might have hindered the interpretation of these results.

In the study conducted by Breyer et al. (3), the information regarding ART usage was absent. On the contrary, in our study all MLWH were receiving ART, which provides contemporary insights into the relationship between MLWH and LUTS in the modern era. Bictegravir-based ART was the most common (74.5%) modality among MLWH in our cohort. We observed no statistically significant differences among subgroups based on ART types regarding the presence of LUTS.

Larouche et al. (16) assessed 177 women living with HIV (WLWH) using the UDI-6. They found that stress urinary incontinence (UI) was the most prevalent urinary symptom, observed in 36.7% of the participants. Another study by Greene et al. (14), including 145 MLWH and 10 WLWH, reported a 25% prevalence of unspecified UI. This finding was associated with the relatively higher median age of patients (57 years). Similarly, in our study, with a median patient age of 40 years, 13 MLWH (25.4%) reported experiencing urinary incontinence, a rate that was higher than in the control group, but the difference remained statistically insignificant.

Potential risk factors for LUTS in HIV-positive individuals could encompass chronic urinary tract inflammation, a background of opportunistic infections, and other sexually transmitted infections, the direct impact of the virus on both the central and peripheral nervous systems, and potential toxicity associated with ART (3,16). In our study, we observed no statistically significant differences between CMIA positive, and negative MLWH, in terms of the presence and severity of LUTS. In another study, urinary tract infections, prostatitis, and gonorrhea were found to be an unlikely underlying cause of bothersome LUTS in HIV-positive individuals (3). Furthermore, the type of ART exhibited no discernible impact on the presence of LUTS or the scores recorded on questionnaires in our study. We speculate the likelihood of the virus and/or the ART, impacting the nervous system and contributing to the increased occurrence of LUTS in MLWH.

Study Limitations

The primary strength of our study was the utilization of multiple validated questionnaires to assess the existence and severity of LUTS among MLWH. Moreover, we compared these results with an HIV-negative control group. However, we omitted the analysis of factors such as sexual orientation/behavior, clinical information, and serological titers related to sexually transmitted diseases in certain individuals with MLWH, but not in the control group. Furthermore, syphilis was solely assessed through CMIA sero-positivity, without conducting any further confirmatory tests in MLWH. Moreover, given its observational nature, our study lacked robust hypotheses that could substantiate our findings from pathophysiological and urodynamic perspectives. Unfortunately, we do not have additional information about comorbidities beyond those specified in the methodology section. This represents another important drawback of our study.

Conclusion

LUTS are more frequently observed in MLWH than in HIV-negative controls. A significantly higher number of MLWH reported symptoms related to the emptying phase as reflected by higher IPSS and MCIQ-LUTS scores. Although not reaching statistical significance, there was a greater tendency for OAB, in MLWH. Continuing to explore this correlation within larger prospective cohorts, including comprehensive information on sexual behaviors, sexually transmitted infections, and urodynamic data, might offer insights into the pathophysiological basis. This will enhance patient counseling, and management strategies for understanding and addressing of LUTS in MLWH.

Ethics

Ethics Committee Approval: This study was conducted according to the principles of the Declaration of Helsinki and was approved by the Koç University Ethics Committee (approval number: 2023. 127.IRB1.039).

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

Footnotes

Authorship Contributions

Concept: E.K., Ö.A., S.T., Design: E.K., Ö.A., S.T., T.T., Data Collection or Processing: E.K., U.C.K., İ.C.A., S.T., Analysis or Interpretation: Ö.A., İ.C.A., T.T., Literature Search: E.K., U.C.K., Writing: E.K., T.T.

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

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Treatment Strategies for Kidney Stones Following ESWL Failure: A Prospective Comparative Study of Three Surgical Approaches

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

Nephrolithiasis is commonly treated with extracorporeal shock wave lithotripsy (ESWL), but in cases of failure, more invasive procedures, like retrograde intrarenal stone surgery (RIRS), mini percutaneous nephrolithotomy (PCNL), and PCNL, are used. However, there is limited consensus on the best approach for patients with 1-2 cm stones post-ESWL. This study provides a direct comparison of these three techniques, showing that RIRS and miniPCNL are associated with shorter hospital stays and fewer complications than PCNL, which, though quicker, requires more analgesia and causes greater hemoglobin reduction.

Abstract

Objective: This study aims to evaluate the efficacy and safety of retrograde intrarenal stone surgery (RIRS), mini-percutaneous nephrolithotomy (miniPCNL), and PCNL in patients with 1-2 cm kidney stones who failed extracorporeal shock wave lithotripsy (ESWL).

Materials and Methods: This prospective study analyzed the medical records of 90 patients who underwent RIRS (n=29), miniPCNL (n=31), or PCNL (n=30) after unsuccessful ESWL treatment. The groups were compared based on operative time, hospital stay, complication rates, narcotic analgesic use, catheterization requirements, perioperative hemoglobin changes, transfusion needs, and treatment efficacy. Statistical analyses were performed using appropriate methods based on variable distribution.

Results: RIRS resulted in significantly shorter hospital stays than miniPCNL and PCNL groups ($p<0.001$). MiniPCNL patients also had a shorter hospital stay than those in the PCNL group ($p=0.047$). The shortest operative time was observed in the PCNL group (59.9 min) compared to both the RIRS and miniPCNL groups ($p<0.05$). However, PCNL was associated with significantly higher narcotic analgesic use, greater hemoglobin reduction, and longer hospitalization. No significant differences were found among the three groups regarding transfusion requirements, residual stone rates, or overall complications.

Conclusion: All three surgical methods were effective and safe for treating kidney stones measuring 1-2 cm in patients who previously failed ESWL. However, considering the shorter hospital stay and lower complication rates, RIRS and miniPCNL may be preferable options, while PCNL should be considered in selected cases.

Keywords: ESWL, kidney stone, miniPCNL, percutaneous nephrolithotomy, RIRS

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Introduction

Nephrolithiasis is a prevalent urological condition with a rising incidence worldwide, significantly affecting both patient quality of life and healthcare systems. Treatment strategies vary based on stone size, location, composition, and patient-specific factors, ranging from conservative medical management to surgical interventions (1-3). Among non-invasive approaches, extracorporeal shock wave lithotripsy (ESWL) is commonly preferred as a first-line treatment for small to medium-sized renal stones. However, its success rate is limited by factors such as stone density, unfavorable anatomical conditions, and lower pole stone location (4,5).

When ESWL fails, more invasive endourological procedures-retrograde intrarenal surgery (RIRS), mini-percutaneous nephrolithotomy (miniPCNL), and percutaneous nephrolithotomy (PCNL)-are utilized (4). According to the 2024 European Association of Urology guidelines, no specific endourological method is prioritized for 1-2 cm kidney stones, and both ESWL and surgical options are recommended. However, for stones larger than 1 cm in the lower pole or in cases where ESWL is not feasible, endo-urological techniques are the preferred treatment approach (6,7).

Although numerous studies have compared the efficacy and safety of RIRS, miniPCNL, and PCNL, most do not specifically focus on patients undergoing surgery after failed ESWL (8-10). Additionally, there is a lack of direct comparisons between these three techniques in this specific patient group. This study aims to fill this gap by prospectively comparing RIRS, miniPCNL, and PCNL in patients with 1-2 cm renal stones who did not benefit from ESWL, thereby providing valuable insights for clinical decision-making.

Materials and Methods

Study Design and Patient Selection

This prospective study was conducted at Düzce University Hospital between January 2015 and July 2017 and included patients who underwent RIRS, miniPCNL, or PCNL due to failed ESWL. Ethical approval was obtained from the Düzce University Clinical Research Ethics Committee (approval number: 2014/63, date: 28/10/2014), and the study was conducted in compliance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients before undergoing surgical intervention. This study was designed and reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure transparency and completeness in the presentation of methods and results.

A total of 113 patients with single renal stones measuring 1-2 cm who had undergone at least two ESWL sessions without successful stone fragmentation were assessed for eligibility. After applying inclusion and exclusion criteria, 90 patients were included in the study. ESWL failure was defined as the absence of stone fragmentation on follow-up radiography or fluoroscopy in at least two applications performed a week apart. It also included patient intolerance due to pain, or inability to complete ESWL sessions, each consisting of 2,500 shocks at 18-22 kV (Stonelith-V5 Lithotripter; PCK Medical Systems, Ankara, Turkiye). The surgical procedure was planned three weeks after the unsuccessful ESWL treatment. Patients were comprehensively informed about all three surgical options-RIRS, miniPCNL, and PCNL-before undergoing the procedure. Following the attainment of patient consent for the surgical procedure selection, patients were prospectively divided into three separate groups according to the surgery being conducted. An intraoperative miniPCNL was performed on one patient in the RIRS group, because the stone could not be reached. The RIRS group included 29 patients, the miniPCNL group included 31 patients, and the PCNL group included 30 patients. Due to the nature of the study, randomization could not be implemented.

The flow diagram showing the patient selection and analysis process of the study is presented in Figure 1. This diagram summarizes the assessment, exclusion criteria, group separation, and final analysis stages of the patients included in the study.

Inclusion and Exclusion Criteria

Patients were eligible for inclusion if they had a single radiopaque renal stone measuring between 1 and 2 cm located in a single calyx or the renal pelvis, confirmed on imaging. They were required to have no active urinary tract infection and to meet the criteria for ESWL failure (no stone fragmentation on control radiography or fluoroscopy after at least two ESWL treatments performed one week apart or the patient was unable to continue treatment due to pain). Stone density was measured in Hounsfield units (HU) using non-contrast computed tomography.

Exclusion criteria included patients younger than 18 years or older than 85 years with a body mass index (BMI) greater than 35 with severe skeletal deformities, and with anatomical abnormalities such as a pelvic kidney or abnormal renal rotation. Patients with active urinary tract infections or those who required immediate emergency intervention were also excluded.

Surgical Procedures

All procedures were performed under general anesthesia after confirming a sterile urine culture and administering prophylactic antibiotic therapy. RIRS was performed using a 7.5 Fr Karl Storz (Karl Storz GmbH & Co. KG, Tuttlingen, Germany)

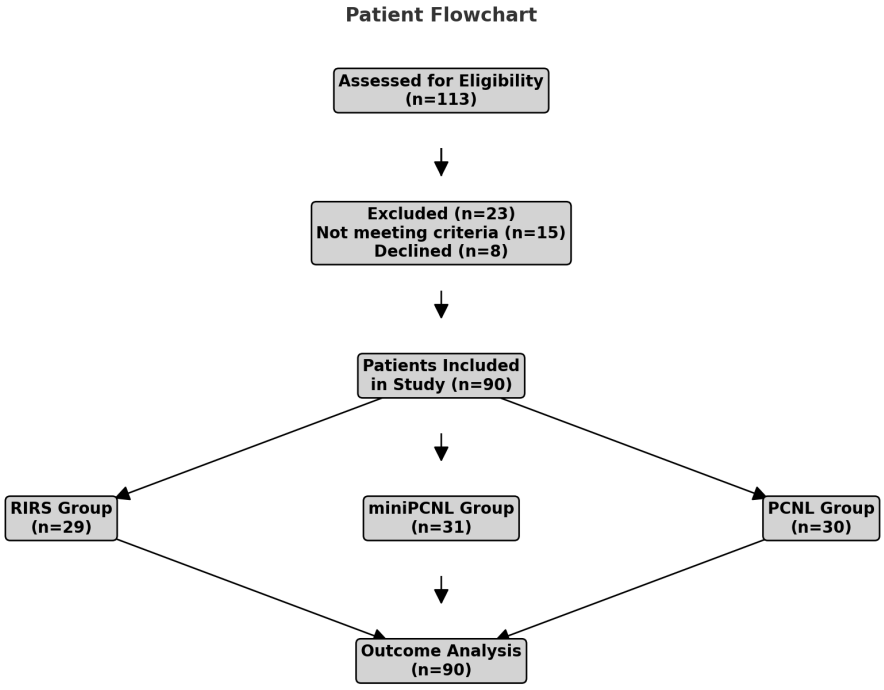

Figure 1. Patient flowchart

RIRS: Retrograde intrarenal stone surgery, MiniPCNL: Mini-percutaneous nephrolithotomy, PCNL: Percutaneous nephrolithotomy

Flex-X2S flexible ureteroscope with a 9 Fr ureteral access sheath. Lithotripsy was performed using a 270-micron laser fiber in dusting mode (0.5 J, 20 Hz), with energy and frequency adjustments made as necessary. A Double-J stent (DJS) was routinely placed postoperatively. MiniPCNL was performed using a 12 Fr nephroscope, part of the Minimally invasive PCNL system, manufactured by Karl Storz. Additionally, a 17.5 Fr sheath was used in this procedure. Stone fragmentation was performed using a 600-micron laser fiber in fragmentation mode (2 J, 10 Hz). Postoperatively, either a Malecot nephrostomy tube or a DJS was placed depending on the clinical indication. PCNL was performed using a 26 Fr Karl Storz nephroscope with a 30 Fr access sheath. A pneumatic lithotripter was used for stone fragmentation. Catheterization methods included the placement of a re-entry catheter, a Malecot nephrostomy tube, or a combination of a nephrostomy tube with a DJS based on intraoperative conditions (11).

Outcome Measures

The primary outcome measures were operative time, hospital stay duration, perioperative hemoglobin changes, transfusion requirements, complication rates classified using the Clavien-Dindo system, narcotic analgesic use, and residual stone presence. Residual stones were assessed using computed tomography (CT) imaging performed within two months postoperatively. Residual stones greater than 4 mm were classified as clinically significant, while those smaller than 4 mm were considered stone-free. Stone distribution according to renal anatomy (upper pole, middle pole, lower pole, and pelvis) was analyzed to determine any potential impact on treatment outcomes.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS v23 software. Parametric variables such as operative time and hemoglobin change were analyzed using ANOVA and post hoc Tukey's tests, while non-parametric variables such as hospital stay were analyzed using the Kruskal-Wallis and Mann-Whitney U tests. Categorical variables, including transfusion requirements and complication rates, were compared using chi-square or Fisher's exact tests as appropriate. A priori power analysis was performed using GPower, and it was determined that a sample size of 75 patients would provide sufficient statistical power for detecting meaningful differences (7). A p-value of less than 0.05 was considered statistically significant.

Results

Between January 2015 and July 2017, 90 patients with 1-2 cm kidney stones following failed ESWL were included in the study. In one patient from the RIRS group, the procedure was switched to miniPCNL due to the inability to access the stone.

The mean age of the patients was 48.4 years, the average stone size was 16.5 mm, and the mean BMI was 25.5, with no significant differences observed between the groups (Table 1).

When examining the operation durations: the average time for all groups was found to be 76.3 minutes (RIRS: 78.17 minutes, miniPCNL: 90.45 minutes, PCNL: 59.9 minutes). A significant difference was found between the RIRS-PCNL and miniPCNL-PCNL groups (p=0.024; p<0.001). However, no significant difference was observed between the RIRS and miniPCNL groups (p=0.20) (Table 1).

The average hospital stay duration was found to be 3.62 days (RIRS: 1.76 days, miniPCNL: 4.13 days, PCNL: 4.9 days), with patients in the RIRS group having a significantly shorter hospital stay compared to the other groups (p<0.001). Additionally, the miniPCNL group was observed to have a shorter hospital stay compared to the PCNL group (p=0.047) (Table 1).

A comparison of the preoperative and postoperative hemoglobin changes between the RIRS and miniPCNL groups showed no significant difference (p=0.404). However, a significant difference was observed between the miniPCNL-PCNL and RIRS-PCNL groups (p=0.03 and p<0.001, respectively). In the PCNL group, two patients received blood transfusions, and in the miniPCNL group, one patient received a transfusion. No transfusions were performed in the RIRS group (Table 2).

No significant difference was found in preoperative and postoperative hemoglobin changes between the RIRS and miniPCNL groups (p=0.404). However, significant differences were observed between the miniPCNL-PCNL and RIRS-PCNL groups (p=0.03 and p<0.001, respectively). In the PCNL group, 2 patients received blood transfusions, while in the miniPCNL group, 1 patient received a transfusion, and no transfusions were performed in the RIRS group (Table 2).

Residual stones were observed in 8 patients in the RIRS group, 3 patients in the miniPCNL group, and 8 patients in the PCNL group. No significant difference was found between the groups (p>0.05) (Table 2).

A total of 5 patients developed complications. The complications were graded according to the standardized Clavien-Dindo classification for PCNL procedures. In the PCNL group, one patient developed a fever postoperatively (Clavien score 2); antibiotic treatment was started. Subsequently, a urinary tract infection was

Table 1. Baseline demographic and clinical characteristics

Features	RIRS (n=29)	MiniPCNL (n=31)	PCNL (n=30)	Total (n=90)	p-value
Age, year	51.10±15.07	47.48±14.76	46.77±18.52	48.41±16.13	>0.05*,**,**
Gender	18/11	22/9	13/17	53/37	>0.05*,**,**
Body mass index (<35)	25.6±3.8	26.1±3.2	24.8±4.1	25.5±3.4	>0.05*,**,**
Stone size	16.31±2.87	16.35±3.85	17.03±2.82	16.56±3.21	>0.05*,**,**
Stone density (Hounsfield unit)	1019.7±119.8	1021±123.8	1029.3±146.8	1023.7±129.3	0.96
Surgery duration (min)	76.17±22.7	90.45±30.31	59.90±23.35	76.31±28.48	0.20* ***0.024**** ***<0.001****
Hospitalization duration (average, min-max, median)	1.76 (1-3, med: 2)	4.13 (3-5, med: 4)	4.9 (2-13, med.: 4)	3.62	***<0.001*,**** ***0.047****

*: RIRS-miniPCNL, **: RIRS-PCNL, ***: miniPCNL-PCNL. Represents the p-value between the groups. Statistically significant differences are indicated in ***bold italics***. Groups with normal distribution are presented as mean and standard deviation, while those without normal distribution are shown with minimum-maximum and median values, RIRS: Retrograde intrarenal stone surgery, MiniPCNL: Mini-percutaneous nephrolithotomy, min-max: Minimum-maximum, PCNL: Percutaneous nephrolithotomy

Table 2. Preoperative and postoperative clinical outcomes

Features	RIRS (n=29)	MiniPCNL (n=31)	PCNL (n=30)	Total (n=90)	p-value
Hgb change (g/dL)	0.16±0.27	0.43±0.53	0.88±0.99	0.49±0.73	0.404* ***0.03**** ***0.001****
Transfusion requirement (n)	0	1	2	3	>0.05*,**,**
Complication (n)	0	2	3	5	>0.05*,**,***
Narcotic analgesia requirement (n)	0	4	13	17	0.125* ***0.004**** ***<0.001****
Residual stone presence (>4 mm, n)	8	3	8	19	0.156*,**,***

*: RIRS-miniPCNL, **: RIRS-PCNL, ***: miniPCNL-PCNL. Represents the p-value between the groups. Statistically significant differences are indicated in ***bold italics***. Groups with normal distribution are presented as mean and standard deviation, RIRS: Retrograde intrarenal stone surgery, MiniPCNL: Mini-percutaneous nephrolithotomy, PCNL: Percutaneous nephrolithotomy

detected in the follow-up urine culture. In the miniPCNL group, one patient developed severe hematuria (Clavien score 3A), and a three-way catheter was applied. The other three complications were transfusions performed due to perioperative hemoglobin drop (Clavien score 2).

In the catheterization information, DJS was inserted in all patients in the RIRS group. In the MiniPCNL group, Malecot nephrostomy was placed in 6 patients and DJS in 25 patients. In the PCNL group, 6 patients underwent malecot nephrostomy, 21 patients underwent re-entry, and 3 patients underwent malecot nephrostomy + DJS (Table 3). The distribution of the stones between the groups is shown in Table 4. There was no statistically significant difference between the groups regarding the surgical procedure and the calyx distribution of the stones between the groups (p=0.33) (Table 4).

In the analysis of the treatment groups, complications were observed in a total of five patients. In the PCNL group, one patient developed postoperative fever (Clavien score 2), was started on antibiotic therapy, and a urinary tract infection was identified in a follow-up urine culture In the miniPCNL group, severe hematuria occurred in three patients, requiring the placement of a three-way catheter (Clavien score 3A). The other three complications involved perioperative low hemoglobin levels, which necessitated blood transfusions (Clavien score 2). Although the complication rates between the groups were not statistically significant, it was observed that no complications occurred in the RIRS group.

Table 3. Postoperative catheterization methods

	RIRS	MiniPCNL	PCNL	Total
DJ catheter	29	25	0	54
Nephrostomy	0	6	6	12
Re-entry	0	0	21	21
Nephrostomy + DJ catheter	0	0	3	3
Total	29	31	30	90

RIRS: Retrograde intrarenal stone surgery, MiniPCNL: Mini-percutaneous nephrolithotomy, PCNL: Percutaneous nephrolithotomy, DJ: Double J

Table 4. Stone distribution across groups

	RIRS	MiniPCNL	PCNL	Total	p-value
Upper pole	10	6	5	21	0.33
Middle pole	7	11	9	27	
Lower pole	4	8	11	23	
Pelvis	8	6	5	19	
Total	29	31	30	90	

RIRS: Retrograde intrarenal stone surgery, MiniPCNL: Mini-percutaneous nephrolithotomy, PCNL: Percutaneous nephrolithotomy

Discussion

In this study, the efficacy and safety of RIRS, miniPCNL, and PCNL were prospectively compared in patients with 1-2 cm kidney stones who had previously failed ESWL treatment. The results demonstrated that while all three surgical approaches were effective in achieving stone clearance, they differed in terms of operative time, hospital stay, perioperative complications, and analgesic requirements. RIRS and miniPCNL were associated with shorter hospital stays and lower perioperative morbidity, whereas PCNL had the advantage of a shorter operative time but was associated with greater hemoglobin decline and higher analgesic requirements.

The findings align with previous studies that have evaluated the outcomes of these surgical techniques separately (12,13). A systematic review and meta-analysis by Cabrera et al. (14) comparing miniPCNL and RIRS for 10-20 mm lower pole stones concluded that both techniques had similar stone-free rates, but miniPCNL was associated with a longer operative time and greater blood loss. Another study by Chen et al. (15) comparing PCNL and RIRS found that PCNL had a higher stone-free rate but was associated with greater morbidity. Similarly, our study supports the notion that PCNL remains a robust option for stone removal, but may be less favorable due to its increased invasiveness and postoperative recovery period.

The mean operative time in our study was the shortest in the PCNL group (59.9 minutes), which is consistent with prior research showing that PCNL is generally faster than RIRS and miniPCNL for stones of this size range. However, this shorter duration may be counterbalanced by the increased morbidity associated with PCNL, as seen in the higher rates of perioperative hemoglobin reduction and narcotic analgesia requirements. Previous studies have reported similar trends, with PCNL showing a significantly greater need for postoperative pain management, likely due to the larger renal access sheath and increased tissue trauma, compared to the other methods (16,17).

One of the most critical factors influencing treatment decisions is hospital stay duration. Our study found that RIRS had the shortest hospital stay (1.76 days), followed by miniPCNL (4.13 days), while PCNL had the longest hospitalization period (4.9 days). These results are in accordance with prior studies in which RIRS is consistently associated with a faster recovery due to its minimally invasive nature and lack of renal tract dilation (9,18). A multicenter study by Karakoç et al. (19) evaluating lower pole stones found that hospital stays were significantly shorter in patients undergoing RIRS compared to those undergoing PCNL, reinforcing the findings observed in our study.

Despite the differences in perioperative morbidity, no significant difference was observed in residual stone rates among the three

techniques. The presence of residual stones (>4 mm) was slightly higher in the RIRS and PCNL groups than in miniPCNL, although this difference was not statistically significant. The stone-free rate is an important consideration in treatment selection, as residual stones may increase the risk of recurrence. While PCNL is traditionally considered superior in achieving complete stone clearance, recent advances in RIRS technology, including improved flexible ureteroscope designs and enhanced laser lithotripsy techniques, have significantly improved the stone-free rates associated with this approach (20,21).

Complications in our study were relatively low across all three techniques, with no major adverse events reported. PCNL had a higher incidence of perioperative hemoglobin drop, and required transfusions more frequently than miniPCNL and RIRS. These findings are consistent with a meta-analysis by Qiu et al. (22), which demonstrated that miniPCNL is associated with significantly less bleeding than standard PCNL. Furthermore, while RIRS was associated with fewer complications, it had a slightly higher residual stone rate, which is a known limitation of this method in cases where the stone burden is higher.

Additionally, ESWL failure can be attributed to factors such as stone density, location (especially in the lower pole), and stone size. Hard stones, in particular, are less likely to fragment efficiently under ESWL, as they resist the shock waves more effectively than softer stones. The hardness of the stone is often associated with its density, typically measured in HU; high-density (hard) stones may not break apart as effectively during ESWL treatment (23,24). Furthermore, the chemical composition of the stone plays a significant role; calcium oxalate stones, for example, are harder and may not respond well to ESWL, reducing its effectiveness. In our study, 113 patients, who did not achieve successful stone fragmentation despite undergoing at least two sessions of ESWL, were included. This highlights the limitations of ESWL in certain patient populations. Additionally, patient intolerance to the procedure and the inability to complete the recommended number of shock waves are key factors contributing to ESWL failure. These failures necessitate the use of more invasive treatments, such as RIRS, miniPCNL, and PCNL, which offer effective solutions for patients who do not respond to ESWL.

One of the key clinical implications of our study is the importance of individualized treatment selection. The choice between RIRS, miniPCNL, and PCNL should be based on patient-specific factors such as stone location, anatomy, comorbidities, and surgeon expertise. While PCNL remains the most efficient technique for large stone burdens, its increased morbidity may limit its use in cases where a less invasive approach could be equally effective. RIRS, on the other hand, offers a safer profile with a quicker recovery but may require staged procedures for complete stone clearance in larger stone burdens. MiniPCNL appears to be a middle ground, providing better stone clearance than RIRS while maintaining a lower complication profile than standard PCNL (25).

Study Limitations

This study has several limitations that must be considered when interpreting the results. Although the study was conducted prospectively, randomization was not feasible. Patients were provided with information regarding all three surgical options-RIRS, miniPCNL, and PCNL-before the procedure. As a result, the lack of random assignment may have introduced selection bias, influenced by patient preferences or physician recommendations. These factors could have contributed to the unequal distribution of confounding variables, including surgeon choice, patient-specific anatomical features, and stone characteristics. To minimize such biases and strengthen the evidence, a prospective, randomized controlled trial would be required.

Second, this study was conducted at a single center, limiting the generalizability of the findings to other institutions with different surgical expertise, technological capabilities, and patient demographics. The results might not fully reflect the variability in surgical outcomes that could be observed in multi-center or international studies. Additionally, the experience and technique of individual surgeons performing RIRS, miniPCNL, and PCNL can significantly influence outcomes such as operative time, complication rates, and stone-free rates, which were not standardized in this study.

Another limitation is the lack of long-term follow-up data. The primary outcome measures were assessed within two months postoperatively, focusing on short-term perioperative outcomes. Long-term factors such as stone recurrence rates, retreatment necessity, and overall patient satisfaction were not evaluated. Since nephrolithiasis is a chronic and recurrent disease, understanding long-term effectiveness and recurrence prevention strategies is crucial for optimizing treatment decisions. Future studies should incorporate follow-up periods of at least 12 months to assess stone regrowth, new stone formation, and potential complications such as ureteral stricture development or renal function deterioration.

Additionally, while stone-free status was evaluated using CT, the criteria for residual stone significance (>4 mm) is subject to debate. Some studies suggest that even residual fragments as small as 2 mm, although commonly used in the literature, could increase recurrence risk. Furthermore, factors such as infundibulopelvic angle, calyx neck width, stone-skin distance, and stone composition were not assessed, despite their known impact on stone fragmentation and clearance. The inclusion

of these parameters, which were not assessed in our study, could provide more comprehensive insights into the factors influencing ESWL failure and surgical outcomes.

A further limitation is the lack of standardized pain assessment and postoperative recovery parameters, beyond hospital stay duration and narcotic analgesic requirements. While the study highlights that PCNL was associated with higher analgesic needs, the absence of a structured pain scoring system such as the visual analog scale makes it difficult to quantify and compare pain severity across groups objectively. Including validated pain assessment tools in future research would allow for a more precise evaluation of postoperative comfort and recovery trajectories.

Lastly, the cost-effectiveness of each procedure was not analyzed. While RIRS and miniPCNL demonstrated advantages in terms of shorter hospital stays and lower morbidity, the financial implications of these approaches compared to PCNL were not assessed. Factors such as procedure duration, equipment costs, hospital resource utilization, and patient return-to-work times play a significant role in clinical decision-making. Future studies should incorporate economic analyses to determine the most cost-effective strategy for treating ESWL-resistant kidney stones.

Conclusion

All three surgical methods-RIRS, miniPCNL, and PCNL-were found to be effective and safe for the treatment of 1-2 cm kidney stones following failed ESWL. RIRS and miniPCNL were associated with shorter hospital stays and lower perioperative morbidity, while PCNL demonstrated the shortest operative time but had higher analgesic requirements and greater hemoglobin decline. The choice of surgical technique should be tailored to individual patient characteristics, considering factors such as stone burden, renal anatomy, and patient recovery expectations. Future prospective studies with larger sample sizes and long-term follow-up are needed to further refine treatment algorithms for patients with ESWL-resistant kidney stones.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Düzce University Clinical Research Ethics Committee (approval number: 2014/63, date: 28/10/2014).

Informed Consent: Written informed consent was obtained from all patients before undergoing surgical intervention.

Footnotes

Authorship Contributions

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

Conflict of Interest: Ali Tekin MD is section 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.

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Evaluating Surgical Outcomes: Anterior Colporrhaphy *versus* Transobturator Tape Surgery on Urinary Incontinence and Sexual Function

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

Urinary incontinence symptoms are quite common among women. It has a significant impact on quality of life, and creates personal and social financial burdens. Stress urinary incontinence (SUI) is considered the most common type of urinary incontinence, especially in women of menopausal and reproductive age. Various quality of life questionnaires, such as the Female Sexual Function Index (FSFI) and the 12-question Pelvic Organ Prolapse Urinary Incontinence Sexual Questionnaire (PISQ), have been developed to assess the impact of SUI. This study investigated the effects of various surgical treatments for SUI on FSFI and PISQ results, as well as the effectiveness of these results in monitoring treatment response.

Abstract

Objective: Sexual desire is considered to be the sum of positive and negative components of sexuality. The aim of our study was to compare the effects of anterior colporrhaphy and transobturator tape (TOT) surgery on urinary incontinence and sexual function.

Materials and Methods: One hundred and eighty-eight patients who were admitted to our hospital between January 2018 and October 2023, diagnosed with stress urinary incontinence (SUI) and pelvic organ prolapse and who were then operated on, were evaluated retrospectively. The patients were divided into two groups: anterior colporrhaphy and TOT, and the presurgery and postsurgery the Female Sexual Functıon index (FSFI) and Pelvic Organ Prolapse Urinary Incontinence Sexual Questionnaire (PISQ) scores of the two groups were evaluated retrospectively.

Results: No significant difference was found between the groups when PISQ scores were compared in the pre-surgery and post-surgery periods according to surgery type ($p>0.05$). No significant difference was found between the groups when FSFI scores were compared in the pre-surgery and post-surgery periods, according to surgery type, ($p>0.05$). When the presurgery and postsurgery periods were compared within both groups, a significant increase in the PISQ score was found in the postsurgery period ($p<0.05$). A significant increase in sexual satisfaction score was found in the TOT group in the post-surgery period ($p=0.016$).

Conclusion: It has been found that anterior colporrhaphy and TOT surgeries are effective in the treatment of stress urinary incontinence, and have significant effects on urinary incontinence complaints during sexual intercourse. Sexual function is multifactorial, and anatomical corrections made with surgical methods alone are not sufficient to correct different aspects of sexual function such as orgasm, sexual desire, sexual problems in the partner, and satisfaction. PISQ and FSFI measurements may provide insight into the evaluation of sexual function after SUI and pelvic organ prolapse surgery.

Keywords: Anterior colporrhaphy, FSFI, pelvic organ prolapse, transobturator tape, sexual function, stress urinary incontinence

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Introduction

Sexual desire can be expressed as the sum of the factors that push us towards or away from sexuality. Sexual desire should be evaluated in a wide range of aspects such as disgust, reluctance, interest, a need and passion. Many individuals have a characteristic pattern of desires throughout their adult life, and this spectrum can change significantly, influenced by various factors (1). The World Health Organization (WHO) defines sexual health as "a state of physical, emotional, mental and social well-being related to sexuality". It does not define sexual health as the absence of any disease, dysfunction or disability (2). WHO defines sexual health as the integration and harmony between the mind, emotion, and body, which leads to the development of social, intellectual, communication, and love aspects of an individual's personality. Therefore, any disorder that causes inconsistency, dissatisfaction, and withdrawal from sexual intercourse can lead to sexual dysfunction (3). In various studies, the prevalence of sexual dysfunction among sexually active women is between 30% and 50% (4-7). In our country, the prevalence of sexual dysfunction was determined to be 29.5% (8). Studies in the literature have shown that sexual dysfunctions affect the quality of life of women and that the evaluation of sexual function plays an important role in assessing quality of life (9,10). Sexual dysfunction is a prevalent problem in women. Studies in the literature have shown that pelvic floor disorders such as urinary incontinence and pelvic organ prolapse affect sexual function (11-13). The study by Tok et al. (14) showed that pelvic organ prolapse affects some aspects of sexuality, but not others, such as orgasm and sexual satisfaction. Population studies conducted in many countries have reported that the prevalence of urinary incontinence varies between approximately 5% and 70%, while most studies indicate it is in the range of 25-45% (15). Urinary incontinence is one of the factors affecting sexual function and can lead to feelings of shame and guilt in women during or after sexual intercourse due to incontinence during intercourse. Stress urinary incontinence (SUI) has a prevalence of between 4% and 35% in the population. The clinical definition of SUI has been established by the International Continence Society (16). Its epidemiological definition has not yet been established, resulting in a wide range of prevalence rates reported in studies (16). Although urinary incontinence is not directly related to sexual function, it plays a crucial role in affecting human sexual function. Sexual health is integral to the overall quality of life and should be emphasized because it is linked to a woman's self-esteem, emotional well-being, and even cognitive function (17). There is currently no highly effective medical treatment for urinary incontinence. Drugs such as estrogens, alpha-adrenergic receptor agonists, beta-adrenergic receptor agonists, and tricyclic antidepressants are used in the treatment of urinary incontinence, and their potential for effectiveness is low. In these patients, surgery is considered an alternative treatment option. The main purpose of urinary incontinence surgery is based on the logic of correcting the urethrovesical angle to prevent the urethra from descending by providing support when intra-abdominal pressure increases (18). In incontinence surgery, sling placement surgeries under the urethra, including the classic pubovaginal sling using autologous sling materials (such as rectus fascia and fascia lata), anterior colporrhaphy, and tension-free vaginal tape and transobturator tape (TOT) are performed. Various quality of life questionnaires, such as the International Incontinence Consultation Questionnaire, the Incontinence Severity index, and the Incontinence impact questionnaire, have been developed to assess the impact of SUI on quality of life, but their results may vary. The aim of our study was to compare the effects of anterior colporrhaphy and TOT surgery on urinary incontinence and sexual function.

Materials and Methods

Our study was designed as a retrospective cohort study. The study was designed according to the Helsinki Declaration and informed consent forms were obtained from all patients. The study was initiated after receiving approval dated 09/10/24 and numbered KA-24/311 from the Başkent University Rectorate Medical and Health Sciences Research Board. In our study, 248 patients diagnosed with SUI and pelvic organ prolapse between January 2018 and October 2023 were evaluated retrospectively. Sixty patients, who had incomplete data, lacked a sexual function questionnaire test, and met the exclusion criteria, were excluded from the study. Data from 188 patients who underwent anterior colporrhaphy and TOT were evaluated retrospectively. Ninety-eight patients were included in the anterior colporrhaphy group and ninety patients in the TOT group. While TOT was performed on patients with stress urinary incontinence, anterior colporrhaphy was performed on patients with anterior compartment defect. The questionnaire forms, used to evaluate the sexual function of all patients preoperatively and at 6 months postoperatively, were evaluated retrospectively. Body mass index (BMI), gravida, parity, education level and delivery method of all patients were evaluated retrospectively. Inclusion criteria included patients giving consent to participate in the study, stress urinary incontinence, active sexual life, and pelvic organ prolapse. Exclusion criteria included having given birth within the last year, history of pelvic and breast surgery, history of narcotic drug or antidepressant use in the patient or partner, history of diabetes, hypertension and heart disease in the patient or partner, and sexual problems in the partner (premature ejaculation and impotence). In the anterior colporrhaphy method, the patient is placed in the lithotomy position after spinal anesthesia is applied. An incision is made in the anterior wall of the vagina from the bladder neck level

to the vaginal arch, and the vaginal epithelium and endopelvic fascia are dissected from each other. After the dissection, the endopelvic fascia on both sides is closed and repaired with 2-0 Vicryl sutures using the interrupted technique. 0-number chromic suture is used for primary repair of the vaginal mucosa. In the presence of urinary incontinence, the urethra is angled using Kelly sutures in the endopelvic fascia below the bladder sphincter. In the TOT method, the patient is placed in the lithotomy position after spinal anesthesia is applied. First, the guide point is determined where the line intersects the femoral line 1 cm above the clitoris. A 2 cm incision is made in the vaginal mucosa in the suburethral region, below the urethral os point. The paraurethral space is then opened from the vagina, and the finger is directed behind the symphysis pubis. After ensuring that the obturator space is entered, TOT is placed using the TOT applicator from the determined point from the outside to the inside, using the TOT applicator from the determined point the vaginal mucosa is primarily repaired. A Foley catheter is inserted for 24 hours to evaluate the quality and quantity of urine. The 12-question Pelvic Organ Prolapse Urinary Incontinence Sexual Questionnaire (PISQ) consists of questions covering three main points: behavior and excitement (4 questions); physical factors such as urinary incontinence during sexual intercourse, feelings of fear, feelings of shame and guilt, and lack of comfort in the bedroom (5 questions); and factors related to the sexual partner (3 questions). The PISQ is scored on a Likert scale from 0 to 4 as "never", "rarely", "sometimes", "usually", and "always" (19,20). The Female Sexual Function Index (FSFI) questionnaire, assessing six different domains: desire, arousal, lubrication, orgasm, satisfaction, and pain/discomfort, which used a scale from 0 (no sexual activity in the last 4 weeks) and 1 (very dissatisfied) to 5 (very satisfied) at weeks 0, 4, 8, and 12. Throughout the study, a full-scale score ranging from 2.0 (severe dysfunction) to 36.0 (no dysfunction) was employed to evaluate sexual function, with increased FSFI scores considered to be associated with symptom improvement (21). An optimal cut-off score of 26, reported by Wiegel et al. (22), is used to distinguish women with and without current sexual dysfunction.

Statistical Analysis

Statistical analysis was conducted by utilizing the SPSS 26.0 (IBM Inc., Chicago, IL, USA). The normality of the distribution was evaluated with the Kolmogorov-Smirnov test and Shapiro-Wilk test. Data analysis was done using the chi-squared test, independent t-test, and paired t-test. The quantitative data of the patients were reported as mean ± standard deviation (SD) (minimum-maximum). The results were evaluated with a 95% confidence interval. The p-value <0.05 was regarded as statistically significant. The G * Power 3.1 program (Erdfelder, Faul and Buchner, Düsseldorf, Germany) was used for post hoc power analysis. The α error probability, effect size, and power of the study were 0.05, 0.3, and 0.95, respectively. The total required sample size was calculated as 176.

Results

The mean age of the women in our study was 42.7±25.8, and the mean BMI was 30.7±4.76 kg/m^2. Among the operated patients, improvement in complaints was observed in 176 (93.6%) women. No significant difference was found between the groups in terms of demographic and obstetric data (Table 1).

In the anterior colporrhaphy group, behaviour and emotions scores were found to be significantly higher in the after-surgery period compared to the before-surgery period. Mean behavior and emotions scores increased from 7.67 to 10.96 (p<0.001). In the anterior colporrhaphy group, physical factor scores and total score were found to be significantly higher after surgery compared to before surgery. Mean physical factor scores

Table 1. Comparison of demographic and obstetric data of patients

Variables	Anterior colporrhaphy group (n=98)	TOT group (n=90)	p-value
	Mean ± SD		
Age (year)	42.60±26.54	42.94±25.18	0.86
BMI (kg/m^2)	30.84±4.64	30.58±4.88	0.77
Parity	2.88±1.18	2.92±1.24	0.82
Gravidity	3.14±1.29	3.11±1.31	0.79
***Level of education** (n-%)			0.89
Middle and high school	71 (72.4%)	64 (71.1%)	
University	27 (27.6%)	26 (28.9%)	
***Mode of delivery** (n-%)			0.87
NSVD	63 (64.2%)	59 (65.5%)	
C/S	35 (35.8%)	31 (34.5%)	

TOT: Transobturator tape, BMI: Body mass index, NSVD: Normal spontaneous vaginal delivery, C/S: Cesarean section, SD: Standard deviation

Table 2. Comparison of PISQ measurements between and within groups			
Variables	**Anterior colporrhaphy group (n=98)**	**TOT group (n=90)**	****p-value**
	Mean ± SD		
Behaviour and emotions			
Before surgery	7.67±1.82	8.15±2.16	0.78
After surgery	10.96±1.36	11.22±1.18	0.84
*p-value	<0.001	<0.001	
Physical factor			
Before surgery	14.82±1.18	14.14±1.86	0.69
After surgery	16.60±1.08	16.35±1.72	0.72
*p-value	<0.001	<0.001	
Factors related to sex partner			
Before surgery	5.22±1.54	5.14±1.25	0.88
After surgery	5.60±1.66	5.50±1.32	0.92
*p-value	0.68	0.72	
Total score			
Before surgery	27.71±4.28	27.43±5.09	0.86
After surgery	33.16±4.08	33.07±4.18	0.92
*p-value	<0.001	<0.001	

*: p-value: Match test; **: p-value: Independent test, SD: Standard deviation, TOT: Transobturator tape, PISQ: Pelvic Organ Prolapse Urinary Incontinence Sexual Questionnaire

increased from 14.82 to 16.60 (p<0.001). Total score increased from 27.71 to 33.16 (p<0.001). In the TOT group, scores for behavior and emotions were found to be significantly higher in the after-surgery period compared to the before-surgery period. Mean behaviour and emotions scores increased from 8.15 to 11.22 (p<0.001). In the TOT group, physical factor scores and total scores were found to be significantly higher in the after-surgery period compared to the before-surgery period. Mean physical factor scores increased from 14.14 to 16.35 (p<0.001). Total score increased from 27.43 to 33.07 (p<0.001) (Table 2).

In the TOT group, sexual satisfaction scores were found to be significantly higher in the after-surgery period compared to the before-surgery period. Mean FSFI score increased from 3.88 to 4.24 (p=0.016) (Table 3).

Discussion

When patients who underwent surgery for pelvic organ prolapse and SUI were evaluated, no significant difference was found in the pre- and post-surgery sexual function scores of patients who underwent TOT and anterior colporrhaphy surgery, depending on the type of surgery. In the study conducted by Pauls et al. (23), despite anatomical and functional improvements after pelvic organ prolapse and urinary incontinence surgery, no change was detected in sexual function, and it was stated that this could be due to postoperative dyspareunia. Pastore et al. (24) found significant improvement in all subparameters of FSFI scores in patients who underwent surgery for SUI. In the study conducted by Zalewski et al. (25), it was revealed that the operation significantly reduced the feeling of pain during sexual intercourse, decreased sexual arousal, and worsened vaginal wetness after urinary incontinence surgery. Horosz et al. (26) demonstrated that successful treatment of SUI significantly improves the quality of sexual life. It is thought that the difference in results between studies in the literature may be due to the difference in the number of samples and the wide spectrum of data regarding the time elapsed after surgery. In our study, after anterior colporrhaphy and TOT surgeries, significant improvements were observed in urinary incontinence during sexual intercourse, as well as fear, shame, guilt, and lack of comfort in the bedroom. These criteria are accepted as behavior and emotions, and physical factor subscales. In the study conducted by Handa et al. (11), it was determined that urinary incontinence due to SUI in women was associated with decreased libido, vaginal dryness and dyspareunia, and that the treatment of this disorder had a positive effect on these complications. Brubaker et al. (27) stated that sexual dysfunctions due to SUI improved after surgery, but this was not related to the surgical method. Our study also revealed that the type of surgery had no effect on the parameters of sexual function in the postsurgery period. Dursun et al.'s (28) meta-analysis evaluated sexual function in patients who underwent TOT, and revealed that TOT surgery improved female sexual function. Bicudo-Fürst et al. (29) state that the effect of urinary incontinence surgery on sexual function is not definitive and there is inconsistency between studies. Energin and Eric Horasanli (30) reported that short-term improvement in sexual function was achieved in women who underwent

Table 3. Comparison of FSFI measurements between and within groups			
Variables	**Anterior colporrhaphy group (n=98)**	**TOT group (n=90)**	****p-value**
	Mean ± SD		
Sexual desire			
Before surgery	3.76±1.36	3.70±1.58	0.77
After surgery	3.56±1.18	3.77±1.38	0.82
*p-value	0.72	0.9	
Sexual arousa			
Before surgery	3.99±1.26	3.94±1.16	0.8
After surgery	4.08±1.36	4.09±1.21	0.94
*p-value	0.86	0.76	
Vaginal moisturizing			
Before surgery	4.26±1.41	4.12±1.39	0.82
After surgery	4.47±1.28	4.06±1.36	0.46
*p-value	0.56	0.69	
Orgasm			
Before surgery	3.99±1.64	3.76±1.18	0.78
After surgery	4.07±1.49	3.93±1.14	0.85
*p-value	0.62	0.48	
Pain			
Before surgery	4.22±1.28	4.1±1.36	0.66
After surgery	4.04±1.02	3.92±1.18	0.94
*p-value	0.82	0.07	
Sexual satisfaction			
Before surgery	3.82±1.38	3.88±1.18	0.81
After surgery	4.06±1.28	4.24±1.26	0.77
*p-value	0.18	0.016	
Total score of sexual function			
Before surgery	24.04±5.38	23.5 ±5.67	0.36
After surgery	24.28±5.98	24.01±5.22	0.76
*p-value	0.78	0.37	

*: p-value: Match test; **: p-value: Independent test, SD: Standard deviation, TOT: Transobturator tape, FSFI: Female Sexual Function Index

anterior colporrhaphy surgery due to pelvic organ prolapse. Jafarzade and Ulu (31) found that orgasm was significantly reduced in women who underwent anterior colporrhaphy. They also stated that it is appropriate to recommend conservative or alternative treatments for the early stages of cystocele. In our study, the FSFI scales and sub-parameters were evaluated during the presurgery and postsurgery periods, and no significant difference was found between the groups according to the type of operation. However, no significant difference was found between the groups in terms of changes in FSFI scales, and subparameters in the pre-surgery and post-surgery periods. Although a significant improvement was achieved in the sexual satisfaction score in the TOT group at the 6th month follow-up, no additional supporting FSFI subgroup score could be obtained. The variable effects of surgery on sexual function reported in the literature may be attributed to the sexual index scales used in the evaluation and the subjective responses of patients to these scale questions. In our study, 72.3% of women had urinary incontinence during sneezing, coughing, or sexual intercourse, and 93.6% of these cases improved after surgery. Pace and Vicentini (32) reported that 67% of women experienced urinary incontinence during intercourse, 96% during penetration, and 4% during orgasm. 97.1% of women who underwent TOT reported that their urinary incontinence improved; 90.1% reported relative improvement in their sexual life, while 9.9% reported poor sexual function (32). In our study, 42.5% (80/188) of the women had desire problems, 38.2% (72/188) had arousal problems, and 44.6% (84/188) had lubrication problems. In our study, 47.8% (90/188) of the women had orgasm problems, 37.2% (70/188) had satisfaction problems, and 11.7% (22/188) had pain during sexual intercourse. Maaita et al. (33) also reported similar results regarding the prevalence

of sexual dysfunction. In the study by Kamińska et al. (34), a significant improvement was found in PISQ scores after SUI and pelvic organ prolapse surgery. In a study by Rogers et al. (35), on the contrary, sexual satisfaction was found to have decreased three and six months after surgery. In the study by Glass Clark et al. (36), women who underwent anti-incontinence surgery showed general improvement in sexual function from baseline to 24 months after surgery, without significant differences depending on the surgical procedure. Most of this improvement occurred in the first 12 months and was stated to continue for an additional 12 months, lasting a total of 24 months. In our study, significant improvement was found in PISQ total score, behaviour and emotions score, and physical factor scores regardless of the type of operation. In the study conducted by Kammerer-Doak (37) on the sexual satisfaction of women with pelvic floor problems, better performance was reported regarding physical factors and partner-related factors in women after urinary incontinence and pelvic organ prolapse surgery. Significant improvement was found in the subscales of the PISQ questionnaire. However, no significant improvement was found in sexual function measures such as orgasm and arousal. In our study, significant improvement in PISQ scores was found in the post-surgery period for both types of surgery, while no significant improvement was found in FSFI scores. The reason for this is that it is easier to see the direct effects of the operation in the PISQ group, since it includes parameters that evaluate the presence of incontinence and prolapse; this inference, however, is not valid for the FSFI questionnaire. In our study, anterior colporrhaphy and TOT surgeries were found to be effective in the treatment of stress urinary incontinence, and significant improvements were found in complaints of urinary incontinence during sexual intercourse and in feelings of shame or guilt experienced during intercourse. However, no significant difference was found in the results depending on the type of surgery. However, there is no basic element of active sexual life.

Study Limitations

One of the main limitations of the study is its retrospective design. However, the difficulties in expressing sexual dysfunction due to the ethical constraints of the patients in the study may be considered as a second reason.

Conclusion

It has been found that anterior colporrhaphy and TOT surgeries are effective in the treatment of SUI and have significant effects on urinary incontinence complaints during sexual intercourse. Sexual function is multifactorial, and anatomical corrections made with surgical methods alone are not sufficient to correct different aspects of sexual function such as orgasm, sexual desire, sexual problems in the partner and satisfaction. PISQ and FSFI measurements may provide insight into the evaluation of sexual function after SUI and pelvic organ prolapse surgery. Prospective studies with longer follow-up periods and larger numbers of patients are needed for women who underwent anterior colporrhaphy and TOT surgeries.

Ethics

Ethics Committee Approval: The study was initiated after receiving approval dated 09/10/24 and numbered KA-24/311 from the Başkent University Rectorate Medical and Health Sciences Research Board.

Informed Consent: Declaration and informed consent forms were obtained from all patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: U.A., B.Ö., Concept: U.A., B.Ö., Design: U.A., Data Collection or Processing: B.Ö., Analysis or Interpretation: M.U.M., Literature Search: U.A., Writing: U.A., B.Ö.

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ORIGINAL RESEARCH
General Urology

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An Objective Quantitative "Quality Factor" for Scientific Meetings, Is It Possible? A New Formula

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

Many scientific conferences are organized in the medical field. how can the quality of a conference be measured? In the literature, there is no comprehensive method to evaluate the quality of scientific conferences. We offer a comprehensive approach to this problem. With the formula we have developed, we aim to measure the quality of conferences.

Abstract

Objective: Numerous local and international meetings are held in the field of medicine. Up-to-date information and experiences are shared at these meetings. It also provides an opportunity to pave the way for collaborations. There is a need for an objective and reliable tool to evaluate conference quality. In our study, we aimed to develop an objective and understandable quality factor (QF) that evaluates scientific congresses.

Materials and Methods: Between 2021 and 2022, abstract books of four national meetings of the Society of Urological Surgery in Turkey (MSUST) were reviewed [(2012 (MSUST1), 2014 (MSUST2), 2016 (MSUST3), 2018 (MSUST4)]. A total of 1,436 abstracts were evaluated. The publication status of the abstracts presented at a conference in scientific articles a scientific journal within the first two years was investigated in scientific journals using the Web of Science, PubMed, and Google Scholar databases. The impact factors of the scientific journals in which Abstracts were published and the H Indices of the scientists invited as speakers to the congress were taken from the Web of Science database. The H-index values of the speakers at the time of their participation in the meeting were considered. Considering these three parameters, we created a QF for scientific congresses. QF = [(abstracts publication rate in two years x average impact factor of journals) + average H Index of speakers]/10.

Results: MSUST1, MSUST2, MSUST3, and MSUST4 had a follow-up of 96, 72, 48, and 24 months, respectively. The percentages of abstracts in MSUST1, MSUST2, MSUST3, and MSUST4 were 31.6%, 19.9%, 13.8%, and 14.1%, respectively, with no time limit set for inclusion, and all were published in a scientific journal. Median publication times of Abstracts in MSUST1, MSUST2, MSUST3, and MSUST4 were 23 (-2 to 88), 11 (-2 to -60), 10.5 (-2 to -39), and 7 (-2 to -24) months. The average H-index of the speakers at the UCD4 meeting was 13.6±11.5, the average impact factor of the journals in which abstracts was published was 2.029±0.84, and the rate of publication of abstracts in a 24-month period was 14.1%. With the formula we suggested, the QF of the MSUST4 meeting was calculated as 4.22 [(14.1x2.029)+13.6]/10=4.22.

Conclusion: The QF we recommend is easy to calculate and can be used objectively to evaluate the quality of scientific meetings. However, our primary goal is to draw attention to this direction, instead of developing this formula. We believe this tool will help physicians manage their time, energy, and financial resources.

Keywords: Scientific congresses, formula, quality, h-index, impact factor

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Introduction

An immense number of annual meetings are held in the medical field on local and international scales. These meetings provide an environment for sharing the most up-to-date information and precious experience, as well as creating opportunities for networking that pave the way for future collaboration. From this point of view, international congresses play an important role in education and development of young professionals; therefore, they are promoted by relevant medical societies. However, it is a controversial topic.

Some colleagues argue against certain aspects of international congresses, mentioning their negative impact on carbon emissions, while others defend them (1). Ioannidis J. P. A. argues that conferences have little to do with scientific knowledge dissemination and suggests reevaluating our standpoint on international gatherings (2).

With advances in communication technology as well as an increase in alternatives for conventional meetings, the rationale for large in-person gatherings becomes unclear. Considering recent restrictions imposed on both national and international meetings by local authorities to prevent the spread of Coronavirus disease 2019, attending an international congress is a decision of crucial importance. This development forces us to reconsider our perspective on participation. In this regard, we believe that there is a vital need for an objective and reliable tool to assess congress quality.

The aim of the present paper is to propose an objective criterion to determine the scientific value of any given congress, thus facilitating the decision-making process. We believe that this tool would be of great assistance to physicians in managing their time, energy and financial resources.

Materials and Methods

Abstract books of four national meetings of the Society of Urological Surgery, in Turkey (MSUST), were reviewed [2012 (MSUST1), 2014 (MSUST2), 2016 (MSUST3), 2018 (MSUST4)]. A total of 1,485 abstracts from these 4 meetings held between 2021 and 2022 were reviewed. Poster (visual or oral) presentations were not included in the study. A total of 1,436 abstracts from four meetings were included in the study.

The publication status of these abstracts in a scientific journal within the first two years after the meeting was investigated using the Web of Science, PubMed, and Google Scholar databases. The databases were searched, by the first author of the abstracts. When first author searching was unsuccessful, the search was conducted with subsequent authors. Published papers identical to the abstracts in hypothesis, study design, and conclusion were considered a match and included in the study. Abstracts published more than three months before the congress date were excluded from the study. The publication time was calculated as the time interval between a meeting and the online availability of an abstract. Publication rates in the first two years were calculated. The median publication time was determined for all meetings.

In the fourth MSUST, studies that were published as abstracts and later published in a journal were identified. The impact factors of the journals in which these studies were published were obtained.

The H-indices of the lecturers who attended the fourth MSUST as speakers were taken from Web of Science. The H-index values of the speakers at the time of their participation in the meeting were considered.

Considering these three parameters, we created a scientific congress quality factor. Quality factor (QF) = [(Abstracts publication rate in two years x average impact factor of journals) + average H-index of Speakers]/10.

Statistical Analysis

Data were analyzed using SPSS 23.0 software. Non-parametric data were presented as median (minimum-maximum). Parametric data were presented as mean ± standard deviation. The Kaplan-Meier survival analysis was used for assessing publication times. The distribution of publication times was examined by survival analysis.

Results

Forty-nine of 1,485 abstracts were excluded because they were published more than three months before the meetings. A total of 1,436 abstracts were investigated. The 1st MSUST, 2nd MSUST, 3rd MSUST, and 4th MSUST had a follow-up time of 96, 72, 48, and 24 months, respectively.

The overall publication rates of the 1st MSUST, 2nd MSUST, 3rd MSUST, and 4th MSUST were 31.6%, 19.9%, 13.8%, and 14.1%, respectively (Figure 1). The median publication time of the 1st MSUST, 2nd MSUST, 3rd MSUST, and 4th MSUST was 23 months (-2 - 88), 11 months (-2 - 60), 10.5 months (-2 - 39), and 7 months (-2 - 24), respectively. Using survival analysis of the abstracts published, 24-month publication rates of 1st MSUST, 2nd MSUST, 3rd MSUST, and 4th MSUST were 59.3%, 81%, 86%, and 100%, respectively (Figure 2). The publication curves for all times are provided in Figure 3. Accordingly, we used a publication time interval of two years. The publication rates for the first two years of the 1st MSUST, 2nd MSUST, 3rd MSUST, and 4th MSUST were 18.8%, 16.3%, 12%, and 14.1%, respectively (Figure 4).

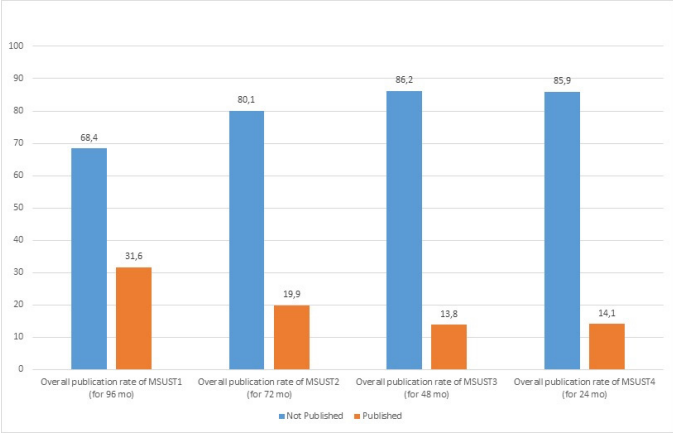

Figure 1. Overall publication rate

MSUST: Meetings of the Society of Urological Surgery in Turkey

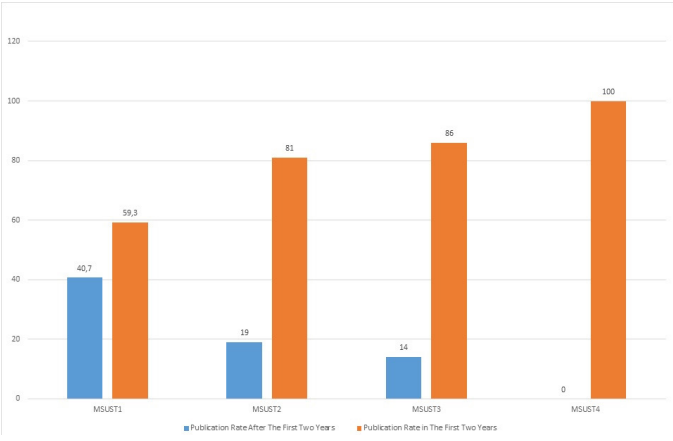

Figure 2. Publishing rates of published abstracts in the first two years

MSUST: Meetings of the Society of Urological Surgery in Turkey

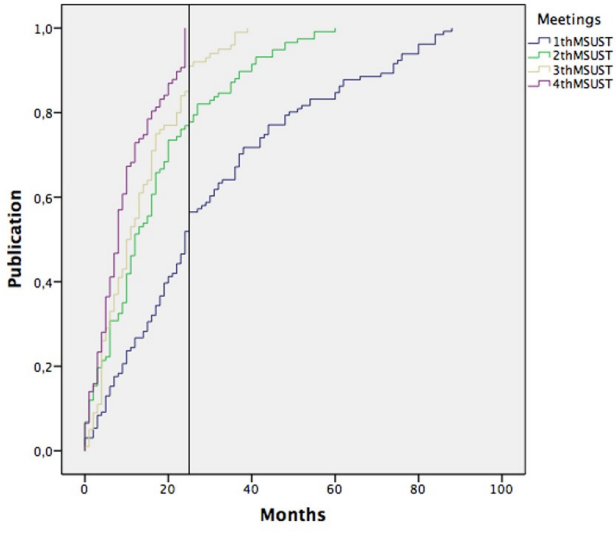

Figure 3. The publication curves for the MSUSTs

MSUST: Meetings of the Society of Urological Surgery in Turkey

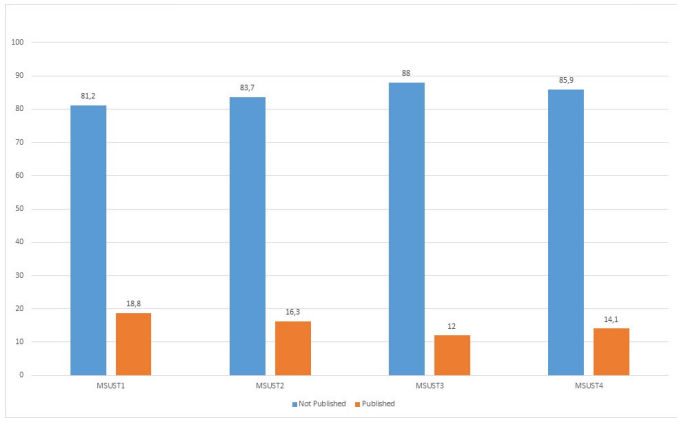

Figure 4. The publication rates for the first two years

MSUST: Meetings of the Society of Urological Surgery in Turkey

At the fourth meeting of MSUST, the average H-index of lecturers participating as speakers was 13.6±11.5, and the average impact factor of journals of published abstracts was 2.029±0.840.

In summary, at MSUST's fourth meeting, the rate of publication in a journal in the first two years, the mean impact factor of journals, and the average H-index of speakers were 14.1%, 2.029, and 13.6, respectively.

In summary, with the formula we suggested, the QF of the MSUST4 meeting was calculated as 4.22 [(14.1x2.029)+13.6]/10=4.22. We tried to simplify the result by taking 10% of the obtained value, therefore, we divided the output by 10.

Discussion

Every year, international or national scientific meetings are held in several scientific fields around the world. Scientific meetings are especially important for young scientists to follow and discuss the developments in their fields, to present their own research, and to reveal new ideas. However, there is no objective, widely used assessment system that compares congresses or measures the quality index of a congress. The issue that has been popular especially in the last two decades is the publication rates of congresses. These rates in almost all fields have been evaluated (3). These papers explore the factors associated with the publication of abstracts accepted to the congress and provide publication rates of scientific congresses. In fact, the publication rate is an important matter of prestige for congresses. Especially in urology, prestigious associations such as the American Urological Association, European Association of Urology, Société Internationale d'Urologie, and European Society for Pediatric Urology also reported the publication rates of their own congresses (4-7). However, examination of these publications shows differences in the databases used to review the publications, the methods of matching publications and

abstracts, and, more importantly, the follow-up times of studies. Therefore, although the publication rates provide information about congresses, it is very difficult to make a comparison due to the aforementioned reasons. Thus, these parameters need to be standardized. However, it is believed that the publication rate alone would be insufficient to compare the congresses in terms of scientific value.

The important factor to be considered while examining the publication rates is follow-up. There are studies conducted with a long follow-up of up to 120 months (8-10). Scherer et al. (3) examined 181 studies in their systematic review with follow-up time using survival analysis and showed an increase in the publication rate over time. The authors also established a publication rate of 68.7% and 44.9% for randomized-controlled studies and other types of studies, respectively, at a 10-year follow-up. Examination of their survival graphs shows that more than half of the studies of all study designs were published within two years. In our study, we observed that more than half of all publications, including the 1st MSUST, which had the longest follow-up (96 months), were within the first two years of their follow-up periods. Although the publication rate in the first two years does not include the overall publication rate of congresses, we believe that it can be used as a better indicator.

Today, bibliometric indicators are used by researchers and journals. Although there are some controversial aspects, the use of these bibliometric measurements is accepted by the scientific community. The H-index was proposed to assess the scientific output of an individual researcher (11). Although Hirsch first defined the H-index for the field of physics, it was later applied to almost all fields over time. The H-index was defined by Hirsch as the number of papers with a citation number of ≥ h. For example, if a researcher's H-index is 5, it means that the researcher has 5 publications that have been cited at least 5 times. However, the H-index also has limitations. The most important limitation is that the researcher must engage in scientific research for a certain length of time. Therefore, its correlation with age is not surprising. Another limitation of the H-index is self-citation, and friendly cross-citations, thus, the H-index of researchers may increase quickly (12,13). Another issue is the contribution of the authors to the study. Since citations received by a study affect all authors equally, the first and last authors will be evaluated in the same way as other authors (13). The H-index should vary by field. This is because it would not be fair to compare researchers working in two different fields, where the total numbers of citations and articles during given periods are very different. The H-index is a currently applicable bibliometric indicator despite its obvious limitations.

The bibliometric indicator commonly used for journals is the impact factor. The impact factor is calculated by dividing the number of citations received by a journal in the two years, by the total number of publications in that time period (14). However, a high impact factor of the journal does not indicate the high quality of every article. Since the impact factor is calculated over the total number of citations, it may not accurately represent the citation impact of all articles published in the journal. Furthermore, the I impact factor is affected by factors such as the journal's subject category, specialty, type of publication, and number of publications (15).

What is known on the subject is that the process that started with examining the publication rates of the meetings has not yet developed to a point of comparing the meetings. In their study published in 2018, De Simone et al. (16) argued that a congress impact factor (IFc) should be assigned to congresses. The authors believe that IFc, which is derived by dividing the mean H-index of lecturers by the number of lectures on the topic at the congress, with normalization for lecture topic, is an important indicator for congresses. We believe that congresses are not just about the presentations of invited lecturers. Additionally, the calculation method is difficult for large and heterogeneous congresses. Although it is a method that can be used for standardization, we believe that this parameter is insufficient to calculate the quantitative index of a congress. This is because in our opinion, a congress is not just a meeting where lecturers make presentations. Presenting and discussing abstracts of new studies is also an important component of congresses. The study adds that we proposed a more inclusive formula. In this formula, we included the H-index of the lecturers, the publication rates of the accepted abstracts, and the impact factor of the journals publishing the abstracts. This system can be easily calculated by multiplying the publication rate and the impact factor of the journals, and then adding the mean H-index of the lecturers. We suggest that ten percent of the output value should be taken for simplification. It will not be easy to find every parameter of this assessment system, but meeting organizers can request the H-index of the lecturers invited to the meeting, to collect such data. Publication rates and impact factors of journals, may seem more difficult to obtain than the previous parameter. We believe that a single database should be used for this purpose, and only the publications indexed in the database used should be included in the calculation, because the use of multiple databases would change the publication rates and would also complicate the calculation. Perhaps introducing a common questionnaire about the course of the author's previous submission as part of the abstract submission page may successfully solve this issue. Perhaps it can be followed by a fixed serial number assigned to all abstracts across congresses.

Study Limitations

The most important limitation of this study is the lack of validity of the formula. For the result obtained from the calculation to

be considered good or bad, it would be appropriate to compare it with other scientific methodologies. Similarly, evaluating the meetings through participants' feedback or survey forms could be useful for ensuring the accuracy of the results. The effectiveness of the QF formula could be enhanced by including variables such as citations received by the papers. The lack of validation of the calculated QF is one of the limitations of the study. However, our primary goal is to introduce the QF and highlight this approach. Another important limitation of the present study is the lack of information on non-published abstracts. The purpose of examining meetings organized by a single society is accurately calculating the authors' H-index and easily accessing information on past congresses. The calculation of QF based on the H index and impact factor also cause certain insufficiencies, leading to limitations as mentioned above. Therefore, we suggest that our QF index should be used for each discipline. For example, comparing the QF of an oncology meeting with the QF of a urology congress may yield inaccurate results depending on the parameters. However, meetings within each scientific discipline can be compared using the proposed formula. The last point of our proposed QF is the requirement for monitoring for a period of at least 2 years after the meeting.

Conclusion

In our world where science is universal, several disciplines organize congresses periodically. We believe that the scientific quality index of these congresses would be a guide for both the prestige of the congress and participants. The QF we recommend is easy to calculate and can be used objectively to evaluate the quality of scientific meetings. However, our primary goal is to draw attention to this direction instead of developing this formula. There is a need for a standard calculation tool that shows the quality of congresses. We believe this tool will help physicians manage their time, energy and financial resources. The formula and its components can be improved.

Ethics

Ethics Committee Approval: Not necessary.

Informed Consent: Not necessary.

Footnotes

Authorship Contributions

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

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LETTER TO THE EDITOR
Endourology

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J Urol Surg 2025;12(2):99-100

Letter to the Editor: "Effect of Prilocaine Infiltration into the Nephrostomy Tract After Percutaneous Nephrolithotomy on Postoperative Pain"

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Dear Editor,

"Effect of Prilocaine Infiltration into the Nephrostomy Tract After Percutaneous Nephrolithotomy on Postoperative Pain" by Akdoğan et al. (1), provides valuable insights into the utility of local anesthetic infiltration for reducing postoperative pain following percutaneous nephrolithotomy (PCNL). While the study sheds light on a critical aspect of postoperative care, I would like to highlight a few points that could further refine the interpretation and generalizability of the findings.

The study states that Amplatz sheaths were used in all patients but does not specify the diameter. Increasing the diameter of the Amplatz sheath is associated with greater postoperative pain due to increased renal parenchymal stretching. Research has demonstrated that smaller Amplatz sheath sizes are associated with less postoperative discomfort, highlighting the importance of reporting this parameter (2). Clarifying the sheath diameters used could provide better context to the reported pain scores.

The duration of the PCNL procedures is not mentioned in the study. Procedural time is a well-established factor influencing postoperative pain, with prolonged surgeries typically resulting in higher pain levels. Studies have identified operation time as an independent risk factor for moderate-to-severe postoperative pain, with longer durations correlating significantly with increased pain levels (3). Including this variable would strengthen the study's analysis of pain outcomes.

The criteria for patient group allocation were not clearly defined. Specifying whether the groups were homogeneous in terms of demographic and clinical characteristics would enhance the study's methodological rigor and internal validity of the study.

The study mentions that stones were fragmented using either pneumatic lithotripsy or holmium laser energy. However, no subgroup analysis was performed to evaluate whether the type of energy source affected postoperative pain scores. As the energy source could have a significant impact on tissue trauma and, consequently, pain severity, a subgroup analysis would provide more nuanced insights into the observed pain outcomes.

It is unclear whether all surgeries were performed by the same surgeon or by surgeons with varying levels of experience. Surgical expertise can influence both complication rates and the degree of postoperative pain. Clarifying this aspect would enhance the study's reproducibility and generalizability.

It is important to note that factors such as psychiatric disorders, anxiety, alcohol use, and chronic analgesic use can influence visual analog scale (VAS) scores. This study did not explicitly mention whether these conditions were excluded, which may have introduced confounding effects (4). A discussion on the potential impact of these variables would enhance the study's findings, and future research should consider controlling for these factors to enhance the reliability of VAS-based pain assessments.

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In the original study, patients who did not receive a local anesthetic underwent both supine and prone procedures, whereas the group that received local anesthetic included only patients who underwent the prone approach. As previous studies suggest that postoperative pain levels may vary between these two positions, this discrepancy introduces a potential confounding factor that may limit the validity of direct comparisons. Acknowledging this limitation and considering uniform procedural positioning in future studies would enhance comparability and strengthen the validity of the conclusions.

In conclusion, the findings of Akdoğan et al. (1) are highly valuable in advancing our understanding of postoperative pain management in PCNL. Addressing the above points in future studies could further enhance the clinical implications and applicability of their work.

Thank you for this significant contribution to the field.

Ethics

Informed Consent: Retrospective study.

Footnotes

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BRIEF REPORT
Andrology

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The Andrology Working Group of the Society of Urological Surgery in Turkiye: Bridging Academic Gaps and Advancing Male Reproductive or Sexual Health

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Abstract

The Andrology Working Group of the Society of Urological Surgery in Turkiye was established to address the lack of a formal andrology subspecialty in Turkiye and to advance male reproductive and sexual health. With a youth-driven approach-where young professionals play a leading role in organizing educational programs, conducting research, and contributing to advancements in clinical practice-the group fosters collaboration in key subspecialties, including male infertility, erectile dysfunction, and ejaculation disorders. By bridging academic gaps and supporting young professionals, the group plays a pivotal role in shaping the future of andrology in Turkiye. Notably, the group has facilitated over 25 national and international training programs and contributed 14 peer-reviewed publications, directly impacting andrology education and clinical practice in the region.

Keywords: Andrology, basic science, general urology

Introduction

Andrology, the branch of medicine that addresses male reproductive and sexual health, has a rich history dating back to ancient times. Early descriptions of male reproductive health and sexual dysfunction can be found in ancient Egyptian and Greek medical texts, underscoring humanity's long-standing interest in understanding and addressing these issues (1,2). In the modern era, andrology emerged as a distinct field in the mid-20th century, gaining momentum with advances in endocrinology, microsurgery, and reproductive technologies (3).

Despite significant global progress, the absence of an official andrology subspecialty within urology in Turkiye has created a substantial educational and academic gap. This has limited the development of systematic training and comprehensive research in the field. The shortage of scientific publications and weak collaborations with international societies have further contributed to insufficient online education programs, restricting access to up-to-date knowledge and training. Additionally, female sexual health and transgender urology remain underrepresented within urology, resulting in limited awareness and structured educational efforts. Addressing these deficiencies required a systematic approach that integrated both theoretical and practical training while fostering inclusivity in sexual and reproductive health education. Recognizing this need, the Society of Urological Surgery in Turkiye (SUST) established the Andrology Working Group on March 31, 2018. This initiative aims to provide academic support, empower young professionals, and advance male reproductive and sexual health in Turkiye. While some European countries, such as Germany and Hungary, officially recognize andrology as a subspecialty, others, including Italy and Spain, offer structured master's programs for certification in the field (4). Similar challenges exist in countries

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where andrology lacks subspecialty status, underscoring the global relevance of this initiative.

Since its establishment, the group has played a pivotal role in medical education, research, and professional development. Regular meetings and scientific discussions provide members with opportunities to critically analyze emerging advancements in andrology. Unlike traditional academic settings, where senior experts typically lead discussions, the group promotes an inclusive environment, actively encouraging early-career professionals to engage in academic discourse and present their research. This approach has enhanced the visibility of young researchers in national and international congresses, fostering knowledge exchange and professional networking within the global andrology community. Through structured training programs, mentorship initiatives, and multidisciplinary collaborations, the group not only strengthens clinical expertise but also ensures the continuous academic development of its members.

Establishment and Vision

The Andrology Working Group was founded with a clear mission: to bridge the existing gaps in education and research, inspire the younger generation, and provide a collaborative platform for clinicians and researchers passionate about andrology. By focusing on both male infertility and sexual health, the group aspires to lead transformative efforts in advancing andrology as a discipline. In a short period, the group has grown to include over 100 members, the majority of whom are academicians working in university hospitals across various geographical regions of the country (Figure 1) including a significant number of young specialists. Membership is open to urologists who have completed their specialty training and wish to advance their expertise in andrology. Interested professionals can apply through the SUST, which oversees the membership process. Through structured mentorship programs, the group provides guidance for early-career researchers, fostering long-term academic growth in andrology.

Activities and Initiatives

The Andrology Working Group has undertaken a range of activities to achieve its mission, including:

1. Comprehensive Andrology Training Programs: The Andrology Working Group has implemented a comprehensive training strategy combining hands-on surgical courses and virtual education to enhance the skills of urology specialists across Turkiye. Live surgical workshops provide direct experience in penile prosthesis implantation, Peyronie's disease surgeries, microsurgical varicocelectomy, microdissection testicular sperm extraction, and microsurgical vaso-vasostomy. These courses attract urologists from various regions, ensuring advanced surgical techniques are accessible beyond major medical centers. This nationwide participation ensures andrological expertise is disseminated more evenly across Turkiye, reducing disparities in access to specialized care. In-service training programs also address specialized topics, such as sexual therapy for psychogenic erectile dysfunction.

To further expand educational reach and overcome geographical limitations, the group has developed online and semi-live courses under the "Easily Accessible, Up-to-Date, and Standardized Training Model in Urology: E-Learning Residency Training Programme". This ongoing initiative provides video-based theoretical, clinical, and surgical content on male reproductive health and sexuality. With over 1,000 participants actively engaging in its modules, the program has been associated with reported improvements in clinical knowledge and skills. Additionally, in collaboration with the International Society for Sexual Medicine (ISSM), the group has organized six expert-led online courses, covering critical topics such as Peyronie's disease treatment, penile prosthesis surgery, priapism management, urethral stricture disease, penile implant complications, and penile enlargement surgery.

2. Conferences and Symposia: Organization of national and international events to share knowledge and foster collaboration.

3. Affiliations with Institutions: Collaborations with leading academic and clinical organizations, including the ISSM, the European Society for Sexual Medicine, the European Association of Urology, Young Academic Urologists, Working Group of Sexual and Reproductive Health, and the Global Andrology Forum to promote multidisciplinary research, educational initiatives, and best clinical practices in andrology. These collaborations involve activities such as joint research projects, shared training programs, and participation in international scientific meetings.

4. Publication of Books: Contributions to national and international books on andrology and male fertility, including titles such as *Male Sexual Health and Fertility*, *Andrological Surgery Atlas*, *Treatment of Prostate Diseases and Sexuality*, and *Testosterone* (5).

5. Updates on Specific Topics: Series focused on the latest developments in key areas such as erectile dysfunction and premature ejaculation.

6. Multicenter Research Studies: The Andrology Working Group has spearheaded numerous multicenter research projects, contributing to a deeper understanding of various aspects of male reproductive and sexual health (6-15). Among the numerous research projects, two particularly impactful studies stand out:

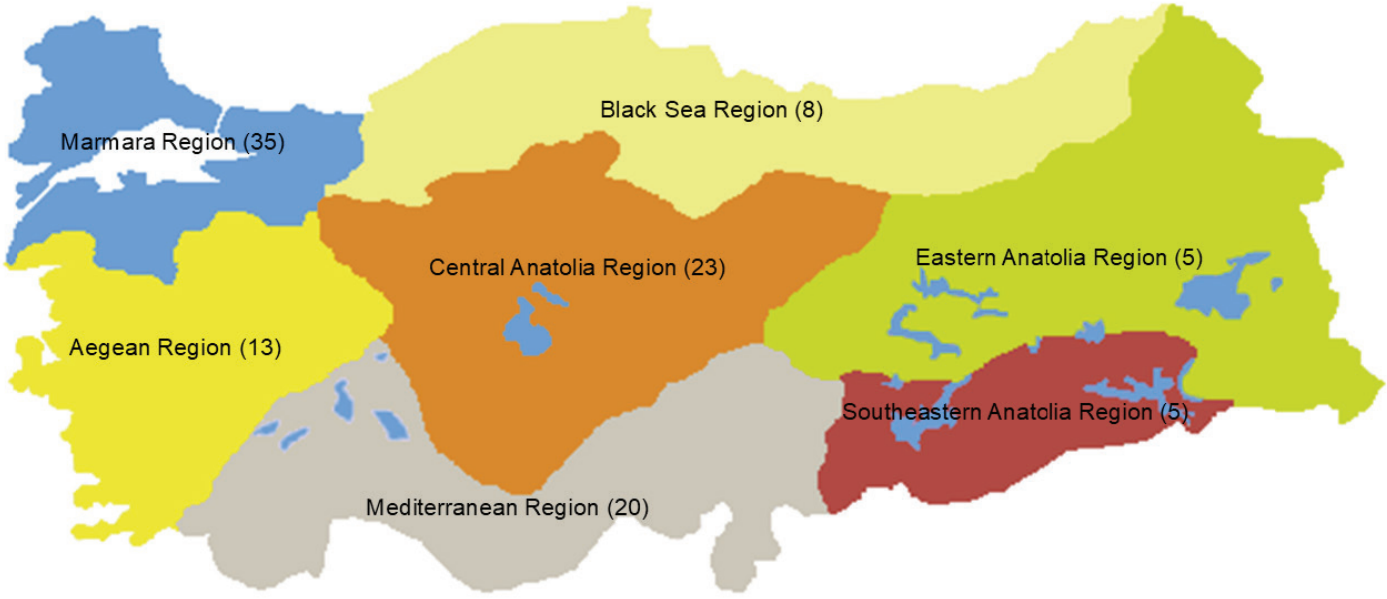

Figure 1. Geographic distribution of members as of March 2, 2025. The number of members in each region is indicated in parentheses

A survey-based study exploring the impact of different sexual positions on ejaculation was conducted, providing new insights into how positional variations may influence ejaculatory function and satisfaction. This study is one of the first to systematically examine this relationship, offering clinically relevant findings that may inform sexual therapy practices (6).

A multicenter case-control study investigates a potential relationship between blood groups and varicocele, offering a novel perspective on the genetic factors that may contribute to varicocele development. Unlike previous research, which primarily focused on environmental and anatomical factors, this study explores an overlooked genetic link, opening new avenues for further investigation (7).

7. Scholarships: Financial support for young researchers and clinicians pursuing careers in andrology. These scholarships are open to all professionals in the field and are awarded based on research potential and contribution to the field, with priority given to studies focusing on andrology education and innovation.

8. Presenting Papers at National and International Congresses: Disseminating findings and insights to the global andrology community.

9. Digital Resources via the Group's Website: The working group maintains an official website (https://www.androlojiucd.com), serving as a comprehensive resource hub for both clinicians and patients. The platform provides open-access materials, allowing physicians to stay updated on advancements in andrology while ensuring patients have access to reliable medical information (5). The website features educational content, including written materials and videos on male reproductive and sexual health as well as surgical notes, consent forms, and a collection of the group's academic contributions, such as books, update series, and research publications. By consolidating academic resources and training materials, the website plays a crucial role in supporting the group's educational mission and enhancing knowledge dissemination within the andrology community.

10. In-service Training Programs as Part of Social Responsibility Projects: The Andrology Working Group has actively contributed to social responsibility initiatives by organizing educational programs aimed at promoting sexual health awareness. Importantly, these initiatives have reached a significant number of educators and healthcare professionals, ensuring the dissemination of accurate information on male reproductive and sexual health to a broader audience. Notably, training sessions were conducted in collaboration with Darüşşafaka Society, one of Turkiye's first non-governmental organizations in the field of education, which has upheld the mission of "Educational Opportunity for All" since 1863, for educators in two separate periods. These sessions focused on adolescent sexual health education as well as comprehensive instruction on the genital and reproductive systems in boys and girls. In collaboration with Darüşşafaka Society, the group has reached over 100 educators through education programs.

Subspecialized Focus Areas

The Andrology Working Group operates with six specific subspecialty groups to address the diverse needs of male reproductive and sexual health. Members have the opportunity

to join one or more of these subspecialty groups based on their interests and expertise. The six subspecialty groups are:

1. Male infertility subgroup
2. Erectile dysfunction and Peyronie's disease subgroup
3. Ejaculation disorders subgroup
4. Prostate diseases and hypogonadism subgroup
5. Female sexual health subgroup
6. LGBT+ sexual health subgroup

These subspecialty groups allow members to focus on their specific areas of interest while fostering collaboration and innovation within the broader framework of the working group.

Youth-oriented Approach

A key characteristic of the Andrology Working Group is its predominantly young membership. With most members in the early stages of their careers, the group benefits from their enthusiasm, innovation, and forward-thinking perspectives. This dynamic energy allows the group to address longstanding challenges with fresh approaches while fostering the next generation of andrology leaders. At the same time, the group acknowledges the crucial role of experienced mentors in guiding young professionals. Through structured mentorship programs and collaborations with senior experts, a program facilitates the transfer of knowledge and expertise across generations, ensuring long-term sustainability.

Academic Impact

The group has made substantial contributions to the academic landscape by publishing articles in high-impact journals and organizing events that address critical topics in male reproductive and sexual health. By creating opportunities for young professionals to engage in research and clinical practice, the group is not only addressing current needs but also ensuring sustainable growth in andrology.

Conclusion

The Andrology Working Group of the Society of Urological Surgery serves as a model for innovation and collaboration in addressing educational and academic gaps in andrology. By fostering the integration of young professionals with experienced mentors, the group ensures both continuous advancement and long-term sustainability in the field. Through its diverse initiatives, the group contributes to the development of andrology and encourages similar efforts at both national and international levels.

Footnotes

Authorship Contributions

Concept: G.Ç., H.D., Ü.G., T.T., Design: G.Ç., Data Collection or Processing: All authors, Analysis or Interpretation: G.Ç., H.D., Ü.G., T.T., Literature Search: G.Ç., Writing: G.Ç., H.D., Ü.G., T.T.

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CASE REPORT
Pediatric Urology

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J Urol Surg 2025;12(2):108-111

Infected Pelvic Cyst: A Postoperative Complication in a Patient with Zinner Syndrome: A Case Report

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Abstract

Zinner syndrome is a rare disorder characterized by congenital seminal vesicle cysts, multicystic dysplastic kidney, and ipsilateral upper urinary tract anomalies. Although at least 80% of patients are asymptomatic, they may suffer from dysuria, urinary tract infections, bladder dysfunction, and infertility. Excision of cysts may be considered as an option to relieve symptoms, but it carries risks and potential complications due to the deep localization of seminal vesicles. There is limited knowledge regarding postoperative complications. In this case, an asymptomatic patient underwent surgery because of enlargement of the seminal vesicle cysts. However, an infected cyst was developed as a complication. Seminal vesicle cyst excision in asymptomatic patients with Zinner syndrome may result in postoperative complications, and the decision to have an operation should be made with great care and consideration.

Keywords: Zinner syndrome, seminal vesicle cyst, pelvic cyst, case report

Introduction

Zinner syndrome is a rare congenital disorder caused by a developmental anomaly of the mesonephric duct (1). It is characterized by unilateral renal agenesis, ipsilateral seminal vesicle cysts, and upper tract urinary anomalies (2-4). Although it is rarely diagnosed in pediatric populations (5), patients frequently remain asymptomatic; however, the most common symptoms include dysuria, frequent urination, perineal or scrotal pain, and painful ejaculation (5). Magnetic resonance imaging (MRI) serves as the gold standard for diagnosis. Treatment strategies range from conservative approaches to minimally invasive or surgical interventions, depending on the size of the cyst and the patient's symptoms.

To the best of our knowledge, this case represents the first report of a pelvic cyst subsequent to surgical excision of the seminal vesicle cyst in Zinner syndrome. We discuss the risks of surgery and the management of an infected pelvic cyst as a complication of surgical intervention.

Case Presentation

In October 2023, a 45-year-old male patient presented to our outpatient clinic, reporting persistent perineal pain for 1 year. The pain was further exacerbated during urination, defecation, and ejaculation. The patient's body mass index was measured as 23.9 kg/m^2, and besides lumbar scoliosis, no other chronic diseases were noted.

A comprehensive review of the patient's medical history was systematically analyzed. Five years ago, the patient had undergone surgical resection of an incidental right seminal vesicle cyst because of its progressive enlargement. There were no complaints before the operation. Preoperative contrast-enhanced computed tomography revealed the absence of the right kidney and identified a cystic lesion within the right seminal vesicle (Figure 1A, 1B). Although preoperative MRI was unavailable, documentation indicated an inferior positioning of the prostate relative to its typical location, along with the presence of a 4.5x2.8 cm cystic lesion within the seminal vesicle, extending toward the right posterolateral aspect of the bladder.

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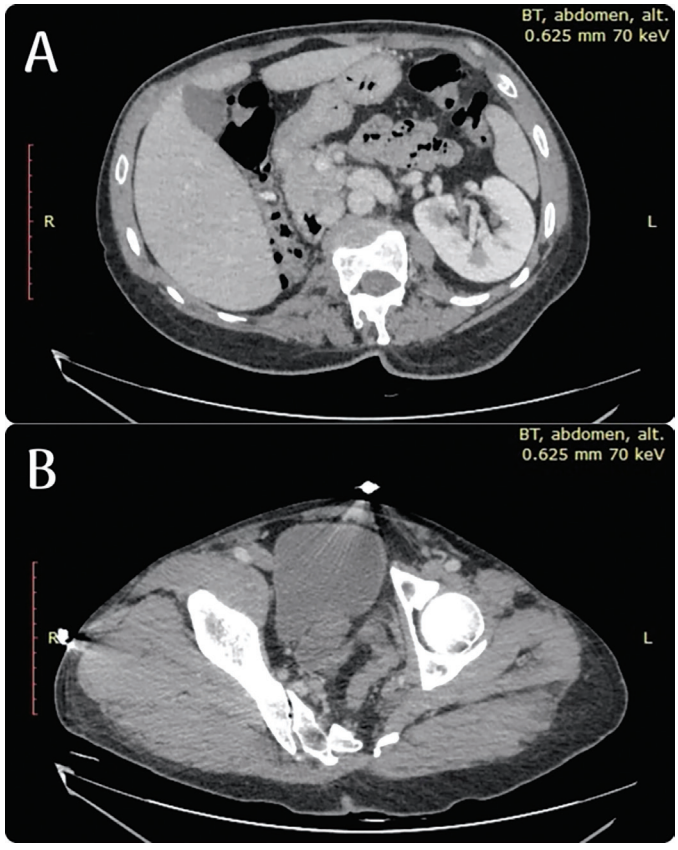

Figure 1. A. Preoperative post-contrast axial CT image of the right renal agenesis, B. Preoperative post-contrast axial CT image of the right seminal vesicle cyst

CT: Computed tomography

Preoperative cystoscopy revealed a slight elevation of the right hemitrigone and an absence of the right ureteral orifice. Histopathological examination of the excised tissue confirmed cystic structures consistent with a dilated ureter lined by urothelial epithelium (Figure 2).

During the physical examination, the prostate was palpated and characterized as a medium-sized adenoma, while examination of the testis, epididymis, and vas deferens revealed no anomalies. Biochemical, seminal, and urinalysis parameters were within the normal range. The uroflowmetry test showed an obstructive voiding pattern, a maximum flow rate (Q_{max}) of 11.1 mL/s, and a postvoiding residual urine volume of 35 mL. The ultrasound examination identified a cystic lesion measuring 66x23 mm in the posterior right-side of the bladder. Subsequent MRI revealed a 66x23 mm densely enhancing cyst localized at the level of the obturator muscle in the right posteroinferior aspect of the bladder (Figure 3). The cyst was considered as infected and postulated to have arisen as a consequence of prior surgical intervention, with the patient's symptoms attributed to this cystic lesion.

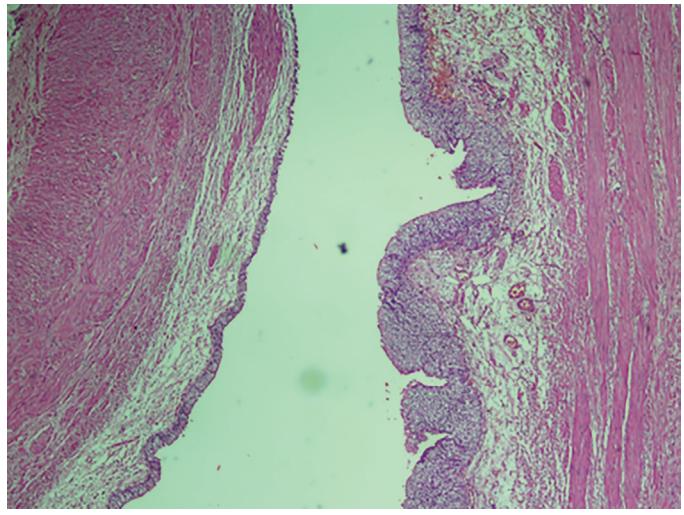

Figure 2. Seminal vesicle cyst lined with urothelium epithelium (hematoxylin-eosin, 40x)

Following comprehensive evaluation, the diagnosis of Zinner syndrome was established, and the patient subsequently underwent computed tomography-guided percutaneous drainage (Figure 4), which resulted in symptomatic relief. Written informed consent to participate and publish was obtained.

Discussion

Acquired seminal vesicle cysts are often unilateral and typically develop in adulthood because of inflammation and obstruction of the ejaculatory ducts (6). However, congenital genitourinary tract anomalies typically result from abnormal development of the ipsilateral mesonephric ducts, including the vas deferens, kidney, and ureter (7-10).

Cystoscopic findings in patients with Zinner syndrome may reveal the absence of hemitrigone or an ectopic ureter (11). Similarly, in this case, the absence of the right orifice was observed in the preoperative cystoscopy, and the pathological examination revealed an ectopic ureter opening into the seminal vesicle.

In asymptomatic patients, annual clinical examination and follow-up ultrasound are recommended. Surgical excision is an option in the management of symptomatic patients and those who have not responded to conservative treatment (12). In a systematic review by Liu et al. (4), of 193 patients with treatment details, 127 were treated surgically (open surgery, laparoscopic surgery, and robot-assisted laparoscopic surgery). Of the 127 patients, 39 were treated by open surgery. In this case, the patient underwent excision of the seminal cyst due to enlargement during follow-up, although he was asymptomatic.

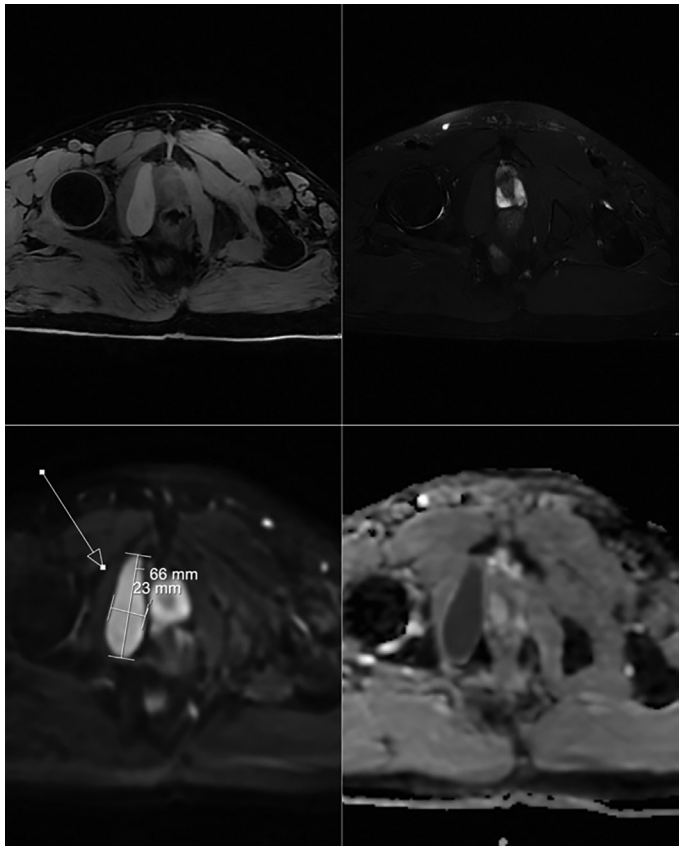

Figure 3. Axial T1 and T2 magnetic resonance imaging shows an infected cystic lesion 66x23 mm with T1A hyperintense, T2A hypointense, diffusion restriction in the right posterolateral near the bladder at the level of the obturator

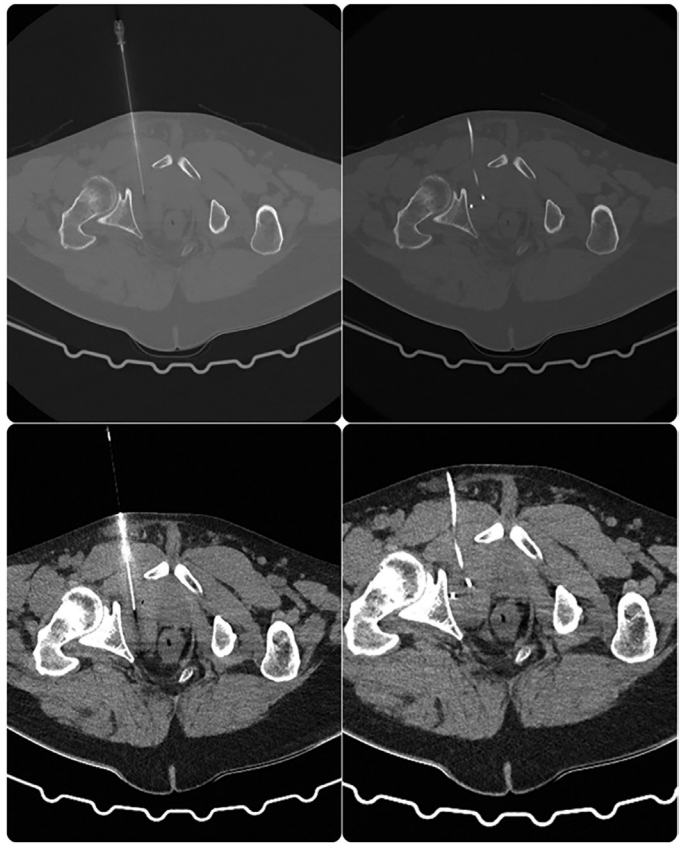

Figure 4. Aspiration of the infected cyst using a 6 Fr catheter under computed tomography guidance

Surgical intervention necessitates extensive dissection because of the deep location of the seminal vesicles within the pelvis, resulting in a high rate of morbidity. This morbidity includes risks such as injury to the erectile neurovascular bundle, rectal or bladder wall, ureter, or formation of a pelvic urinoma (11). Percutaneous drainage of the cyst, compared to surgical removal, is less invasive and can treat symptoms without causing new complications.

Conclusion

Zinner syndrome is a rare syndrome that should be considered in the presence of seminal vesicle cysts and renal abnormalities. It is important to note that excision of seminal vesicle cysts may result in postoperative complications. Therefore, the decision to undergo surgery should be made with great care and consideration.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Footnotes

Authorship Contributions

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

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CASE REPORT
Urooncology

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A Rare Neoplasm of the Kidney: A Female Patient as the First Case Possibly Triggered by Pregnancy

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Abstract

Mixed epithelial and stromal tumor (MEST) is a rare, biphasic adult renal tumor composed of solid and cystic areas with spindle cell stroma and epithelium. Tumors expressing estrogen and progesterone receptors are affected by hormonal changes, often in post-menopausal women on hormone replacement therapy. Since it can be challenging to differentiate between MEST and malignant tumors, it should be considered as a differential diagnosis. To our knowledge, this is the first case postulated to be caused possibly by pregnancy-related hormonal changes. It is noteworthy that the tumor is affected by changing estrogen and progesterone hormone levels during pregnancy, thus rapidly progressing in a brief time.

Keywords: Mixed epithelial stromal tumor, early age, pregnancy

Introduction

Mixed epithelial stromal tumor (MEST) is defined as a distinct renal tumor according to the World Health Organization Classification in 2004. The tumor has cystic and solid components comprising branched glandular structures and smooth muscle-like bundles. To our knowledge, there are only one hundred reported cases in the current literature. MEST has a unique pattern that includes mesenchymal and epithelial components with characteristic estrogen and progesterone receptor-positive immunoreactive mesenchyme, mimicking ovarian stroma. Hormones are considered risk factors for these tumors, especially in women who have a history of long-term estrogen therapy post-menopause for the treatment of gynecological disorders (1-4). They are usually benign although they can rarely exhibit showing malignant behavior. The only treatment method for the tumor is surgical excision (2).

Case Presentation

A 17-year-old female patient presented to the outpatient urology clinic with a history of right flank pain for the past 7 months. She had not received any hormone therapy previously and had no significant features in her medical history except for a recent delivery and three packs/per-year of smoking. The patient had given birth two years prior to her complaints and her kidneys were found to be normal in an ultrasound (US) conducted routinely during the postpartum period. A year after her delivery and 7 months before her admission, the patient began experiencing right flank pain. A computed tomography (CT) scan at another healthcare clinic revealed a 75 mm renal mass. A magnetic resonance imaging (MRI) done 7 months later showed a 90x70 mm high-density mass with a multicystic area in the right lower pole of the right kidney (Figure 1). The patient underwent partial nephrectomy the kidney was accessed through a right subcostal incision and the renal artery and vein were exposed and controlled. The surgical margin was then determined at the edges of the mass in the lower pole, and the mass was removed using cold ischemia for 13 minutes. Bleeding was controlled with Tissel and Surgicel, and the incision was closed with 1/0 Vicryl. A benign mesenchymal tumor was found in the frozen specimen sent intraoperatively. In our standard practice, we typically do not send frozen sections for partial nephrectomies. In this case, the patient's age was inconsistent with the development of renall cell carcinoma (RCC), prompting the need to determine a surgical approach for the tumor. Thus, frozen sections were specifically sent for this case to ensure an accurate diagnosis and appropriate treatment plan.

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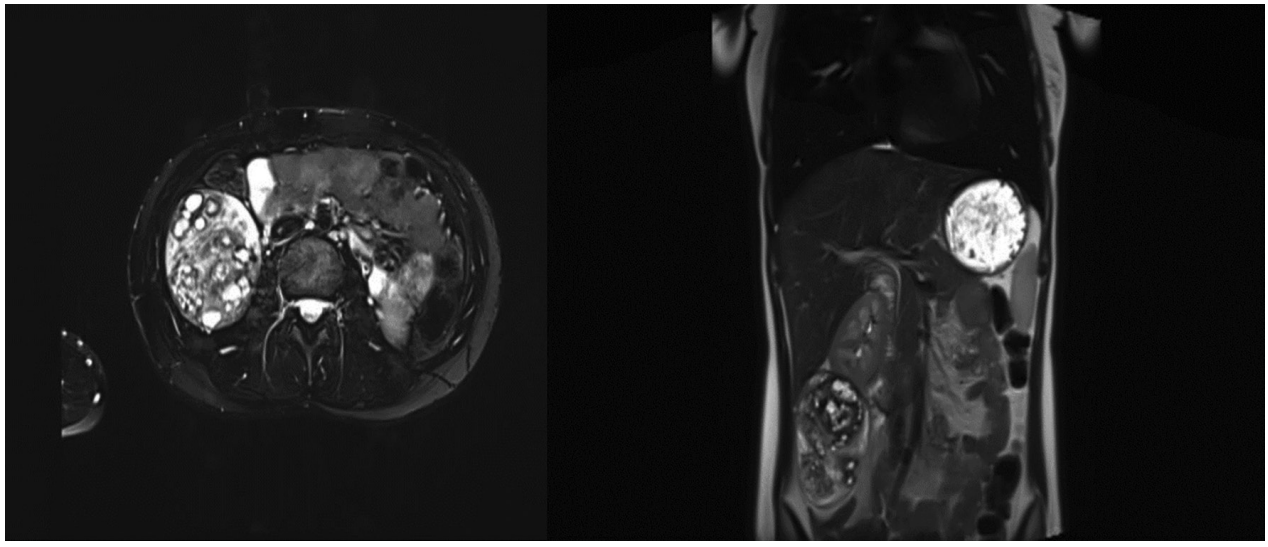

Figure 1. MRI scan image of a right renal tumor contrast retaining in transverse section and coronal section

MRI: Magnetic resonance imaging

Figure 2. Partial nephrectomy specimen showing a predominantly solid mass with microcystic areas

After surgery, the pathologic examination, revealed negative surgical margins. No invasion was observed in the renal pelvis or hilar blood vessels. There were no complications during the surgery or in the recovery period. The pathology report of a 14x8.5x5 cm mass indicated as MEST (Figure 2). The pathological evaluation of the mass lesion showed smooth muscle bundles, adipose tissue lobes, and thick-walled blood vessels in a hypocellular stroma with hyalinized and myxoid features. Multiple areas contained tubule structures and epithelial cysts of various sizes. The solid portion of the mass was composed of moderately cellular areas of ovoid-spindle cells resembling ovarian-type stroma and rare lipocytes. There was no evidence of a blastic component nor stromal overgrowth. Cysts were lined by flattened to cuboidal, mostly bland-looking, partly hobnailed epithelial cells. Some tubules exhibited eosinophilic secretions in their tubular lumina. Immunohistochemistry demonstrated that estrogen and progesterone receptors were positive in the stromal cells while Human Melanoma Black-45 and inhibin were found to be negative.

Discussion

Mixed epithelial tumors were first described by Michal and Syrucek (5), and Adsay et al. (2) in 1998 as adult mesoblastic nephroma, cystic hamartoma of the renal pelvis, and adult nephroblastic tumors. In 2004, they were categorized as renal tumors (6). It is a rare tumor with approximately one hundred documented cases in the literature. Post-menopausal hormone therapy is the most common cause of the condition, which is typically observed in women aged 17 to and 78 years. The male to female ratio is 1:10, with rare occurrences reported in men who received hormonal therapy. Only one pediatric case has been reported. Although MEST may present with abdominal distension, flank pain, hematuria, and urinary tract infection, it is typically asymptomatic and often detected incidentally (1).

MESTs appear as well-circumscribed thin or thick multi-septate cystic components or cystic and solid areas on MRI and CT; therefore, it is difficult to distinguish them from cystic nephroma (CN) and congenital mesoblastic nephroma (7,8). On CT, the tumor can be evaluated as Bosniak type 3 and type 4 cystic lesions because they enhance contrast in the late phase

and have solid components (1). The macroscopic appearance of heterogeneous areas may include necrosis and calcification. MESTs rarely contain sinus fat tissue (9).

Our case was characterized by the development of a renal mass after pregnancy. One of the key factors that contribute to the pathogenesis of MEST is the hormonal mechanism, which is often seen in women using hormone replacement therapy during the post-menopausal period. In addition, positive staining of estrogen and progesterone receptors in immunohistochemical examination of the tumor supports this mechanism. The spindle cells found in the lesions are thought to originate from the periductal fetal mesenchyme around the epithelial structures of organs such as the kidney, pancreas, and liver. The perimenopausal period triggers the proliferation of this mesenchyme due to unopposed estrogen levels, which leads to the development of the epithelial part and the growth of tumors (2). Considering that the patient became pregnant at a young age and the tumor grew 5 cm in just two months between the MRI and surgery, it was hypothesized that the rapid proliferation of fetal mesenchymal cells was induced by hormonal changes during pregnancy.

Conclusion

The MEST family can be challenging to differentiate radiologically from other tumors, whether malignant or benign. Although exceptionally rare in children, it should be included in the differential diagnosis for Wilms tumor, CN, or pediatric RCC. In our case, the patient, who became pregnant at a young age, exhibited positive estrogen and progesterone receptors, suggesting that these hormones might have contributed to tumor stimulation. This mirrors the mechanism observed in postmenopausal patients undergoing hormone therapy. While the definitive cause of the tumor remains unclear, it is possible that hormonal fluctuations during pregnancy were influential.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.Ç., M.Ö.T., Concept: K.Ş.E., S.Ç., M.Ö.T., Design: K.Ş.E., S.Ç., M.Ö.T., Data Collection or Processing: K.Ş.E., S.Ç., M.U., İ.I.G., M.Ö.T., Analysis or Interpretation: K.Ş.E., S.Ç., M.U., İ.I.G., M.Ö.T., Literature Search: K.Ş.E., S.Ç., M.Ö.T., Writing: K.Ş.E., S.Ç., M.Ö.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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VIDEO ARTICLE
Pediatric Urology

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Excision of Prostatic Utricle: When? How?

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Abstract

The prostatic utricle is a rare anomaly in the urogenital system and is generally thought to develop from remnants of the Müllerian duct. Prostatic utricle is usually accompanied by hypospadias, renal agenesis, and cryptorchidism, and it is mostly asymptomatic. Symptoms such as recurrent urinary tract infection, epididymo-orchitis, abdominal pain, voiding disorders, and stones are observed. Surgery in symptomatic patients is recommended. Prostatic utricle cyst was detected as a result of abdominal imaging in two of our patients who had a history of hypospadias repairs, and who presented with complaints of recurrent epididymo-orchitis and abdominal pain. We report two cases of laparoscopic utricle cyst excision.

Keywords: Prostatic utricle, hypospadias, epididymo-orchitis

Introduction

The prostatic utricle is a sinus, lined with mucosal epithelium, opening between the two ejaculatory ducts on the verumontanum (1). It is located in the midline, in the lower half of the pelvic cavity, between the bladder and the rectum, and is usually associated with the prostatic urethra. Utricular anomalies result from incomplete regression of the Müllerian duct remnants or incomplete androgen-mediated closure of the urogenital sinus (2). It is rare in the normal population and is mostly asymptomatic. Surgery in symptomatic patients is recommended.

Case Presentations

1. A 1-year-old male patient was admitted to our clinic due to proximal hypospadias. There was nothing notable in the patient's history, except that he was born prematurely, and had undergone right inguinal hernia operation together with right orchiopexy. Physical examination revealed penoscrotal hypospadias, right inguinal scar, and left undescended testicle. After the patient's chromosome analysis was 46-XY, left orchiopexy and two-stage hypospadias repair (chord release and Byar flap with prepuce + Thiersch-Duplay procedure) were performed. As urethrocutaneous fistula developed in the following months, fistula repair was performed. As epididymo-orchitis developed after fistula repair, cystoscopy was planned. A cystic lesion was observed on the posterior wall of the bladder in the ultrasonography performed before cystoscopy. Cystoscopy revealed stenosis in the distal urethra and a utricle opening into the prostatic urethra. Ultrasonography was repeated simultaneously with cystoscopy, and the utricle diameter was measured as 4.5 cm. No pathological lesion was found in the bladder. A guidewire was advanced to the bladder, the stenosis in the distal urethra was cut with Bugbee cautery, and the urethra was dilated to 12F. The patient was admitted with complaints of left epididymo-orchitis 2 weeks after the procedure. Under general anesthesia, a cystostomy was opened and the utricle was fulgurized. After the procedure, the patient was admitted again with complaint of left epididymo-orchitis. Ultrasonography revealed a 34 x 20 mm prostate utricle in the posterior part of the bladder. He was admitted to the hospital with plans for laparoscopic utricle cyst excision.

2. A 10-year-old patient presented with the complaint of abdominal pain. He had four previous operations due to hypospadias and a history of epididymo-orchitis in the post-operative period. As a result of abdominal magnetic resonance imaging, a 7 x 1 cm cystic lesion was observed in the rectovesical area. Since the complaints of blunt pain in the lower abdominal quadrant, nausea, and vomiting continued, he was hospitalized with plans for laparoscopic utricle cyst excision.

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Informed consent from the parents of the patients was provided. The surgical procedure is described in the video (Video 1).

First, a cystostomy catheter was placed in the bladder, and a ureteral catheter was placed in the utricle under cystoscopy guidance. Then, the laparoscopic case was started. Visualization was achieved by injecting methylene blue into the utricle. The peritoneum was incised from the midline, and the utricle wall was reached. The 8F Foley catheter was advanced into the utricle. The balloon was inflated and placed at the neck of the utricle. The utricle wall was dissected, freed, and excised. The remaining mucosal area within the utricle was fulgurized. The neck of the utricle was then sutured and closed. A 12F sump drain was placed in the surgical area and the procedure was terminated. On the 3rd postoperative day, the patient's drain was removed and they were discharged. During the nine-month follow-up, no complications or recurrent epididymo-orchitis were observed.

Discussion

Prostatic utricle, a vestigial remnant of the Müllerian duct, is a rare pathology. Although its true incidence is not known exactly, it is seen in 14% of patients with proximal hypospadias, and approximately 50% of patients with perineal hypospadias (3). As the severity of hypospadias increases, the incidence of prostatic utricle increases (4). Most of the patients are seen in the triad: Proximal hypospadias, cryptorchidism, and a prostatic utricle. Although most patients are asymptomatic, 29% have various clinical presentations such as including lower urinary tract symptoms, epididymo-orchitis, urinary tract infection, stones, secondary incontinence, and urinary retention (5). As in our patient, a prostatic utricle should be considered when lower urinary tract symptoms such as recurrent epididymo-orchitis are seen in patients with a history of proximal hypospadias and undescended testicles. Diagnosis is possible with an accessible examination such as pelvic ultrasonography. Surgical excision is recommended in symptomatic patients. However, there is no standard surgical method yet (6). There are many different surgical approaches. Endoscopic, open and minimally invasive procedures have been described. Schuhrke and Kaplan (7) reported endoscopic transurethral cyst catheterization and aspiration, cyst orifice dilatation, incision or deroofing. It may be suitable for small utricles, but the recurrence rate is high (8). Open excision is a successful method. A wide variety of approaches have been described, including the abdominal transperitoneal, perineal, combined abdomino-perineal, anterior sagittal, posterior sagittal transrectal, suprapubic extravesical, and transvesical transtrigonal approaches (9). However, it may require extensive pelvic dissection. It carries risks such as pelvic organ injuries and inadequate utricle excision during dissection. With the developing technology, minimally invasive interventions have become popular. Yeung et al. (10) reported the first successful laparoscopic excision series of four cases. Jia et al. (11) reported a retrospective comparison between the open transvesical approach and the laparoscopic approach, involving a total of 14 patients. It has been observed that, in the laparoscopic technique, better cosmetic results are obtained with shorter operative time, hospital stay, and catheter time. Other advantages of the laparoscopic technique can be listed as follows: i) Clear view of the deep pelvic structures; ii) Enabling examination of the rest of the abdomen and urogenital system; iii) Complete excision (12). Minimally invasive techniques have been preferred in recent years with their successful results (13-15).

In patients with proximal hypospadias and undescended testis, pelvic ultrasonography may be beneficial to identify possible utricle pathologies preoperatively. The existence of a prostatic utricle does not necessitate preemptive intervention unless symptoms develop. In the case of surgical intervention for the giant prostatic utricle, the laparoscopic approach seems feasible as it facilitates total excision by a minimally invasive method and is advantageous compared to the open surgical approach, which might be challenging due to the difficult anatomic location.

Video 1.

Ethics

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

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.S.D., S.T., Concept: H.K., H.S.D., S.T., Design: G.K., H.K., H.S.D., Data Collection or Processing: G.K., H.K., Analysis or Interpretation: H.S.D., S.T., Literature Search: G.K., H.K., S.T., Writing: G.K., H.S.D.

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VIDEO ARTICLE
Urooncology

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Robot-assisted Radical Cystectomy with Orthotopic Neobladder (Pitcher Pot): Point of Technique

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Abstract

Robot-assisted radical cystectomy with orthotopic neobladder reconstruction represents a significant advancement in the surgical management of muscle-invasive bladder carcinoma. This report presents the case of a 48-year-old male who underwent a robot-assisted radical cystectomy with an intracorporeal orthotopic neobladder of "Pitcher Pot" configuration. The "Pitcher Pot" technique, a neo-urethral modification of the ileal orthotopic neobladder, is designed to enhance urethral anastomosis and functional outcomes. The procedure was completed successfully with no intraoperative complications, and the patient exhibited satisfactory postoperative recovery, including self-voiding and improved continence. This case highlights the potential for improved quality of life and long-term functional outcomes associated with advanced surgical techniques in appropriately selected patients.

Keywords: Basic science, reconstructive urology, urooncology

Introduction

Muscle-invasive bladder carcinoma (MIBC) is a significant urological malignancy requiring prompt and effective management. Radical cystectomy with urinary diversion is the standard treatment, and orthotopic neobladder reconstruction is often preferred in younger, motivated patients due to its superior quality of life outcomes, including natural voiding patterns and better body image. The "Pitcher Pot" configuration, described by Dr. Sudhir Rawal, is a neo-urethral modification of the ileal orthotopic neobladder. This design facilitates tension-free urethral anastomosis by incorporating an additional ileal segment to create a neourethra (1). This case report details the first robotic replication of this technique, emphasising its technical feasibility and clinical outcomes.

Case Presentation

A 48-year-old male presented with painless gross haematuria for one year. Detailed evaluation, including contrast-enhanced computed tomography (CECT) of the abdomen, revealed a 4×4 cm heterogeneously enhancing mass on the right lateral wall of the urinary bladder. Histopathology from transurethral resection of the bladder tumour confirmed MIBC. Staging investigations showed no evidence of metastasis. Given the patient's younger age, creatinine clearance >60 mL/min, and motivation for orthotopic neobladder reconstruction, he underwent a robot-assisted radical cystectomy with the "Pitcher Pot" configuration.

The surgical procedure involved bilateral ureteric dissection and division, posterior, lateral, and anterior bladder dissections, deep venous complex ligation, urethral transection, bilateral standard pelvic lymph node dissection, and creation of the orthotopic neobladder using an ileal segment. The total operative time was 440 minutes, with a console time of 400 minutes and an estimated blood loss of 250 mL. Postoperative recovery was uneventful, and the patient was discharged on day 10 with stable renal function (serum creatinine: 1.0 mg/dL). Histopathology revealed pT2bN0 disease with tumour-free margins. After one month, the per-urethral catheter was removed. At three months post-surgery, the patient demonstrated satisfactory voiding function and gradual improvement in continence, using 3-4 pads per day for intermittent leakage. Informed consent is taken from the patients for the use of video recordings for scientific purposes and for publishing in scientific journals (Video 1).

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Discussion

Orthotopic neobladder reconstruction is preferred for younger patients due to its potential for better quality of life, body image, and natural voiding patterns compared to ileal conduits (2,3). The "Pitcher Pot" configuration enhances functional outcomes by enabling a tension-free urethral anastomosis (1). This case underscores the importance of patient selection, including the absence of urethral involvement and sufficient renal function, to achieve optimal outcomes (2,4).

Robotic-assisted radical cystectomy has demonstrated reduced perioperative morbidity and shorter recovery times compared to open surgery (4). The sparing of neurovascular bundles during surgery, as performed in this case, has been associated with improved continence outcomes (1,5). Studies indicate that the "Pitcher Pot" neobladder provides satisfactory long-term continence and negligible rates of clean intermittent self-catheterization (1). However, postoperative continence depends on factors such as preoperative pelvic floor muscle training and patient compliance (2,3).

In this case, the application of the "Pitcher Pot" technique robotically underscores its feasibility and clinical benefits. The patient exhibited no intraoperative complications, satisfactory postoperative recovery, and promising early functional outcomes, reinforcing the technique's viability. However, long-term follow-up is essential to evaluate continence, voiding function, and quality of life outcomes.

Conclusion

The "Pitcher Pot" configuration of the orthotopic neobladder represents a novel advancement in the surgical management of MIBC, combining technical innovation with enhanced functional outcomes. This case demonstrates the successful robotic replication of the technique, achieving favourable perioperative and short-term postoperative outcomes. Patient selection, including consideration of renal function, absence of urethral involvement, and strong patient motivation, is critical for successful outcomes. Continued research and long-term follow-up are warranted to validate these findings and further refine patient selection criteria.

Video 1.

Ethics

Informed Consent: Informed consent is taken from the patients for the use of video recordings for scientific purposes and for publishing in scientific journals.

Footnotes

Authorship Contributions

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

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