E-ISSN: 2148-0532

ENDOÜROLOJİ BÜLTENİ
ENDOUROLOGY BULLETIN

Period: Triannual Founded: 2008 Publisher: Endourology Society Volume 18 / Number 3

www.endouroloji.org

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Publisher
Pera Yayıncılık Hizmetleri
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Değerli Meslektaşlarımız,

Endoüroloji Bülteni Editör Kurulu olarak, akademik yayıncılık yolculuğumuzun 2026 yılındaki üçüncü ve son sayısında sizleri yeniden selamlamanın gururunu yaşıyoruz. Bu sayımızda, ürolojinin farklı alt disiplinlerinden en güncel araştırmaları ve klinik pratikleri mercek altına alan zengin bir içerikle karşınızdayız.

Yayınımızda yer alan çalışmalar arasında, ipsilateral üreter ve böbrek taşlarına yönelik güncel yaklaşımlar, chatbotlardan elde edilen böbrek kisti bilgileri, üroloji pratiğinde frailty (kırılganlık) kavramının önemi (Modified Frailty Index) ve retrograd üreteral stentlemenin başarı oranları dikkat çekmektedir. Ayrıca HoLEP sırasında komorbidite yükünün etkileri, istatistiksel doğruluğun ötesinde PCN yaklaşımları, robotik parsiyel nefrektomide Zero Ischemia deneyimleri, robot yardımlı radikal prostatektomi sonuçları ve Avicenna Roboflex® ile konvansiyonel yöntemlerin karşılaştırılması geniş yer bulmaktadır.

Klinik pratiklerin cerrahi ve onkolojik boyutlarının yanı sıra, primer mesane tümörlerinde ameliyat yaklaşımları, akut karın başvurularında üriner taş kliniği, Türkiye'deki ürologlar arasında mesleki eğilimler, prostat kanseri tedavisinin tercihinde belirleyici faktörler ve üriner sistem enfeksiyonlarının immünolojik yönleri gibi çok yönlü konular da bu sayımızın merkezindedir.

Dergimizin bilimsel çıtasını her geçen sayı daha yukarı taşımayı amaçlarken, bu süreçte emeği geçen tüm yazarlarımıza, akademik tarafsızlığı koruyan hakemlerimize ve yayın kurulumuza en içten teşekkürlerimi sunuyorum. www.endourolojibulteni.com adresi üzerinden dijital ortamda erişebileceğiniz bu çalışmaların, bilim camiamıza ve günlük klinik uygulamalarınıza katkı sağlamasını diliyorum.

Bilimin ışığında, ortak başarılarımıza yenilerini ekleyeceğimiz gelecek sayılarda görüşmek dileğiyle.

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):117–125. doi: 10.54233/endourolbull-1840851

The Efficacy of Simultaneous Ureterorenoscopy for Ipsilateral Ureter and Kidney Stone: A Single-Center Experience

İpsilateral Üreter ve Böbrek Taşlarında Eş Zamanlı Üreterorenoskopinin Etkinliği: Tek Merkez Deneyimi

Ilkin Hamid-Zada*, Özgür Arıkan, Talha Nuroğlu, Elbrus Fehruzlu, Ferhat Keser, Asıf Yıldırım

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ABSTRACT

Objective: This study aimed to evaluate the efficacy and safety of simultaneous endourological management of ureteral and ipsilateral renal stones and to identify predictive factors associated with stone-free outcomes.

Materials and Methods: A retrospective analysis was conducted on seventy-nine patients who underwent single-session treatment for concurrent ureteral and ipsilateral renal stone. Demographic data, stone characteristics, operative details, and postoperative outcomes were collected. Stone-free rates (SFR) were assessed on postoperative day 1 and at 1 month. Comparative analyses were performed to determine factors associated with 1-month SFR.

Results: The overall 1-month SFR was 75.9%. Renal stone size, ureteral stone density (HU), hydronephrosis grade, and number of stones were significant predictors of SFR ($p < 0.05$). Patients who were stone-free on postoperative 1 day were significantly more likely to remain stone-free at 1 month ($p < 0.001$). Larger renal stones and a higher number of stones were associated with decreased success rates. Complication rates were low, with 6.3% experiencing postoperative events, most of which were minor. Auxiliary procedures were required in 16.5% of patients during follow-up.

Conclusion: Simultaneous management of ureteral and ipsilateral renal stones is a safe and effective treatment option, providing high SFR with low morbidity. Stone size and number of stones are the key determinants of postoperative success and should be considered during preoperative planning.

Keywords: lithotripsy, simultaneous treatment, ureteral and renal stone, ureteroscopy

Cite As: *Hamid-Zada I, Arikan O, Nuroglu T, Fehruzlu E, Keser F, Yildirim A. The Efficacy of Simultaneous Ureterorenoscopy for Ipsilateral Ureter and Kidney Stone: A Single-Center Experience. Endourol Bull. 2026;18(3):117–125.* https://doi.org/10.54233/endourolbull-1840851

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Received : December 12, 2025 ***Accepted*** : May 11, 2026

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ÖZET

Amaç: Bu çalışma, üreteral ve ipsilateral renal taşların eşzamanlı endoürolojik tedavisinin etkinliğini ve güvenliğini değerlendirmeyi ve taşsızlık sonuçlarıyla ilişkili prediktif faktörleri belirlemeyi amaçlamıştır.

Gereç ve Yöntemler: Üreteral ve ipsilateral renal taşın eşzamanlı olarak tek seansta tedavi edildiği yetmiş dokuz hastaya ait retrospektif bir analiz gerçekleştirildi. Demografik veriler, taş özellikleri, operatif detaylar ve postoperatif sonuçlar kaydedildi. Taşsızlık oranları (SFR), postoperatif 1. gün ve 1. ayda değerlendirildi. Bir aylık taşsızlık ile ilişkili faktörleri belirlemek amacıyla karşılaştırmalı analizler yapıldı.

Bulgular: 1 aylık taşsızlık oranı %75,9 olarak saptandı. Renal taş boyutu, üreteral taş yoğunluğu (HU), hidronefroz derecesi ve taş sayısı SFR için anlamlı prediktörlerdi ($p < 0.05$). Postoperatif 1. günde taşsız olan hastaların 1. ayda da taşsız kalma olasılığı anlamlı olarak daha yüksekti ($p < 0.001$). Daha büyük renal taşlar ve daha yüksek taş sayısı başarı oranlarının azalmasıyla ilişkili bulundu. Komplikasyon oranları düşük olup, hastaların %6.3'ünde çoğunluğu minör olan postoperatif olaylar izlendi. Takip sürecinde hastaların %16.5'inde ek girişimlere ihtiyaç duyuldu.

Sonuç: Üreteral ve ipsilateral renal taşların eşzamanlı yönetimi, yüksek taşsızlık oranı ve düşük morbidite ile güvenli ve etkili bir tedavi seçeneğidir. Taş boyutu ve taş sayısı, postoperatif başarının temel belirleyicileridir ve preoperatif planlama sürecinde dikkate alınmalıdır.

Anahtar kelimeler: litotripsi, eş zamanlı tedavi, üreter ve böbrek taşı, üreteroskopi

INTRODUCTION

Urolithiasis is becoming increasingly common worldwide and currently affects approximately 20% of the population. This rising prevalence has established urolithiasis as one of the most common urological conditions (1). Urinary system stones can be asymptomatic for long durations or pass spontaneously, but they are also capable of presenting symptoms such as pain, hematuria, infection, and damage to renal function (2). New endoscopic equipment and laser devices with powerful and functional optics have revolutionized kidney stone treatment and made RIRS safe and efficient (3). According to European Association of Urology (EAU) recommendations, ureteroscopy (URS) is the first-line treatment for ureteral stones measuring greater than 10 mm in the proximal or distal ureter. If the stone is less than 10 mm, either URS or extracorporeal shockwave lithotripsy (ESWL) can be used for initial management (4).

Several investigations have reported that performing endoscopic procedures—such as URS and percutaneous nephrolithotomy within the same session may reduce the number of anesthetic exposures, shorten hospitalization, and increase overall efficiency (5–6). Despite these potential advantages, single-session procedures may prolong operative time and increase intrarenal pressures, which may lead to infectious complications, postoperative discomfort, or, in some cases, bleeding and ureteral injury (7,8).

Given these considerations, further evaluation is required to clarify the safety and effectiveness of simultaneous stone removal. The present study aims to assess the outcomes of treating ureteral and ipsilateral renal stones during the same operative session.

MATERIALS AND METHODS

We retrospectively analyzed seventy-nine patients treated with flexible URS / Retrograde Intrarenal Surgery (RIRS) for simultaneous ureteral and ipsilateral renal stones from January 2024 to May 2025. The study was in accordance with the Declaration of Helsinki, and ethical approval was obtained from the Medeniyet University Ethics Committee (Approval no.: 2025/0300, Date: 2025-11-11). All patients were assessed by non-contrast spiral computed tomography (CT) scanning. Exclusion criteria included the ureteropelvic junction obstruction, ureteral strictures, presence of congenital renal anomalies, and the presence of a urinary tract infection. Prior to the procedure, patients underwent routine laboratory evaluations comprising a complete blood count, urine culture, and serum creatinine measurement. A single dose of a second-generation parenteral cephalosporin was administered to all patients preoperatively for

antibiotic prophylaxis. Patients were placed in the lithotomy position under general anesthesia. Ureter stones were treated using a 9.5 French (Fr) ureteroscope (Richard Wolf, Knittlingen, Germany). Following the complete removal of the ureteral calculus, 11.5 Fr Ureteral Access Sheath (UAS) of appropriate length was inserted to facilitate the RIRS procedure. The flexible ureteroscope (7.5 Fr Karl Storz Flex-X2, Tuttlingen, Germany) was advanced through the access sheath to reach the renal pelvis. In patients in whom the UAS could not be advanced, direct visualization was achieved by advancing the flexible ureteroscope over the guidewire. The renal stones were fragmented using a Holmium YAG laser probe. Following a detailed inspection of the collecting system to ensure no residual fragments remained, a double-J (DJ) stent was placed and left in situ for 2 to 4 weeks.

Preoperative and postoperative characteristics, Hounsfield unit (HU), complication rate, hospital duration, and Stone-free rate (SFR) were evaluated. Postoperatively, patients underwent radiographic assessments, X-ray, or non-enhanced CT scan at 1 day and 1 month for follow-up. SFR was defined as residual stones <2 mm on a postoperative imaging study.

Statistical analyses were performed using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics for patient demographics and baseline characteristics are presented in Table 1. Continuous variables are reported as mean ± standard deviation. Comparisons between SFR-positive and SFR-negative groups are presented in Table 2. Continuous variables were compared using the independent samples t-test. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate (particularly when expected cell counts were <5). Patient follow-up data are summarized in Table 3. A p value <0.05 was considered statistically significant.

RESULTS

Seventy-nine patients were included in the study. The mean ureteral stone size was 8.66 ± 2.8 mm, while the mean ipsilateral renal stone size measured 10.47 ± 6.1 mm. The average HU were 985 ± 267.1 for ureteral stones and 1101 ± 235.8 for renal stones. Regarding stone location, 48.8% of ureteral stones were in the proximal ureter, 39% in the distal ureter, and 20.2% in the mid-ureter. Renal stones were most frequently identified in the lower pole (35.4%), followed by the renal pelvis (26.6%), middle pole (22.7%), and upper pole (15.3%). The median number of stones per patient, including both renal and ureteral stones, was 3.16 (range 2–10). Hydronephrosis was present in varying degrees, with Grade 2 being the most common (41.7%), whereas only 1.6% of patients demonstrated Grade 4 hydronephrosis. The mean operative time was 50.06 ± 13.1 minutes. UAS was used in 53.2% of cases. Intraoperative complications were rare, observed in only 2 patients (2.6%). Postoperative complications were recorded in 5 patients (6.4%). SFR on postoperative day 1 was 53.2%, increasing substantially to 75.9% at 1 month follow-up.

Patients were categorized into two groups according to their 1-month stone-free status: SFR-positive (n=60) and SFR-negative (n=19). Ureteral stone HU was significantly lower in the SFR-positive group compared to the SFR-negative group (981.8 ± 263 vs. 842 ± 256.4 HU, p = 0.047). Patients with SFR-negative outcomes had significantly larger ipsilateral renal stones than those in the SFR-positive group (14.74 ± 7.5 mm vs. 11.2 ± 4.8 mm, p = 0.018). Hydronephrosis severity demonstrated a statistically significant distribution between groups (p = 0.010), with ≥ Grade 2 hydronephrosis being more significant in the SFR-positive group. The mean number of stones per patient was significantly higher in the SFR-negative group compared with the SFR-positive group (4.1 ± 2.4 vs. 2.8 ± 1.6, p = 0.037). Lateralization, prior surgical intervention history, ureteral and renal stone localization demonstrated no statistically significant differences between the groups.

The mean follow-up duration was 14.1 ± 5.7 months. Thirteen patients (16.5%) required an auxiliary procedure. Among these interventions, five patients (38.4%) underwent URS, four patients (30.8%) underwent RIRS, and four patients (30.8%) were treated with ESWL. Postoperative complications occurred in five patients (6.3%). Of these, two patients (40%) developed fever or infection requiring antibiotic therapy, two patients (40%) experienced stent

migration necessitating reinsertion, and one patient (20%) presented with postoperative hematuria. According to the Clavien–Dindo classification, complications were distributed as follows: one patient (20%) had a Grade I event, two patients (40%) had Grade II events, and two patients (40%) experienced Grade III complications. No Grade IV complications were observed. The mean time to DJ stent removal was 2.8 ± 0.9 weeks.

Table 1. Descriptive Statistics of Patient Demographics and Clinical Outcomes

Variables	Patients, n (%)
Age (years), (mean ± SD)	48.3 ± 15.7
Gender, n (%)	
Male	60 (75.9)
Female	19 (24.1)
Ureteral stone size, (mean ± SD)	8.66 ± 2.8
Ureteral stone HU, (mean ± SD)	985 ± 267.1
Kidney stone size, (mean ± SD)	10.47 ± 6.1
Kidney stone HU, (mean ± SD)	1101 ± 235.8
Operative Time (min), (mean ± SD)	50.06 ±13.1
Lateralization, n (%)	
Right	41 (51.9)
Left	38 (48.1)
Prior surgery, n (%)	
No	43 (54.4)
Yes	36 (45.6)
Ureteral stone location, n (%)	
Distal	30 (39)
Mid-ureter	16 (20.2)
Proximal	33 (48.8)
Kidney stone location (%), n (%)	
Renal Pelvis	21 (26.6)
Upper calyx	12 (15.3)
Middle calyx	18 (22.7)
Lower calyx	28 (35.4)
Grade of Hydronephrosis (SFU), n (%)	
Grade 0	22 (27.8)
Grade 1	15 (18.9)
Grade 2	33 (41.7)
Grade 3	8 (10)
Grade 4	1 (1.6)
Usage of UAS, n (%)	
None	37 (46.8)
Yes	42 (53.2)
Peroperative complications, n (%)	
None	77 (97.4)
Yes	2 (2.6)
SFR postoperative 1.day, n (%)	
None	37 (46.8)
Yes	42 (53.2)
SFR postoperative 1. month, n (%)	
None	19 (14.1)
Yes	60 (75.9)
Number of stones, median (min-max)	3.16 (2-10)

UAS: Ureteral access sheath; SFR: Stone-free rate; SFU: Society of Fetal Urology; HU: Hounsfield Unit

Table 2. Comparison of Demographic and Operative Outcomes between Stone-Free Positive and Stone-Free Negative Patient Groups

	SFR 1. month (Negative) (N=19)	SFR 1. month (Positive) (N=60)	P value
Age (years), (mean ± SD)	42 ± 17.6	45.3 ± 14.6	0.466
Gender, n (%) Male Female	 14 (73.7) 5 (26.3)	 46 (76.7) 14 (26.3)	0.767
Ureteral stone size, (mean ± SD)	9.2 ± 3.5	8.4 ± 2.6	0.367
Ureteral stone HU, (mean ± SD)	981.8 ± 263	842 ± 256.4	**0.047**
Kidney stone size, (mean ± SD)	14.74 ± 7.5	11.2 ± 4.8	**0.018**
Kidney stone HU, (mean ± SD)	1101.3 ± 241.6	1101.2 ± 235.7	0.998
Operative Time (min), (mean ± SD)	53.16 ± 13.1	49.08 ± 13.03	0.239
Lateralization, n (%) Right Left	 8 (42.1) 11 (57.9)	 33 (55) 27 (45)	0.431
Preoperative surgical procedure, n (%) No Yes	 8 (42) 11 (58)	 35 (58.3) 25 (41.7)	0.216
Ureteral stone location, n (%) Distal Mid-ureter Proximal	 4 (21) 7 (36.8) 8 (42.2)	 26 (43.3) 9 (15) 25 (41.7)	0.071
Kidney stone location (%), n (%) Renal Pelvis Upper calyx Middle calyx Lower calyx	 4 (21) 2 (10.5) 4 (21) 9 (47.5)	 17 (28.3) 10 (16.6) 14 (23.3) 19 (31.8)	0.641
Grade of Hydronephrosis (SFU), n (%) Grade 0-1 ≥ Grade 2	 4 (21) 15 (79)	 33 (55) 27 (45)	**0.010**
Usage of UAS, n (%) None Yes	 7 (36.8) 12 (63.2)	 30 (50) 30 (50)	0.317
Perioperative complications, n (%) None Yes	 19 (100) 0	 58 (96.7) 2 (3.3)	0.420
SFR 1.day, n (%) None Yes	 18 (94.8) 1 (5.2)	 20 (33.3) 40 (66.7)	**<0.001**
Number of stones, (mean ± SD)	4.1 ± 2.4	2.8 ± 1.6	**0.037**

UAS: Ureteral access sheath; SFR: Stone-free rate; SFU: Society of Fetal Urology; HU: Hounsfield Unit

Table 3. Follow-up data of patients

Variables	
Follow-up (mo.), (mean ± SD)	14.1 ± 5.7
Patients required auxiliary procedure, n (%)	13 (16.5)
Auxiliary procedures, n (%)	
URS	5 (38.4)
RIRS	4 (30.8)
ESWL	4 (30.8)
Postoperative complications rate, n (%)	5 (6.3)
Postoperative complication, n (%)	
Fever/Infections requiring antibiotics	2 (40)
Stent migration requires reinsertion	2 (40)
Postoperative hematuria	1 (20)
Clavien Dindo	
Grade 1	1 (20)
Grade 2	2 (40)
Grade 3	2 (40)
Grade 4	0
Removal of DJ stent (week), (mean ± SD)	2.8 ± 0.9

URS: Ureteroscopy; RIRS: Retrograde Intrarenal Surgery; ESWL: Extracorporeal Shock Wave Lithotripsy; DJ: Double-J

DISCUSSION

In this single-center study, we evaluated the outcomes of simultaneous endourological management of ureteral and ipsilateral renal stone, demonstrating that this combined approach is both feasible and effective, with acceptable complication rates. Our findings support previously published literature suggesting that advances in flexible ureteroscopy, improved laser technologies, and optimized intrarenal pressure control have facilitated comprehensive single-session stone management (9).

The overall 1-month stone-free rate (SFR) of 75.9% in our cohort is comparable with earlier reports demonstrating SFR values between 70–85% for simultaneous stone removal for ureteral and ipsilateral renal stone (10-11). Ozden et al., who reported SFR rates between 72–81% in patients undergoing combined ureteroscopy and renal stone treatment (5). Similarly, Zhu et al. observed that single session ureteroscopy for multi-level stones yielded high success rates with minimal morbidity, supporting the feasibility of treating both ureteral and renal stones concurrently (12).

Importantly, our comparative analysis identified several predictive factors influencing surgical success. Patients in the SFR-negative group had significantly larger renal stones, higher stone burden, and more advanced hydronephrosis. Our findings are consistent with prior studies of stone size and hydronephrosis as major determinants of SFR (13). Increasing stone size has been consistently associated with longer operative times, less effective fragment clearance and making complete stone removal more difficult. Patients with larger renal stones had significantly lower SFR rates, which provides evidence to indicate that stone size remains one of the strongest determinants of endourological success (8).

Some studies have similarly demonstrated the benefits of combining URS and Percutaneous Nephrolithotomy (PCNL) for patients with complex stone burdens. Desai et al. reported that synchronous URS and PCNL reduced overall anesthesia exposure and shortened hospital stay without compromising safety or efficacy (14). Their findings also highlighted that combined treatment is particularly advantageous in patients with high stone burden, in our study, where patients with larger renal stones showed lower SFR, emphasizing the importance of stone size in predicting outcomes. Zeng et al. showed that synchronous intrarenal surgery and ureteroscopy improved operative efficiency in

patients with multiple stones and avoided the need for staged procedures (15). Our findings are consistent with this observation, as 16.5% of patients required additional procedures during follow-up, comparable to the auxiliary rates in combined URS/PCNL series that reported 12–20% secondary intervention rates (16).

Multiple stones increase laser fragmentation time and elevate the risk of residual fragments. Therefore, in patients with multiple stones, the complete removal of stones has decreased, and our findings are agree with previously published studies (17).

Despite the inclusion of patients with high stone burdens, the procedure demonstrated a low perioperative (2.6%) and postoperative complication rate (6.3%). These rates are similar to those found in recent multicenter studies, indicating that performing simultaneous procedures does not increase complication risks when conducted by experienced surgeons (11-12). Additionally, the mean operative time of approximately 50 minutes remained within the acceptable range for combined ureteroscopic and intrarenal procedures.

The primary limitation of this study is its retrospective nature. Another limitation is that the procedures were performed by multiple experienced endourologists. Although this helps maintain consistent and high-quality surgical results, it may limit the generalizability of the findings to centers with less experienced surgeons. Other limitations were the small number of patients and a single center study. Future prospective, multicenter studies with larger cohorts are needed to confirm and expand upon these findings to provide more robust and generalizable evidence

CONCLUSIONS

Simultaneous treatment of ureteral and ipsilateral renal stones was found to be an effective and safe approach, achieving high SFR with low complication rates. Stone size and number of stones, were the strongest predictors of postoperative success. Although these results support the use of single-session management in appropriately selected patients, larger prospective and multicenter studies are needed to confirm these findings and guide optimal clinical decision-making.

Funding: No funding was received for this research.

Conflicts of Interest: There are no conflicts of interest to declare.

Ethical Approval: The study was conducted by the Helsinki Declaration, and ethical approval was obtained from the İstanbul Medeniyet University Ethics Committee (Approval no.: 2025/0300, Date: 2025-11-11).

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):126–133. doi: 10.54233/endourolbull-1848567

Evaluating Kidney Cyst Information from Chatbots: A Comparative Study

Chatbotlardan Elde Edilen Böbrek Kisti Bilgilerinin Değerlendirilmesi: Karşılaştırmalı Bir Çalışma

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ABSTRACT

Objective: Kidney cysts are the most common acquired lesions of the kidney. This study aims to assess the reliability and quality of responses provided by three different artificial intelligence chatbots to questions related to kidney cysts.

Materials and Methods: Using the Semrush platform, we analyzed kidney cyst-related search trends over five years. We examined 25 questions, categorized into four subgroups: "general information", "symptoms and diagnostic methods", "treatment and follow-up procedures", and "side effects and complications". These questions were posed to three chatbots (ChatGPT-4, Gemini Pro, Llama 3.1 Large). Response readability was assessed using Flesch-Kincaid Grade Level (FKGL) test and Flesch Reading Ease Score (FRES) test. Reliability and quality were evaluated using the Ensuring Quality Information for Patients (EQIP) score and modified DISCERN score.

Results: Llama had a significantly higher FKGL score than ChatGPT ($p = 0.022$), with no significant difference between Llama and Gemini ($p = 0.500$), or Gemini and ChatGPT ($p = 0.525$). On the FRES scale, ChatGPT scored higher than Gemini, and Gemini outperformed Llama ($p = 0.006$ and $p = 0.012$, respectively). The median modified DISCERN score was lowest for ChatGPT (2), compared to Gemini (3) and Llama (3) ($p < 0.001$). The mean EQIP score was 71.22 ± 3.91 for ChatGPT, 77.72 ± 1.16 for Gemini and 73.26 ± 2.70 for Llama ($p < 0.001$). ChatGPT had significantly lower quality scores than the other two chatbots.

Conclusion: Although ChatGPT generated the most readable responses according to the FRES score, it demonstrated lower quality and reliability than Gemini and Llama. Overall, chatbot responses remained challenging in terms of readability and comprehension, highlighting the need for further improvements before they can be considered a reliable standalone source of patient education.

Keywords: artificial intelligence, chatbot, ChatGPT, Gemini, kidney cysts, Llama

Cite As: *Koseoglu B, Ordek E, Kutman KG. Evaluating Kidney Cyst Information From Chatbots: A Comparative Study. Endourol Bull. 2026;18(3):126–133.* https://doi.org/10.54233/endourolbull-1848567

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Received : December 24, 2025 ***Accepted*** : August 10, 2026

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ÖZET

Amaç: Böbrek kistleri, böbreğin en sık görülen edinsel lezyonlarıdır. Çalışmanın amacı, böbrek kistleriyle ilgili sorulara üç yapay zekâ sohbet botu tarafından verilen yanıtların güvenilirliğini ve kalitesini değerlendirmektir.

Gereç ve Yöntemler: Semrush platformu kullanılarak böbrek kistleriyle ilişkili arama eğilimleri beş yıllık dönem boyunca analiz edildi. Yirmi beş soru; "genel bilgiler", "semptomlar ve tanı yöntemleri", "tedavi ve takip yaklaşımları" ile "yan etkiler ve komplikasyonlar" olarak gruplandı. Sorular üç sohbet botuna (ChatGPT-4, Gemini Pro, Llama 3.1 Large) yöneltildi. Yanıtların okunabilirliği Flesch-Kincaid Sınıf Düzeyi (FKGL) testi ve Flesch Okunabilirlik Kolaylığı Skoru (FRES) testiyle değerlendirildi. Güvenilirlik ve kalite ise Hastalar İçin Bilgi Kalitesinin Sağlanması (Ensuring Quality Information for Patients – EQIP) skoru ve modifiye DISCERN skoru kullanılarak analiz edildi.

Bulgular: Llama'nın FKGL skoru ChatGPT'ye kıyasla anlamlı derecede yüksekti (p = 0,022); Llama ile Gemini (p = 0,500) ve Gemini ile ChatGPT (p = 0,525) arasında fark saptanmadı. FRES ölçeğinde ChatGPT, Gemini'den; Gemini ise Llama'dan yüksek skor elde etti (sırasıyla p = 0,006 ve p = 0,012). Medyan modifiye DISCERN skoru ChatGPT için en düşük değerdi (2); bu değer Gemini (3) ve Llama (3) ile karşılaştırıldığında anlamlı fark gösterdi (p < 0,001). Ortalama EQIP skoru ChatGPT için 71,22 ± 3,91, Gemini için 77,72 ± 1,16 ve Llama için 73,26 ± 2,70 bulundu (p < 0,001). ChatGPT, diğer sohbet botlarına kıyasla daha düşük kalite skorlarına sahipti.

Sonuçlar: ChatGPT, FRES skoruna göre en okunabilir yanıtları oluşturmasına rağmen, kalite ve güvenilirlik açısından Gemini ve Llama'ya kıyasla daha düşük performans göstermiştir. Genel olarak sohbet botlarının yanıtları okunabilirlik ve anlaşılabilirlik açısından zorlayıcı bulunmuş olup, hasta eğitimi için güvenilir bağımsız bir kaynak olarak değerlendirilebilmeleri için daha fazla geliştirmeye ihtiyaç vardır.

Anahtar Kelimeler: böbrek kistleri, ChatGPT, Gemini, Llama, sohbet botu, yapay zekâ

INTRODUCTION

Renal cysts are the most frequently observed acquired lesions of the kidney (1). Often detected incidentally during imaging studies conducted for other indications, these lesions represent a highly prevalent urological condition and constitute a common finding in routine clinical practice (2). Although most renal cysts are benign and asymptomatic, concerns regarding their malignant potential, follow-up strategies, and treatment options frequently prompt patients to seek additional health information. Consequently, the demand for reliable patient-oriented health information remains considerable.

The internet, which became widespread in the last quarter of the 20th century, has emerged as the primary method for information retrieval today. The rapid development of information and communication technologies has substantially increased public access to health information and continuously reshaped health information-seeking behaviors (3). In recent years, artificial intelligence (AI) technologies have gained prominence as an interactive tool for accessing such information (4). AI encompasses technologies that enable computers to mimic human learning, decision-making, and creativity, and these systems are now integrated into various platforms, allowing patients immediate access to medical information and treatment options (5).

Several studies have examined the quality and reliability of AI chatbots' responses to medical inquiries (5–8). However, to the best of our knowledge, no published study has specifically evaluated chatbots in the context of renal cysts. Therefore, the aim of this study is to evaluate the readability, quality, and reliability of chatbot-generated responses pertaining to renal cysts.

MATERIALS AND METHODS

This cross-sectional observational study was initiated on December 7, 2024. The Semrush platform (Semrush Inc., Boston, MA, USA) was used to identify search trends for "kidney cyst" and related keywords. The 50 most relevant kidney cyst-related questions identified by the platform were screened according to predefined eligibility criteria,

including relevance to kidney cysts, clarity of expression, and suitability for patient-oriented questioning. Duplicate, repetitive, poorly formulated, and unrelated questions were excluded, resulting in a final set of 25 eligible questions (Appendix 1). To avoid bias prior to the study, all personal web browser accounts were logged out, and browsing histories were cleared. A 5-year timeframe was selected from the Semrush data source, and the search volumes and regional distributions were examined. Based on their content, the questions were categorized under four main headings: "general information", "symptoms and diagnostic methods", "treatment and follow-up procedures", and "side effects and complications".

In the second phase of the study, the 25 identified questions were presented once to three publicly accessible chatbot models (ChatGPT-4, Gemini Pro, and Llama 3.1 Large) on December 7, 2024, and all responses were generated and recorded on the same day. Each question was submitted only once to each chatbot without regeneration or repeated prompting, and the first response generated by the chatbot was used for analysis. The number of words, sentences, and syllables in each response was documented. Subsequently, the responses were subjected to statistical analyses focusing on readability, quality, and reliability.

The readability of the responses obtained was evaluated using the Flesch-Kincaid Grade Level (FKGL) and Flesch Reading Ease (FRES) scores. The FKGL score identifies the level of education at which the text can be comfortably read. A lower FKGL score indicates a more readable and easily understandable text (9). Lower scores (0–6) correspond to an elementary school level, while higher scores (>12) indicate a university-level text. The formula for calculating the FKGL score is presented below.

FRES is another metric used to assess the readability of responses. The target score in this system is 60 or above. As the score increases, the readability of the responses also improves (10). A score between 80 and 100 indicates that the text is easily readable, while a score ranging from 0 to 30 suggests that the text is hard to understand. The calculation is shown below.

The quality and reliability of the responses were assessed using the modified DISCERN score and the Ensuring Quality Information for Patients (EQIP) tool. The modified DISCERN score was calculated by asking five questions with yes/no answers. Each "yes" or "no" response was scored as 1 point or 0 points, respectively, by two urologists. In cases of disagreement, a third reviewer was consulted to finalize the score. The questions were as follows: (a) Is the text clear and understandable? (b) Are reliable sources of information used? (c) Is the information presented both balanced and unbiased? (d) Are additional sources of information listed for patient reference? (e) Are areas of uncertainty mentioned? The EQIP tool, on the other hand, is an assessment instrument comprising 20 questions, each of which can be answered with "yes," "partly," "no," or "does not apply". As with the modified DISCERN score, the EQIP score was assigned by two urologists, with "yes" scoring 1 point, "partly" 0.5 points, and "no" 0 points. The calculation of the EQIP score is shown below. According to the EQIP score, 76%–100% indicates adequate quality, 51%–75% indicates good quality with minor issues, 26%–50% indicates serious quality issues, and 0%–25% indicates severe quality issues (11).

Statistical Analysis

Statistical analyses were performed using IBM SPSS (v 27.0.1.0). Descriptive statistics for normally distributed variables were reported as mean ± standard deviation, whereas nonparametric or ordinal data were reported as median (IQR). Normality was assessed using the Shapiro-Wilk test, and homogeneity of variances was evaluated with Levene's test. Comparisons among the three chatbot groups were performed using one-way analysis of variance (ANOVA). When significant differences were detected, Tukey's HSD (Honestly Significant Difference) test was used for post hoc comparisons if the assumption of equal variances was met. In cases of unequal variances, the Games-Howell test was applied. For ordinal variables, including Modified DISCERN scores, the Kruskal–Wallis test was used, followed by Bonferroni-adjusted pairwise comparisons when appropriate. A p value < 0.05 was considered statistically significant.

Because this study did not involve any personal data or patient information, no ethical committee approval was required. The data used in this study were obtained from publicly accessible versions of large language models (LLMs) and open-source databases.

RESULTS

The 25 questions posed to the chatbots were evaluated using readability, quality, and reliability metrics. The average number of words per response for ChatGPT, Gemini, and Llama was 130.16 ± 39.82, 228.80 ± 67.33, and 191.20 ± 71.72, respectively ($p < 0.001$). The average number of sentences per response was 12.92 ± 5.58 for ChatGPT, 17.76 ± 6.75 for Gemini, and 12.40 ± 6.04 for Llama ($p = 0.005$). Post-hoc analyses showed that ChatGPT's responses contained significantly fewer words than those of Gemini ($p < 0.001$) and Llama ($p = 0.002$). However, no statistically significant difference was observed between Gemini and Llama ($p = 0.100$). Additionally, post-hoc analyses indicated that Gemini's responses had significantly more sentences per response compared to ChatGPT and Llama ($p = 0.021$ and $p = 0.009$, respectively), whereas no significant difference was noted between ChatGPT and Llama ($p = 1.00$).

Readability was assessed using FKGL and FRES scores (Table 1). There was a statistically significant difference in FKGL scores among the three chatbots ($p = 0.026$). Pairwise comparisons revealed that Llama had a significantly higher FKGL score than ChatGPT ($p = 0.022$); however, there was no significant difference between Llama and Gemini ($p = 0.500$) or between Gemini and ChatGPT ($p = 0.525$). For the FRES scale, post-hoc analyses showed that ChatGPT had a significantly higher FRES score than Gemini, and Gemini had a significantly higher score than Llama ($p = 0.006$ and $p = 0.012$, respectively).

The reliability and quality of the responses were evaluated using the modified DISCERN score and EQIP tool (Table 1). ChatGPT had lower modified DISCERN scores compared to both Gemini and Llama ($p < 0.001$ and $p = 0.014$, respectively). No statistically significant difference was observed between Gemini and Llama ($p = 0.056$). For the EQIP score, Gemini scored significantly higher than both ChatGPT and Llama ($p < 0.001$ and $p < 0.001$, respectively), and Llama had a significantly higher score than ChatGPT ($p = 0.039$).

Analyses of the responses by question subgroup revealed no significant differences in readability measures. For the questions related to "general information", Gemini's responses had significantly higher modified DISCERN and EQIP scores. In the subgroups of "symptoms and diagnostic methods", and "treatment and follow-up procedures", Gemini had higher EQIP scores than the other chatbots, whereas the modified DISCERN scores were similar across all three. Within the "treatment and follow-up" subgroup, the modified DISCERN scores were also similar for all three chatbots; however, Gemini had a significantly higher EQIP score than the other two. Regarding "side effects and complications", all three chatbots had similar EQIP scores; however, ChatGPT's modified DISCERN score was significantly lower than that of Llama, with no statistically significant difference observed between ChatGPT and Gemini.

Table 1. The results of the readability, quality, reliability evaluation of chatbots

Variables	ChatGPT	Gemini	Llama	p value
FRES, mean ± s.d	51.69±5.45[a]	45.74±5.80[b]	40.25±8.09[c]	<0.001
FKGL, mean ± s.d	20.52±2.53[a]	21.38±1.89[ab]	22.26±2.21[b]	0.026
Modified DISCERN, median (min-max)	2 (1-3)[c]	3 (1-4)[a]	3 (1-4)[b]	<0.001
EQIP, mean ± s.d.	71.22±3.91[c]	77.72±1.16[a]	73.26±2.70[b]	<0.001

Different superscript letters indicate statistically significant differences between groups ($p < 0.05$). EQIP: The Ensuring Quality Information for Patients, FKGL: Flesch–Kincaid Grade Level, FRES: Flesch Reading Ease score, s.d: Standard Deviation

DISCUSSION

The role of AI in healthcare is expanding every day. AI-based LLMs are frequently used by patients and caregivers to obtain information on various diseases (12). Owing to their high prevalence, kidney cysts represent one of the topics most commonly queried in AI chatbots. In this study, we aimed to evaluate the readability, quality, and reliability of answers provided by three chatbots regarding kidney cysts.

To our knowledge, this is the first study in the literature to assess answers generated by AI chatbots for questions related to kidney cysts. According to our findings, ChatGPT provided more readable answers than Llama and Gemini, yet it scored lower than the other two chatbots in terms of quality and reliability. This apparent paradox may be explained by the shorter and more concise nature of ChatGPT's responses. Although brevity may improve readability, it may also reduce the comprehensiveness of the information provided, leading to lower EQIP and modified DISCERN scores. Although Gemini had higher EQIP scores than the other two chatbots, all three chatbots' EQIP scores indicated good quality with minor issues. Gemini's higher scores may be attributable to its provision of longer, more detailed answers. Subgroup analyses showed that Gemini had higher EQIP scores in all but the "side effects and complications" subgroup. These findings suggest that Gemini delivers more detailed, reliable, and higher-quality information, making it a better resource for addressing complex and challenging questions about kidney cysts.

In recent years, the use of chatbots in healthcare has attracted considerable attention, prompting numerous studies on this subject (5–7,13). Nearly all these studies have evaluated the readability and comprehensibility of chatbot responses. Texts that are difficult for patients and their caregivers to understand may lead to the spread of misinformation; therefore, the readability and comprehensibility of chatbot-generated content are of paramount importance (14). One study reported low readability in ChatGPT-generated text on spinal cord injuries (15). In that study, the readability scores, as assessed by FKGL and FRES, were 14.84 ± 1.79 and 26.24 ± 13.81, respectively. Behers and colleagues, in their assessment of responses from four different chatbots—including ChatGPT and Gemini—regarding cardiac catheterization, noted that the responses were difficult to read (10). However, the texts generated by Gemini had a lower FKGL and a higher FRES, indicating that it produced more readable content. Similarly, in an evaluation of educational brochures for urological patients, chatbot-generated answers—including those from Llama—were found to exceed the average adult reading level (16). Consistent with prior research, our findings indicate that chatbot-generated responses are often written at a level that exceeds the average reader's comprehension capacity. Among the evaluated models, ChatGPT produced the most readable content; however, its readability still corresponded to a university-level text according to the FKGL score. The relatively high FKGL values observed in the present study may be explained by the frequent use of multisyllabic medical terminology, disease classifications, and detailed explanatory language generated by the chatbots. Because the evaluated questions focused on specialized concepts such as Bosniak classification, polycystic kidney disease, and minimally invasive treatment approaches, the resulting responses naturally contained vocabulary that increased the calculated reading grade level. Post-hoc comparisons showed that ChatGPT's responses were significantly easier to read than those of Gemini, and Gemini's were in turn more readable than those of Llama. Notably, Llama's outputs aligned with the lowest FRES values and the highest FKGL scores, indicating text that would likely be challenging even for highly educated readers. These results reveal a clear gradient in readability among the chatbots and underscore the importance of optimizing AI-generated health content to meet established readability standards, especially when intended for patient education.

Various assessment tools such as the Patient Education Materials Assessment Tool (PEMAT), the Global Quality Score (GQS), the modified DISCERN score, and the EQIP score have been utilized in recent studies to evaluate the accuracy and overall quality of health-related content produced by AI-powered chatbots (5,17,18). One study that assessed content related to erectile dysfunction compared five different chatbots, including ChatGPT, using the EQIP score (5). In contrast to our findings, that study reported a significantly lower mean EQIP score for ChatGPT (40 ± 4.2), indicating serious quality issues, whereas our results showed acceptable quality with minor issues, reflected by a notably higher

mean score (71.22 ± 3.91). In an evaluation of patient education materials on female urinary incontinence produced by chatbots, the EQIP scores for the Gemini chatbot were higher than those of ChatGPT and Llama (19). These results align with the EQIP scores observed in our study. In our study, while ChatGPT received lower scores for quality and reliability than the other two chatbots, Gemini outperformed both on these metrics.

The modified DISCERN score is another commonly used tool in recent studies for evaluating the reliability of health-related information provided by AI chatbots (4,17). In their study on cardiopulmonary resuscitation content, Arca and colleagues found that Gemini provided more reliable responses than ChatGPT, as reflected by higher modified DISCERN scores, which is consistent with our results (17). In another study, health information provided by AI-powered chatbots regarding premature ejaculation was evaluated. The modified DISCERN score, used to assess reliability, was similar for Gemini and Llama, whereas ChatGPT received a lower score (4). This statistical outcome aligns with the findings of our study.

The reliability and quality of information provided by AI-supported chatbots can vary considerably between different models. Overall, the literature suggests that chatbot responses do not consistently meet adequate quality standards (5,7,20). Therefore, efforts to improve the quality of AI-generated content remain crucial. One strategy to achieve this involves expanding the training datasets used by AI chatbots (5). Incorporating specific healthcare parameters into AI machine-learning processes could facilitate the generation of more accurate responses. In addition, the evaluated chatbots differ in their accessibility and deployment characteristics. Unlike proprietary models such as ChatGPT and Gemini, Llama is an open-source large language model that can be deployed and customized locally, potentially improving accessibility in privacy-sensitive or resource-limited settings. It is also important to remember that no AI-based model can fully replace a comprehensive medical examination or the consultation of a qualified healthcare professional.

From a practical perspective, chatbot-generated information may serve as an introductory educational resource for patients and caregivers. Patients seeking brief and relatively easier-to-read information may benefit from ChatGPT's concise responses, whereas users requiring more comprehensive information may find Gemini more informative despite its lower readability. Therefore, chatbot-generated content should be interpreted as a complementary educational tool rather than a substitute for professional medical advice.

Limitations

This study has several limitations. First, the question set was restricted to the 25 most frequently searched queries identified through the Semrush platform, which may not fully represent the wide range of information needs of patients with kidney cysts. Second, the EQIP tool used to assess response quality was originally developed for evaluating written patient information rather than AI-generated chatbot content. Although it has been widely used in similar studies, dedicated assessment instruments specifically designed for LLM outputs are still needed. Third, all evaluations were performed using English-language responses, which may limit the generalizability of our findings to other languages and cultural contexts. Fourth, only specific versions of three publicly available chatbot models were evaluated at a single time point. Because LLMs are continuously updated, their responses and performance may change over time. Fifth, each question was submitted only once to each chatbot, and only the initial response was analyzed. Since chatbot outputs may vary across repeated interactions due to their probabilistic nature, future studies incorporating multiple response generations may provide a more comprehensive assessment of response quality and reliability. Finally, although the modified DISCERN and EQIP scores were independently evaluated by two urologists and disagreements were resolved through discussion with a third reviewer, formal inter-rater agreement statistics (e.g., Cohen's kappa or intraclass correlation coefficient) were not calculated, which may limit the assessment of scoring consistency.

CONCLUSION

All three chatbots evaluated in this study provided responses to kidney cyst-related questions at a readability level beyond the recommended threshold, rendering their content somewhat challenging to comprehend. Although ChatGPT produced the most readable responses, it demonstrated lower quality and reliability than Gemini and Llama. Since none of the three chatbots achieved optimal scores for quality and reliability, our findings underscore the importance of users exercising caution and seeking assistance from a healthcare professional when relying on chatbot-generated information for matters concerning health. Future research should focus on developing AI-specific scoring systems for quality assessment. Investigators should further examine advancements aimed at delivering comprehensible, high-quality information on kidney cysts to chatbot users. Meanwhile, chatbot developers should strive to enhance the clarity and reliability of the information provided.

Conflict of Interest: The authors have no relevant financial or non-financial interests to disclose.

Funding: None

Ethical Approval: No ethical approval was needed because this is not a human study, but only online information was used.

Informed Consent: No informed consent was needed because this is not a human study, but only online information was used.

Author Contributions: B Koseoglu: Project development, data collection, manuscript writing; KG Kutman: Manuscript editing, supervision; E Ordek: Data collection, data analysis

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):134–140. doi: 10.54233/endourolbull-1878545

Evaluation of the Quality and Reliability of Youtube Videos Related to Commonly Performed Kidney Stone Surgeries in Urology Practice

Üroloji Pratiğinde Sık Uygulanan Böbrek Taşı Cerrahilerine İlişkin Youtube Videolarının Kalite Ve Güvenilirliğinin Değerlendirilmesi

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ABSTRACT

Objective: Patients increasingly turn to online video platforms for information about surgical options before making treatment decisions. YouTube™ is the most commonly used video-sharing website and contains a large volume of health-related material with variable accuracy and educational value. This study evaluated the quality, reliability, and informational content of Turkish-language YouTube videos about kidney stone surgery, with particular emphasis on whether uploader characteristics were associated with video quality.

Materials and Methods: In this cross-sectional study, YouTube™ was searched in January 2026 using the Turkish term "böbrek taşı ameliyatı". The first 200 relevant Turkish-language videos were reviewed. For each video, we recorded duration, view count, likes and comments. Video quality was scored with the Journal of the American Medical Association (JAMA) benchmark criteria and the Global Quality Score (GQS). Uploaders were classified as specialist urologists or academic urologists (associate professor/professor). Surgical procedures mentioned in each video were also documented. Statistical analyses were used to compare video characteristics and quality scores between the two groups.

Results: Among the 200 included videos, 112 (56%) had been uploaded by specialist urologists and 88 (44%) by academic urologists. Videos published by academic urologists showed significantly higher median JAMA and GQS values and also attracted higher view and like counts ($p < 0.05$). Video length was not significantly associated with quality scores. Most videos concentrated on a single operative technique, especially ureterorenoscopy, whereas discussion of complications and alternative treatment options was limited.

Conclusion: Although videos uploaded by academic urologists were generally more reliable and of better quality, Turkish-language YouTube content on kidney stone surgery overall was not sufficient as a stand-alone patient education source. These findings support the need for standardized, evidence-based video materials prepared by professional urological organizations.

Keywords: kidney stone surgery, video analysis, YouTube, health information quality

Cite As: *Ozmez A, Ozgur MO. Evaluation of the Quality and Reliability of YouTube Videos Related to Commonly Performed Kidney Stone Surgeries in Urology Practice. Endourol Bull. 2026;18(3):134–140.* https://doi.org/10.54233/endourolbull-1878545

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Received : January 31, 2026 ***Accepted*** : August 21, 2026

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ÖZET

Amaç: Hastalar tedaviye karar vermeden önce cerrahi seçenekler hakkında bilgi edinmek için çevrim içi video platformlarına giderek daha fazla başvurmaktadır. YouTube, en sık kullanılan video paylaşım platformudur ve doğruluk ile eğitsel değer açısından değişken çok sayıda sağlık içeriği barındırmaktadır. Bu çalışmada, böbrek taşı cerrahisi ile ilgili Türkçe YouTube videolarının kalite, güvenilirlik ve bilgilendirici içeriği değerlendirildi; ayrıca yükleyici özellikleri ile video kalitesi arasındaki ilişki araştırıldı.

Gereç ve Yöntemler: Bu kesitsel çalışmada, Ocak 2026 tarihinde YouTube'da "böbrek taşı ameliyatı" anahtar sözcüğü ile arama yapıldı. Uygun bulunan ilk 200 Türkçe video incelendi. Her video için süre, görüntülenme sayısı, beğeni sayısı ve yorum sayısı kaydedildi. Video kalitesi Journal of the American Medical Association (JAMA) ölçütleri ve Global Quality Score (GQS) kullanılarak değerlendirildi. Yükleyiciler uzman ürolog ve akademik ürolog (doçent/profesör) olarak sınıflandırıldı. Videolarda yer verilen cerrahi yöntemler de ayrıca kaydedildi. Gruplar arasındaki video özellikleri ve kalite skorları istatistiksel olarak karşılaştırıldı.

Bulgular: Çalışmaya alınan 200 videonun 112'si (%56) uzman ürologlar, 88'i (%44) akademik ürologlar tarafından yüklenmişti. Akademik ürologlar tarafından yüklenen videolarda medyan JAMA ve GQS skorları ile görüntülenme ve beğeni sayıları anlamlı olarak daha yüksekti ($p < 0.05$). Video süresi ile kalite skorları arasında anlamlı bir ilişki saptanmadı. Videoların büyük kısmı tek bir cerrahi yönteme, özellikle üreterorenoskopiye odaklanırken, komplikasyonlar ve alternatif tedaviler hakkındaki bilgi çoğu videoda sınırlıydı.

Sonuçlar: Akademik ürologlar tarafından yüklenen videolar görece daha güvenilir ve daha yüksek kaliteli olsa da böbrek taşı cerrahisi ile ilgili Türkçe YouTube içerikleri tek başına hasta eğitimi için yeterli değildir. Bu bulgular, profesyonel üroloji kuruluşları tarafından hazırlanacak standart ve kanıta dayalı video içeriklerine ihtiyaç olduğunu göstermektedir.

Anahtar Kelimeler: böbrek taşı cerrahisi, sağlık bilgisi kalitesi, video analizi, YouTube

INTRODUCTION

Kidney stone disease is one of the most common urological disorders worldwide, representing a significant morbidity and a substantial economic burden due to healthcare utilization. Advances in endourological techniques have led to the widespread adoption of minimally invasive surgical approaches such as ureterorenoscopy (URS), retrograde intrarenal surgery (RIRS), and percutaneous nephrolithotomy (PCNL); open surgery is now only preferred for selected complex cases. The choice of surgical method depends on the size, location, and structure of the stone, anatomical factors, and stone-related complications such as infection, sepsis, or acute renal failure.

With advancements in surgical treatment methods and increased accessibility to technology, patients' health information-seeking behaviors have changed significantly. An increasing number of patients are searching the internet for information about their condition and potential treatments before, and even during, consultations with healthcare professionals. Video-based platforms, particularly YouTube™, have become a primary source of medical information due to their accessibility, visual structure, and ease of use. Previous studies have shown that online health information can influence patients' expectations, treatment preferences, and decision-making processes (1,2).

Despite its popularity and apparent reliability, YouTube™ lacks a peer-review mechanism, and the accuracy and reliability of medical content vary greatly depending on the publisher. Incorrect or incomplete information can lead to unrealistic expectations, increased anxiety, and potentially harmful health decisions. Several studies across different medical and surgical specialties have shown that YouTube videos, even when uploaded by healthcare professionals, often provide low-quality or misleading information (3,4).

Previous research in the field of urology has evaluated YouTube content related to prostate cancer, benign prostatic hyperplasia, urinary incontinence, andrological procedures (5,6). However, data focusing on kidney stone surgery,

particularly in Turkish-language content, is limited and often outdated. Given the high prevalence of kidney stone disease and the frequent recommendation of surgical intervention, evaluating the quality of YouTube content in this area is of great clinical importance.

The present study was designed to assess the quality, reliability, and educational content of Turkish-language YouTube videos addressing kidney stone surgery by using established scoring systems and to determine whether the uploader's academic profile was related to better-quality material.

MATERIALS AND METHODS

Study Design and Search Strategy

Publicly accessible YouTube™ videos were evaluated in this cross-sectional observational analysis. In January 2026, the platform was searched with the Turkish expression for kidney stone surgery, "Böbrek taşı ameliyatı". This keyword was selected because it represents a simple, non-technical phrase that Turkish-speaking patients are likely to use when searching for information about surgical treatment of kidney stones. More technical terms such as ureterorenoscopy, retrograde intrarenal surgery, or percutaneous nephrolithotomy were not used as primary search terms because they may be less familiar to the general patient population and could have narrowed the search toward professionally oriented content. Before the search, browser history and cookies were deleted to reduce personalization effects. The search was performed using a standard web browser without logging into a personal YouTube account in order to further reduce personalization bias. Search results were reviewed according to YouTube's default relevance ranking.

Inclusion and Exclusion Criteria

The first 200 videos were included if they were in Turkish, directly related to kidney stone surgery, and had sufficient audio-visual quality to allow reliable evaluation. Duplicate videos, non-medical videos, advertisements without educational content, and videos without audio narration were excluded from the analysis.

Data Collection

For each video, video duration, number of views, likes, comments, uploader type categorized as specialist urologist or academic urologist, and the surgical techniques mentioned, including URS, RIRS, PCNL, open surgery, or multiple techniques, were recorded. Uploader status was determined according to publicly available professional information provided in the video channel, institutional webpages, hospital profiles, or national academic title information when available. Academic urologists were defined as urologists holding an associate professor or professor title at the time of video evaluation. University-affiliated specialists without an associate professor or professor title were classified within the specialist urologist group.

Quality Assessment

Two urologists independently rated video quality and reliability using the following tools:

- JAMA Benchmark Criteria, evaluating authorship, attribution, disclosure, and currency (score range: 0–4) (7,8).
- Global Quality Score (GQS), a 5-point Likert scale assessing overall educational value and flow of information (7,8).

The JAMA benchmark criteria comprise four items: authorship, attribution, disclosure, and currency. One point is awarded for each criterion, and higher scores indicate greater transparency and reliability. The GQS is scored from 1 to 5; a score of 1 indicates poor quality and limited usefulness, whereas a score of 5 indicates excellent quality, comprehensive information, and high usefulness for patients.

Discrepancies were resolved by consensus. Inter-rater agreement between the two reviewers was evaluated before consensus scoring. Agreement for JAMA and GQS scores was assessed using the intraclass correlation coefficient.

Ethics Statement

This study analyzed only publicly available YouTube™ videos and did not involve human participants, patient records, personal health data, or any intervention. Therefore, formal ethics committee approval and informed consent were not required.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was evaluated using the Shapiro-Wilk test and visual inspection of histograms. Continuous variables with normal distribution were expressed as mean ± standard deviation, whereas non-normally distributed variables were presented as median with interquartile range. Categorical variables were summarized as numbers and percentages. Comparisons between videos uploaded by specialist urologists and academic urologists were performed using the independent samples t-test for normally distributed continuous variables and the Mann-Whitney U test for non-normally distributed continuous or ordinal variables, including JAMA and GQS scores. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. The association between video duration and video quality scores was evaluated using Spearman's rank correlation analysis. A 2-sided p value < 0.05 was considered statistically significant. Inter-rater agreement for JAMA and GQS assessments was calculated using the intraclass correlation coefficient. The final JAMA and GQS scores used for statistical analysis were determined after reviewer consensus.

RESULTS

Inter-rater agreement between the two reviewers was high for both video assessment tools. The intraclass correlation coefficient was 0.86 for JAMA scores and 0.89 for GQS scores, indicating good agreement before consensus scoring. Among the 200 videos analyzed, 112 (56%) were uploaded by specialist urologists and 88 (44%) by academic urologists. The mean video duration was 4.1 ± 3.3 minutes. Videos uploaded by academic urologists demonstrated significantly higher quality and reliability scores than those uploaded by specialist urologists. The median JAMA score was 2.5 (IQR: 2–3) in the academic urologist group and 1.5 (IQR: 1–2) in the specialist urologist group, and this difference was statistically significant ($p = 0.003$). Similarly, the median GQS score was significantly higher in videos uploaded by academic urologists than in those uploaded by specialist urologists [4 (IQR: 3–4) vs. 2 (IQR: 2–3), $p < 0.001$].

DISCUSSION

This study demonstrates that the informational quality of Turkish-language YouTube videos related to kidney stone surgery remains limited, despite the high level of public interest and widespread use of the platform for preoperative information-seeking. Although videos uploaded by academic urologists achieved higher JAMA and GQS scores, substantial content-related deficiencies were identified across the majority of analyzed videos.

One of the most important findings of this study is that information regarding potential surgical complications, postoperative care, and alternative treatment options was inadequately addressed in a considerable proportion of

Table 1. General characteristics of analyzed YouTube videos (n = 200)

Variable	Value
Mean video duration (minutes)	4.1 ± 3.3
Median number of views	29,800 (IQR: 6,400–74,500)
Median number of likes	215 (IQR: 62–610)
Median number of comments	18 (IQR: 4–46)
Uploaded by specialist urologists	112 (56%)
Uploaded by academic urologists	88 (44%)

Table 2. Comparison of video quality scores according to uploader academic status

Parameter	Specialist Urologists (n = 112)	Academic Urologists (n = 88)	p
JAMA score, median (IQR)	1.5 (1–2)	2.5 (2–3)	0.003
GQS score, median (IQR)	2 (2–3)	4 (3–4)	<0.001
Views, median	21,400	41,700	0.021
Likes, median	160	330	0.018

Note: Inter-rater agreement was good for both assessment tools. The intraclass correlation coefficient was 0.86 for JAMA scores and 0.89 for GQS scores before consensus scoring.

Table 3. Surgical techniques discussed in YouTube videos

Surgical technique	Number of videos (%)
Ureterorenoscopy (URS)	96 (48%)
Percutaneous nephrolithotomy (PCNL)	28 (14%)
Retrograde intrarenal surgery (RIRS)	22 (11%)
Open surgery	6 (3%)
Multiple techniques discussed	48 (24%)

videos. From both a clinical and ethical standpoint, insufficient discussion of these topics constitutes incomplete and inadequate patient information. In kidney stone disease—where multiple treatment modalities exist—appropriate surgical decision-making requires that patients be informed not only about the procedure itself, but also about its potential risks, expected postoperative course, and available alternatives.

Although minimally invasive procedures such as ureterorenoscopy (URS), retrograde intrarenal surgery (RIRS), and percutaneous nephrolithotomy (PCNL) are generally considered safe, they are not devoid of complications. Intraoperative events such as ureteral injury, bleeding, and infection, as well as postoperative complications including fever, sepsis, stent-related symptoms, and the need for secondary interventions, may significantly influence patient outcomes and satisfaction. Failure to address these issues in publicly accessible educational videos may contribute to unrealistic patient expectations and could influence patients' understanding of surgical risks and postoperative symptoms (9,10,11).

In addition, postoperative management—including stent-related discomfort, pain control, activity restrictions, and follow-up requirements—was frequently overlooked. As patients commonly experience lower urinary tract symptoms, hematuria, or discomfort following endourological procedures, the absence of preoperative counseling regarding these expected findings may result in unnecessary emergency department visits and dissatisfaction with surgical care.

Another notable observation is that many videos focused exclusively on a single surgical modality—most commonly URS—without adequately discussing alternative management strategies such as conservative follow-up, medical expulsive therapy, shock wave lithotripsy, RIRS, PCNL, or, in selected cases, open surgery. This single-modality emphasis may bias patient perception and undermine individualized treatment planning, which represents a fundamental principle of contemporary urological practice.

The association between academic uploader status and higher video quality observed in this study is consistent with previous YouTube-based analyses in urology and other surgical specialties. Academic urologists may be more inclined to provide balanced, evidence-based content and adhere to professional standards. Nevertheless, even among

academic uploads, discussion of complications and postoperative expectations was often incomplete, suggesting a structural limitation of the platform itself rather than solely individual content quality.

Importantly, no association was identified between video duration and informational quality, indicating that longer videos do not necessarily convey more comprehensive or reliable information. Instead, structured presentation and adherence to evidence-based principles appear to be more critical determinants of educational value.

Taken together, these findings highlight a substantial gap between patient information needs and the content currently available on YouTube. While the platform offers considerable potential as an adjunct educational tool, unregulated and incomplete information—particularly regarding surgical risks and postoperative expectations—may hinder safe and informed patient decision-making. From a clinical communication perspective, inadequate discussion of complications in publicly accessible content could contribute to misconceptions regarding surgical safety and expected postoperative outcomes.

Accordingly, professional urological societies, academic institutions, and healthcare organizations should consider developing standardized, peer-reviewed educational video materials that comprehensively address indications, alternative treatment options, potential complications, and postoperative care. This recommendation is supported by prior research demonstrating that incomplete online surgical information is associated with increased patient anxiety and misinterpretation of postoperative outcomes, and that YouTube videos lacking balanced risk-benefit discussions fail to meet fundamental standards of patient education (12).

This study has several limitations. Only Turkish-language videos were analyzed, and YouTube's dynamic algorithm may affect search results over time. In addition, although the assessment tools are validated, they still involve a degree of subjectivity. Another important limitation is that video upload date and video age were not included in the analysis. Older videos may naturally accumulate higher numbers of views, likes, and comments over time, which may influence engagement-related comparisons independently of video quality. Therefore, engagement metrics such as view and like counts should be interpreted cautiously. In addition, the study used a single Turkish search term, which was selected to reflect common patient search behavior; however, the use of additional search terms could have identified different videos. Finally, YouTube content is dynamic, and videos may be deleted, modified, or newly uploaded over time; therefore, the findings reflect the status of the platform only at the time of data collection.

CONCLUSION

Turkish-language YouTube videos related to kidney stone surgery demonstrate generally low informational quality. Although videos uploaded by academic urologists provide relatively more reliable information, YouTube™ cannot currently be considered an adequate standalone educational resource for patients. The development of high-quality, standardized, evidence-based video content by professional urological organizations is strongly recommended.

Acknowledgments: The authors thank all contributors who supported the preparation and evaluation of this manuscript.

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

Informed Consent: Informed consent was not required.

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

Ethical Approval: Ethical approval was not required for this study because it was based on publicly available online video content and did not involve human participants, identifiable patient data, or patient intervention.

Author Contributions: Abdulkadir Ozmez: Conceptualization, study design, data collection, data analysis, manuscript drafting, final approval.
Mehmet Ozay Ozgur: Data interpretation, critical revision of the manuscript, final approval.

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):141–149. doi: 10.54233/endourolbull-1883616

Frailty Matters: The Success of the Modified Frailty Index-5 Score in Predicting Postoperative Outcomes in Radical Prostatectomy

Frailty Önemlidir: Modified Frailty Index-5 Skorunun Radikal Prostatektomide Postoperatif Sonuçları Öngörmede Başarısı

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ABSTRACT

Objective: Patients undergoing radical prostatectomy generally belong to an older population; therefore, in addition to chronological age, frailty has a substantial impact on clinical outcomes. This study aimed to evaluate the predictive value of the modified frailty index (mFI-5) for post-operative complications and functional outcomes in patients undergoing radical prostatectomy.

Materials and Methods: A retrospective analysis was conducted on 200 individuals who underwent radical prostatectomy between January 2016 and January 2024 in a high-volume tertiary center. Data collection included demographic characteristics, comorbidity profiles, histopathological findings, perioperative variables, postoperative complications and follow-up outcomes. Patients were stratified as having either high risk (≥ 2) or low risk (< 2) according to pre-operative mFI-5 scores. Postoperative complications constituted the primary endpoint, whereas functional outcomes were assessed as secondary endpoints.

Results: The study included 200 male patients, with a mean age of 64.7 ± 6.03 years. Fifty-four out of 200 patients (27%) were in the high-risk group (mFI-5 ≥ 2) while 146 patients (73%) were in low-risk group (mFI-5 < 2). While the rate of major complications (Clavien-Dindo ≥ 3) was significantly higher in high-risk group, the overall complication rate was similar between the groups. Readmission and reoperation rates were increased in the high-risk group; however, the difference did not reach statistical significance. Regarding functional outcomes, erectile dysfunction and urinary incontinence rates were similar between the groups.

Conclusion: This study highlights an association between higher mFI-5 scores and an increased risk of major postoperative complications after radical prostatectomy. Although mFI-5 should not be used as a stand-alone criterion for treatment selection, it may serve as a simple, rapid, and cost-effective adjunctive tool for preoperative risk stratification and individualized surgical decision-making.

Keywords: prostate cancer, radical prostatectomy, modified frailty index-5, complication, functional outcomes

Cite As: *Ipek OM, Dincer E, Sevinc AH, Hanci Sevinc B, Canakci C, Akyol YK, Ozkaptan O. Frailty Matters: The Success of the Modified Frailty Index-5 Score in Predicting Postoperative Outcomes in Radical Prostatectomy. Endourol Bull. 2026;18(3):141–149.* https://doi.org/10.54233/endourolbull-1883616

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Received : February 6, 2026 ***Accepted*** : July 20, 2026

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ÖZET

Amaç: Radikal prostatektomi uygulanan hastalar genellikle ileri yaş popülasyonuna aittir; bu nedenle kronolojik yaşa ek olarak, frailty (kırılganlık) klinik sonuçlar üzerinde önemli bir etkiye sahiptir. Bu çalışmanın amacı, radikal prostatektomi uygulanan hastalarda modifiye frailty indeksinin (mFI-5) postoperatif komplikasyonlar ve fonksiyonel sonuçlarını öngörmedeki başarısını değerlendirmektir.

Gereç ve Yöntemler: Ocak 2016 ile Ocak 2024 tarihleri arasında yüksek hacimli bir üçüncü basamak merkezde radikal prostatektomi uygulanan 200 hastanın verileri retrospektif olarak analiz edilmiştir. Demografik özellikler, komorbidite profilleri, histopatolojik bulgular, perioperatif değişkenler, postoperatif komplikasyonlar ve takip sonuçları değerlendirilmiştir. Hastalar, preoperatif mFI-5 skorlarına göre yüksek risk (≥ 2) ve düşük risk (< 2) olarak sınıflandırılmıştır. Postoperatif komplikasyonlar birincil sonlanım noktası olarak belirlenirken, fonksiyonel sonuçlar ikincil sonlanım noktaları olarak değerlendirilmiştir.

Bulgular: Çalışmaya 200 erkek hasta dahil edilmiş olup, ortalama yaş 64,7 ± 6,03 yıl olarak bulunmuştur. 200 hastanın 54'ü (%27) yüksek risk grubunda (mFI-5 ≥ 2), 146'sı (%73) ise düşük risk grubunda (mFI-5 < 2) yer almıştır. Majör komplikasyon oranı (Clavien-Dindo ≥ 3) yüksek risk grubunda anlamlı derecede daha yüksek bulunurken, toplam komplikasyon oranı gruplar arasında benzer saptanmıştır. Tekrar başvuru ve re-operasyon oranları yüksek risk grubunda daha yüksek bulunmuş, ancak bu fark istatistiksel anlamlılığa ulaşmamıştır. Fonksiyonel sonuçlar açısından, erektil disfonksiyon ve üriner inkontinans oranlarının gruplar arasında benzer olduğu görülmüştür.

Sonuçlar: Bu çalışma, radikal prostatektomi uygulanan hastalarda daha yüksek mFI-5 skorları ile daha yüksek majör komplikasyon oranları arasındaki ilişkiyi ortaya koymaktadır. Frailte değerlendirmesinde basit ve maliyet etkin bir ölçüt olan mFI-5, bu hasta grubunda preoperatif risk sınıflandırması ve hasta seçimi açısından önemli bir rol oynayabilir.

Anahtar Kelimeler: prostat kanseri, radikal prostatektomi, modifiye kırılganlık indeks-5, komplikasyon, fonksiyonel sonuçlar

INTRODUCTION

Prostate cancer is one of the most commonly diagnosed malignancies in men, and its incidence increases progressively with age (1). In these patients, radical prostatectomy (RP) is a curative treatment option and according to guidelines, it is recommended for patients with a life expectancy over 10 years (2). Although radical prostatectomy is a potentially curative treatment, prostate cancer primarily affects older men, who often have a higher burden of comorbidities and an increased risk of postoperative complications (1,3). Therefore, when deciding on RP, it is critically important to minimize risks and complications and to ensure appropriate patient selection for surgery. Several tools have been developed to aid in patient selection for RP, with reported sensitivity rates ranging from 65% to 84% (1,4–7).

In addition to traditional tools such as the American Society of Anesthesiologists classification (ASA) and the Charlson Comorbidity Index (CCI), frailty-based tools have increasingly been used to predict postoperative complications and functional outcomes (8,9). With the progressive aging of populations, frailty has emerged as an increasingly important determinant and has been demonstrated to influence the clinical course and outcomes of a wide range of diseases, including those requiring surgical intervention. Frailty refers to a state of reduced physiological resilience across multiple organ systems and can be evaluated either through phenotypic measures—such as muscle strength, walking speed, and recent falls—or through a deficit accumulation approach that considers existing comorbidities, functional capacity in daily activities, and observable physical impairments (10). Following the development of the 11-item modified frailty index (mFI-11) to enhance clinical practicality (8,9), a shorter version—the 5-item modified frailty index (mFI-5)- was subsequently introduced, with studies demonstrating that it produces outcomes comparable to the original index despite relying on fewer variables. (11). The mFI-5 consists of five variables—congestive heart failure, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, and functional health status—each contributing one point to the total score. Therefore, the present study aimed to evaluate the prognostic value of

the mFI-5 for postoperative complications and functional outcomes in patients undergoing radical retropubic prostatectomy (RRP) and extended lymph node dissection (eLND).

MATERIALS AND METHODS

Ethical Committee, the study was conducted in accordance with the ethical principles of the Declaration of Helsinki (193/2013 revision) and was approved by the Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye (Decision No: 2022/514/230/10; Approval Date: 27 July 2022).

In this study, data from patients who had undergone RRP and eLND for prostate cancer at a tertiary referral center between January 2016 and January 2024 were retrospectively evaluated. Exclusion criteria included incomplete data, radical prostatectomy performed for non-prostate adenocarcinoma indications, receipt of neoadjuvant hormonal therapy or radiotherapy, and the presence of metastatic disease.

All surgical procedures were performed by three experienced surgeons. All patients received cefazolin as antibiotic prophylaxis. Standard postoperative care included intravenous fluid replacement, analgesic therapy, and early mobilization within the first 12 hours after surgery. Low-molecular-weight heparin was administered starting on postoperative day 1 and continued for 30 days.

Data collection included demographic characteristics, comorbidity profiles (with Charlson Comorbidity Index scores), histopathological findings, intraoperative variables—namely operative time and transfusion requirement—and follow-up outcomes. Postoperative recovery parameters included time until first bowel movement, prolonged drain usage, and length of hospital stay.

Complications developing within 90 days postoperatively were prospectively recorded and categorized based on the modified Clavien-Dindo Classification (CDC). In accordance with the CDC, grades 3–5 were defined as major complications, and grades 0–2 as minor or no complications. Outpatient medical records were also reviewed to identify any delayed complications.

Five predefined variables were used to retrospectively derive the mFI-5 score. Based on previous literature, an mFI-5 threshold of 2 was used to classify patients into low-risk (< 2) and high-risk (≥ 2) cohorts (12). The groups were compared regarding baseline characteristics, histopathological results, complications and postoperative outcomes.

Statistical Analysis

Given the retrospective nature of the study, data distribution was evaluated using the Kolmogorov-Smirnov test, which demonstrated non-normal distribution of the variables. Descriptive statistics were expressed as mean ± standard deviation, median with interquartile range (IQR), and frequencies, as appropriate. The Mann-Whitney U test was used to compare continuous variables between groups, while categorical data were evaluated using the Chi-square test or Fisher's exact test when indicated. Analyses were conducted using IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA). 2-tailed *p*-values less than 0.05 were deemed statistically significant. A priori sample size estimation was performed using simple random sampling to ensure adequate statistical power. Assuming a significance level of $\alpha = 0.05$, a 95% confidence level, an expected proportion of 0.5, and a margin of error of ± 0.05, the minimum required sample size was calculated. Based on a total population of 372 patients who underwent radical prostatectomy at a high-volume tertiary referral center between January 2016 and January 2024, the estimated minimum sample size was 189 patients.

RESULTS

The research involved 200 male participants whose ages ranged from 48 to 79 years. The average age was 64.7 ± 6.03 years (median 65). The initial demographic and clinical features of the patients are detailed in Table 1.

A statistically significant difference was observed between the mFI-5 groups with respect to CDC ($p = 0.035$; $p < 0.05$). The incidence of major complications was significantly higher in patients with an mFI-5 score ≥ 2 (14.8%) compared with those with an mFI-5 score < 2 (5.5%). However, no statistically significant difference was found between the mFI-5 groups regarding overall complication rates based on the CDC ($p > 0.05$). Complications occurred in 27.4% of patients with an mFI-5 score < 2 and in 25.9% of patients with an mFI-5 score ≥ 2. There was no statistically significant difference between the mFI-5 groups in terms of overall postoperative complications ($p > 0.05$).

Table 1. Demographic, clinical, perioperative, and pathological characteristics of cohort

		Mean ± SD	Median (IQR)
Age		64.7±6.03	65 (61-68.75)
Length of Stay (day)		7.18±4.4	6 (5-7)
PSA (ng/mL)		11.11±10.68	7.95 (5.9-13)
Intensive care unit length of stay (day)		0.7±1,36	0 (0-1)
Duration of drain (day)		4.41±1.95	4 (3-5)
		N	**%**
Charlson comorbidity index	2	3	1.5
	3	25	12.5
	4	82	41
	5	62	31
	6	18	9
	7	8	4
	8	1	0.5
	9	1	0.5
Complications	Gastrointestinal tract	3	1.5
	Infection	17	8.5
	Genitourinary tract	6	3
	Cardiac	2	1
	Wound infection	10	5
	Pulmonary	5	2.5
	Others	2	1
T stage			
	T2	98	49
	T3	99	49.5
	T4	3	1.5

Although readmission and reoperation rates were numerically higher in patients with an mFI-5 score ≥ 2 compared with those with an mFI-5 score < 2 (readmission: 20.4% vs. 11.0%; reoperation: 13.0% vs. 9.6%), the differences between the groups were not statistically significant ($p > 0.05$). No statistically significant differences were observed between the mFI-5 groups with respect to operative time or length of hospital stay ($p > 0.05$).

Erectile dysfunction and urinary incontinence rates were comparable between patients with an mFI-5 score < 2 and those with an mFI-5 score ≥ 2 (erectile dysfunction: 26.7% vs. 16.7%; urinary incontinence: 55.5% vs. 46.3%), with no statistically significant differences observed between the groups ($p > 0.05$).

Disease recurrence and mortality rates were elevated in patients with a mFI-5 score ≥ 2 compared to those with a mFI-5 score < 2 (recurrence: 24.1% vs. 14.4%; mortality: 11.1% vs. 5.5%); yet these differences were not statistically significant ($p > 0.05$).

Table 2. Comparison of postoperative outcomes between the groups

		mFI-5 < 2 (n=146)	mFI-5 ≥ 2 (n=54)	p
Clavien Dindo Classification	Overall complication	40 (%27.4)	14 (%25.9)	0.835
	Minor (< grade 3)	32 (%21.9)	6 (%11.1)	0.035*
	Major (≥ grade 3)	8 (%5.5)	8 (%14.8)	
Complications	Gastrointestinal tract	3 (%2.1)	0 (%0)	0.565
	Infection	13 (%8.9)	4 (%7.4)	1.000
	Genitourinary	6 (%4.1)	0 (%0)	0.194
	Cardiac	1 (%0.7)	1 (%1.9)	0.468
	Wound infection	8 (%5.5)	2 (%3.7)	1.000
	Pulmonary	3 (%2.1)	2 (%3.7)	0.613
	Others	0 (%0)	2 (%3.7)	0.072
Surgical Margin Positivity		40 (%27.4)	21 (%38.9)	0.117
Re-admission		16 (%11)	11 (%20.4)	0.084
Re-operation		14 (%9.6)	7 (%13)	0.490
Erectile Dysfunction		39 (%26.7)	9 (%16.7)	0.140
Urinary Incontinence		81 (%55.5)	25 (%46.3)	0.248
Anastomosis Stricture		21 (%14.4)	10 (%18.5)	0.473
Recurrence		21 (%14.4)	13 (%24.1)	0.105
Overall Mortality		8 (%5.5)	6 (%11.1)	0.210
Operation Time mean±SD /Median (Q1-Q3)		201.91±57.44/ 190 (160-230)	194,63±65,62/ 180 (150-230)	0.204
Length of stay Median (Q1-Q3)		6 (5-8)	6 (5-7)	0.277

Categorical variables were compared using the Chi-square test or Fisher's Exact test where appropriate. Continuous variables were analyzed using the Mann–Whitney U test. Data are presented as n (%) for categorical variables and median (Q1–Q3) for continuous variables. A p value <0.05 was considered statistically significant.

DISCUSSION

As significance of frailty and biological age in surgical patients has become increasingly recognized, novel scoring systems have been developed to improve the prediction of postoperative outcomes. Due to the limitations of traditional tools, the mFI-5 was introduced in 2017 as a novel frailty-based predictive model for postoperative outcomes in elderly patients (11). This study explored the association of mFI-5 with complications occurring after radical retropubic prostatectomy (RRP) and extended lymph node dissection (eLND). Our findings are concordant with existing evidence, demonstrating a higher incidence of CDC major complications in the high-risk mFI-5 group, while complication subtypes did not differ significantly between groups. The high-risk group demonstrated higher readmission and reoperation rates, but the differences did not achieve statistical significance. Unlike previous studies, we also examined the relationship between frailty and overall survival as well as disease recurrence, but no significant association with higher mFI-5 scores was identified. These findings suggest that the mFI-5 may be a useful adjunctive tool for preoperative risk stratification in patients considered for radical prostatectomy. Rather than serving as a stand-alone determinant of treatment selection, mFI-5 may help identify patients who require more detailed perioperative counseling, optimization of comorbidities, and individualized surgical planning.

Currently, a large number of patients undergoing abdominal surgery are classified as pre-frail or frail (13). In a large-scale study evaluating approximately 92,000 patients who were treated with RP, nearly 1-seventh of the cohort was identified as frail. This study demonstrated that frailty was significantly linked to an elevated risk of postoperative complications and prolonged hospitalization in patients treated with RP (14). Likewise, the literature indicates that frailty remains a significant determinant of postoperative complications in patients treated with RP (15). In a cohort of patients who underwent robotic-assisted radical prostatectomy, the authors observed that higher mFI-5 values were associated with greater overall and high-grade complication rates within 90 days after surgery (16). Similarly, Demirci et al. (17) demonstrated that increasing frailty was correlated with a higher incidence of CDC grade ≥ 3 complications. In another cohort of patients undergoing radical prostatectomy in which the mFI-5 was evaluated, a higher mFI-5 score was identified as an independent predictor of early mortality and adverse postoperative outcomes (18). Additionally, Lascano et al. (15) reported that increasing mFI scores were associated with higher rates of CDC grade IV complications and hospital readmissions. Overall, the findings reported in the literature are consistent with the results of the present study.

Beyond postoperative complications, the relationship between frailty and functional outcomes in patients undergoing radical prostatectomy has also been investigated in the literature. Stankovic et al. (19) demonstrated that higher frailty scores were associated with a reduction in early postoperative continence rates, supporting the notion that frailty adversely affects functional recovery. In contrast, Togashi et al. (20) reported no significant association between frailty and 12-month pad-free continence rates. This discrepancy may be partly explained by differences in surgical approach, as their cohort consisted exclusively of patients undergoing robotic-assisted radical prostatectomy, whereas the present study included patients treated with open radical prostatectomy. In our analysis, postoperative erectile dysfunction and urinary incontinence rates at 12 months were comparable between the mFI-5 groups, aligning more closely with the findings of Togashi et al. (20). However, the absence of detailed baseline functional data, including preoperative erectile function and continence status, limits the interpretation of these outcomes. Therefore, the present findings should not be interpreted as definitive evidence that frailty has no effect on functional recovery after radical prostatectomy.

Frailty has been reported as a potential predictor of overall survival in various malignancies (17,21). In particular, Demirci et al. (17) observed an association between higher mFI-5 scores and poorer overall survival. Despite its predictive value for postoperative complications, the mFI-5 score showed no significant impact on overall survival in this patient population following radical prostatectomy. This lack of concordance with previous reports may be partially explained by methodological differences, including the small cohort and short follow-up period, potentially resulting in insufficient power to identify a meaningful association.

This study is subject to several limitations that warrant consideration in the interpretation of its findings. This study is primarily limited by its retrospective design. The single-center setting and relatively small cohort further constrain the external validity of the findings. Another important limitation is the lack of detailed preoperative functional status data, including baseline erectile function and urinary continence. Therefore, postoperative erectile dysfunction and urinary incontinence rates should be interpreted with caution, as it cannot be determined whether these outcomes developed after surgery or reflected pre-existing functional impairment. This limitation may have reduced the ability of the study to accurately assess the independent relationship between frailty and functional recovery after radical prostatectomy. Furthermore, the inclusion of patients operated on by different surgeons may have introduced potential bias related to variations in surgical technique and surgeon experience. Moreover, although overall survival and disease recurrence were evaluated, cancer-specific survival and data on adjuvant or salvage treatments were not analyzed, which may have affected survival-related outcomes.

Future studies with larger patient populations, multicenter designs, and prospective methodologies are warranted to better clarify the role of frailty in radical prostatectomy outcomes. In addition, investigations incorporating established composite outcome measures, such as trifecta outcomes (erectile function, urinary continence, and oncological control) and pentafecta outcomes (trifecta plus negative surgical margins and reduced perioperative complications), may provide more comprehensive insights and contribute further to the existing literature.

CONCLUSION

In conclusion, higher mFI-5 scores were associated with an increased risk of major postoperative complications after radical prostatectomy. Although mFI-5 should not be used as a stand-alone criterion for treatment selection, it may serve as a simple, rapid, and cost-free adjunctive tool for preoperative risk stratification, perioperative counseling, and individualized surgical planning. Further prospective and multicenter studies are needed to validate its role in predicting functional and oncological outcomes after radical prostatectomy.

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

Conflict of interest: All authors report no conflict of interest

Compliance with ethical standards: Ethical Committee of Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye, 2022/514/230/10, July 27, 2022)

Informed Consent: Written informed consent was waived due to the retrospective nature of the study and the use of anonymized patient data.

Author contributions:

Conceptualization and Methodology: OO, CC, ED ; Investigation: OMI, YKA, BHS ; Resources: YKA, BHS ; Writing - Original Draft; OMI, ED, CC; Writing - Review & Editing; OMI, AHS; Supervision: OO,CC.

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):150–159. doi: 10.54233/endourolbull-1885162

Clinical Outcomes of Antegrade Double-J Stent Placement in Patients with Failed Retrograde Ureteral Stenting

Retrograd Üreteral Stentlemenin Başarısız Olduğu Hastalarda Antegrad Double-J Stent Uygulamasının Klinik Sonuçları

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ABSTRACT

Objective: This study aimed to evaluate the technical and clinical success, complication profile, and clinical effectiveness of antegrade double-J (DJ) stent placement in patients in whom retrograde ureteral stenting had failed.

Materials and Methods: This retrospective study included patients who underwent antegrade DJ stent placement between 2021 and 2025 due to unsuccessful retrograde access. All procedures were performed under ultrasonographic and fluoroscopic guidance. Patients were categorized into single-stage and 2-stage antegrade stenting groups based on their clinical condition. All interventions were performed by a single experienced interventional radiologist. Technical and clinical success rates were assessed, and procedure-related complications were classified according to the Society of Interventional Radiology (SIR) guidelines.

Results: A total of 40 patients were included in the study; 45.0% were treated for benign and 55.0% for malignant ureteral obstruction. Antegrade double-J stent placement was technically successful in all patients, with a significant reduction in the degree of hydronephrosis observed after the procedure. Clinical evaluation demonstrated a statistically significant decrease in serum creatinine levels and visual analog scale (VAS) pain scores at 24 hours post-procedure ($p < 0.001$). No clinically significant decrease in hemoglobin levels was observed. The overall complication rate was 7.5%, and all complications were minor and resolved with conservative management.

Conclusion: Antegrade DJ stenting represents a safe, effective, and minimally invasive alternative in patients with failed retrograde access. When performed within a multidisciplinary framework involving urology and interventional radiology, this approach improves patient comfort and reduces the need for long-term percutaneous nephrostomy.

Keywords: ureteral obstruction, stents, percutaneous nephrostomy, urinary diversion, interventional radiology

Cite As: *Aydin F, Yesilyurt M, İbis E, Demirdogen SO. Clinical Outcomes of Antegrade Double-J Stent Placement in Patients with Failed Retrograde Ureteral Stenting. Endourol Bull. 2026;18(3):150–159.* https://doi.org/10.54233/endourolbull-1885162

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Received : February 11, 2026 ***Accepted*** : June 18, 2026

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ÖZET

Amaç: Bu çalışmanın amacı, retrograd üreteral stent yerleştirmenin başarısız olduğu hastalarda antegrad double-J (DJ) stent uygulamasının teknik ve klinik başarısını, komplikasyon profilini ve klinik etkinliğini değerlendirmektir.

Gereç ve Yöntemler: Bu retrospektif çalışmaya, 2021–2025 yılları arasında retrograd girişimin başarısız olması nedeniyle antegrad DJ stent uygulanan hastalar dahil edildi. Tüm işlemler ultrasonografi ve floroskopi rehberliğinde gerçekleştirildi. Hastalar klinik durumlarına göre tek aşamalı ve çift aşamalı antegrad stentleme gruplarına ayrıldı. Tüm işlemler tek bir girişimsel radyoloji uzmanı tarafından gerçekleştirildi. Teknik ve klinik başarı oranları değerlendirildi. İşleme bağlı komplikasyonlar Society of Interventional Radiology (SIR) sınıflamasına göre kategorize edildi.

Bulgular: Toplam 40 hastanın dahil edildiği çalışmada olguların %45,0'ı benign, %55,0'ı malign nedenlere bağlı üreteral obstrüksiyon nedeniyle tedavi edildi. Antegrad double-J stent yerleştirilmesi tüm hastalarda teknik olarak başarılı olup, işlem sonrası hidronefroz derecelerinde anlamlı gerileme saptandı. Klinik değerlendirmede, serum kreatinin düzeyleri ve VAS ağrı skorlarında işlem sonrası 24. saatte istatistiksel olarak anlamlı düşüş izlendi ($p < 0,001$). Hemoglobin düzeylerinde klinik olarak anlamlı bir kayıp izlenmedi. Komplikasyon oranı %7,5 hesaplandı ve yalnızca minör düzeyde olup konservatif tedavi ile düzeldi.

Sonuçlar: Antegrad DJ stentleme, retrograd girişimin başarısız olduğu olgularda güvenli, etkili ve minimal invaziv bir alternatif olarak öne çıkmaktadır. Üroloji ve girişimsel radyoloji disiplinlerinin multidisipliner yaklaşımı ile uygulandığında hasta konforunu artırmakta ve uzun süreli perkütan nefrostomi gereksinimini azaltmaktadır.

Anahtar Kelimeler: üreteral obstrüksiyon, stent, perkütan nefrostomi, üriner diversiyon, girişimsel radyoloji:

INTRODUCTION

Ureteral obstruction is a clinically significant condition that may arise from a wide range of benign or malignant etiologies and, if left untreated, can lead to irreversible renal damage. Common benign causes include ureteral calculi, ureteropelvic junction obstruction, ureteral strictures, and retroperitoneal fibrosis. In addition to frequently encountered urological malignancies such as prostate and bladder cancer, gynecological and colorectal tumors are also well-recognized causes of malignant ureteral obstruction (1,2).

The primary goals in the management of ureteral obstruction are to achieve effective urinary drainage and to preserve renal function. Retrograde double-J (DJ) stent placement and percutaneous nephrostomy are among the most commonly used treatment options. Over time, the indications for ureteral stenting have expanded substantially, and stent placement has become a standard therapeutic approach, particularly in the management of malignant or complicated benign obstructions (3,4).

Conventionally, DJ stents are placed via a retrograde cystoscopic approach. However, retrograde access may be technically challenging or impossible in certain clinical scenarios, including advanced pelvic malignancies, prior pelvic surgery, or severe ureteral strictures. In such cases, percutaneous antegrade ureteral stent placement has emerged as an effective alternative for achieving internal urinary drainage (5,6). When performed under fluoroscopic and ultrasonographic guidance, this minimally invasive technique has been shown to provide high technical success rates with an acceptable complication profile (7,8).

The success of antegrade stent placement largely depends on a multidisciplinary collaboration between urology and interventional radiology. Careful patient selection, thorough pre-procedural imaging assessment, appropriate technical planning, and coordinated post-procedural follow-up are essential factors that directly influence treatment outcomes (8).

The aim of this study is to evaluate the technical and clinical success of antegrade DJ stent placement in patients with failed retrograde access and to contribute to the development of optimal, collaborative management strategies

between urology and interventional radiology. In addition to common malignant and benign causes of ureteral obstruction, our study includes complex clinical scenarios such as ureterovesical anastomotic strictures following renal transplantation and urinary diversion. By encompassing this broad range of indications, the present series represents one of the most comprehensive evaluations of antegrade DJ stent placement reported in the literature.

MATERIALS AND METHODS

Study Design

This retrospective study included 40 patients who underwent antegrade DJ (double J) stent placement at our institution between 2021 and 2025 after unsuccessful retrograde ureteral stent insertion. The study was approved by the local ethics committee (Approval No: B.30.2.ATA.0.01.00/898). Patients with obstructive uropathy in whom retrograde ureteroscopic or cystoscopic stent placement failed and who subsequently underwent percutaneous antegrade stent placement were included. All benign and malignant etiologies requiring DJ stenting were considered. Patients with uncorrectable coagulopathy, those who could not tolerate the prone position or for whom an adequate access angle could not be achieved in the supine position, and patients with incomplete clinical or imaging data were excluded.

All patients underwent routine pre-procedural evaluation, including renal function tests, coagulation parameters, and complete blood count. In cases of culture-proven active urinary tract infection, the procedure was performed after appropriate antimicrobial treatment. All interventions were conducted under sterile conditions with ultrasonographic and fluoroscopic guidance. Procedure time (defined as the interval from needle puncture of the collecting system to successful placement of the DJ stent) and fluoroscopy time were obtained from procedural records. The need for sedation or general anesthesia was determined collaboratively with the anesthesia team based on the patient's clinical status. All procedures were performed by a single experienced interventional radiologist (F.A.).

Antegrade DJ stent placement was categorized into single-stage and 2-stage procedures.

Single-stage antegrade stenting was preferred in clinically stable patients without signs of urinary tract infection, in whom the obstruction was isolated and percutaneous access could be safely completed. In these cases, urinary drainage and stent placement were achieved during the same session. 2-stage antegrade stenting was primarily performed in patients presenting with sepsis, associated pyonephrosis, severe hydronephrosis, anticipated technical difficulty, or acute obstruction in a solitary kidney. In this group, initial percutaneous nephrostomy was performed to achieve urgent decompression, followed by antegrade DJ stent placement after clinical stabilization and infection control. The choice between single-stage and 2-stage procedures was determined based on clinical status, presence of infection, imaging findings, and operator judgment.

Patients were monitored for 24 hours after the procedure for vital signs and urinary drainage. Stent position and adequacy of drainage were assessed 24 hours post-procedure using ultrasonography and plain abdominal radiography of the urinary tract. Pain intensity was evaluated using a 10-point Visual Analog Scale (VAS). Pain scores at presentation and 24 hours after the procedure were recorded and categorized as mild (1–3), moderate (4–6), or severe (7–10), according to commonly accepted classifications in the literature.

Technical success was defined as the successful positioning of the DJ stent at the end of the procedure, with the proximal end in the renal pelvis and the distal end in the bladder lumen, followed by urinary drainage and regression of hydronephrosis. Clinical success was defined as a reduction in serum creatinine levels and resolution of pain symptoms.

Antegrade Double-J Stent Placement Technique

Percutaneous access to the pelvicalyceal system of the affected kidney was obtained under ultrasonographic guidance using an 18-gauge Chiba needle through an appropriate calyx (Figure 1a, b). A posterior approach targeting the lower pole calyx was preferentially selected. After needle placement, contrast material was injected to opacify the collecting system (Figure 1c). A 0.035-inch guidewire was advanced into the collecting system, the Chiba needle was removed, and the access tract was appropriately dilated over the guidewire (Figure 1 d, e). A diagnostic vascular catheter was then advanced into the renal pelvis (Figure 1f), and antegrade pyelography was performed to identify the level of ureteral obstruction. Based on the location of the stricture and the presence of ureteral tortuosity, an appropriate guidewire was selected to traverse the obstruction. Using the guidewire-catheter combination, the catheter was advanced to the level of the stricture (Figure 1 g, h). The obstruction was crossed using hydrophilic or polytetrafluoroethylene (PTFE) guidewires with different tip configurations and access to the bladder was achieved (Figure 1i, j). Subsequently, the guidewire was exchanged through the catheter for a stiff hydrophilic or super-stiff PTFE guidewire. Over the stiff guidewire, a double-J stent of appropriate length (typically 4.8–6 Fr, 22–28 cm) was advanced from the renal pelvis into the bladder (Figure 1k, l). Stent diameter and length were selected according to the patient's anatomy, ureteral characteristics, and extent of obstruction. No systematic reduction in stent caliber was performed during antegrade placement, and stents of similar dimensions to those routinely used in retrograde ureteral stenting were generally preferred. Correct positioning was confirmed under fluoroscopic guidance.

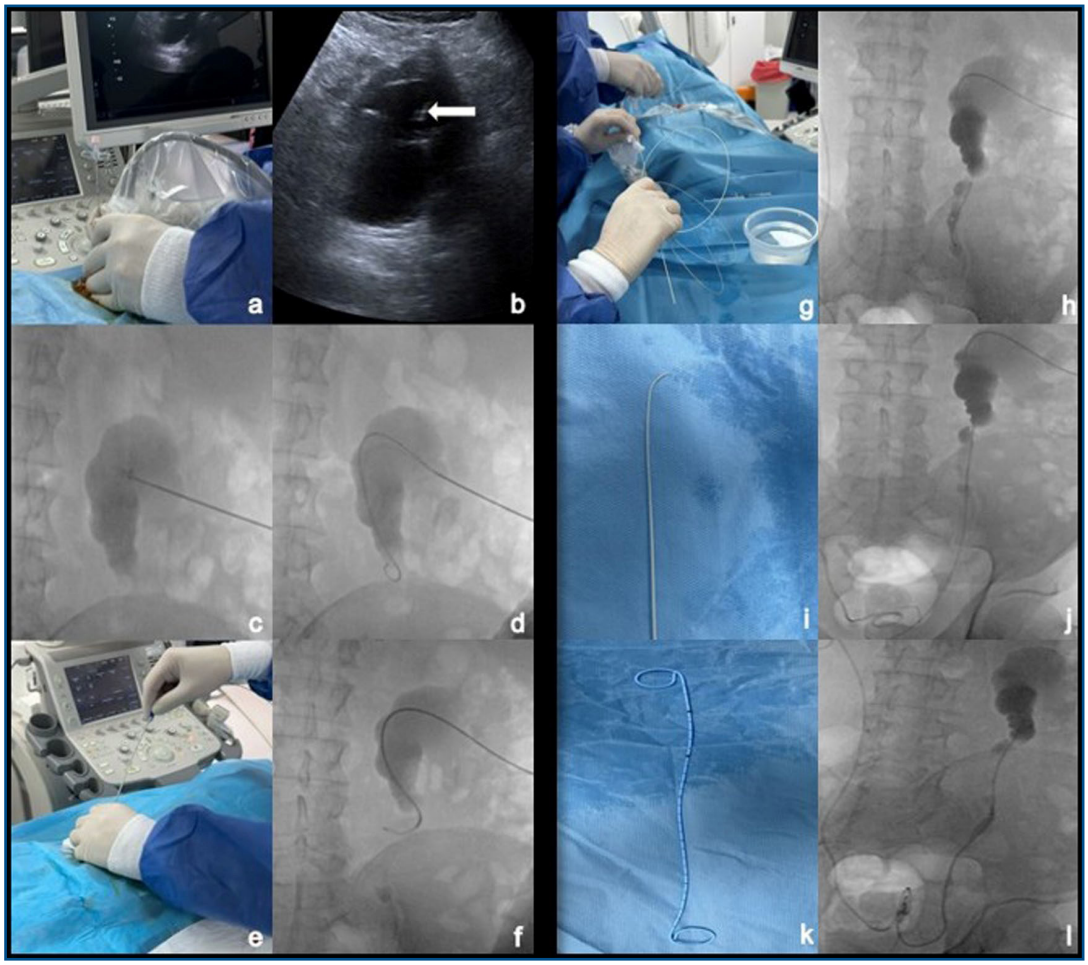


Figure 1. Step-by-step illustration of antegrade double-J stent placement performed under interventional radiology guidance. (a) Ultrasound-guided identification of an appropriate calyx and access to the collecting system using a Chiba needle. (b) Visualization of the needle tip within the collecting system (arrow). (c) Opacification of the collecting system following contrast injection. (d) Placement of a J-tip guidewire into the collecting system. (e) Tract dilation

performed over the guidewire. (f) Advancement of a diagnostic catheter into the renal pelvis. (g) Advancement of the diagnostic catheter together with an appropriate guidewire. (h) Advancement of the diagnostic catheter to the level of the ureteral stricture. (i) Use of an angled hydrophilic guidewire to cross the stricture. (j) Advancement of the hydrophilic guidewire through the stricture into the bladder. (k) Selection of the appropriate double-J stent. (l) Placement of the double-J stent over a stiff hydrophilic guidewire.

Procedure-related complications associated with antegrade double-J stent placement were evaluated according to the standard classification system defined by the Society of Interventional Radiology (SIR). Complications occurring during or after the procedure were recorded as minor (A-B) or major (C-F).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software. Continuous variables were assessed for normality. Normally distributed variables were expressed as mean ± standard deviation, whereas non-normally distributed variables were presented as median (Q1–Q3). Comparisons between pre-procedural and post-procedural continuous variables were performed using the Wilcoxon signed-rank test. Categorical variables were presented as numbers and percentages. A p-value of < 0.05 was considered statistically significant for all analyses.

A post-hoc power analysis was performed using G*Power software (version 3.1, Heinrich-Heine University, Düsseldorf, Germany) based on the observed change in serum creatinine levels. With a sample size of 40 patients, an effect size of 1.20, and a significance level of 0.05, the calculated statistical power of the study was 0.99 (99%).

RESULTS

A total of 40 patients were included in the study. The mean age was 65.5 ± 11.4 years, and 27 patients (67.5%) were male. Indications for antegrade DJ stent placement were benign in 18 patients (45.0%) and malignant in 22 patients (55.0%). The benign group also included patients with ureterovesical anastomotic strictures following renal transplantation. Single-stage antegrade stenting was performed in 33 patients (82.5%) (Table 1).

The mean procedure time was 30.0 ± 9.4 minutes, and the mean fluoroscopy time was 6.2 ± 2.3 minutes. Antegrade double-J stent placement was successfully completed in all patients. A significant reduction in the degree of hydronephrosis was observed in all cases after the procedure, resulting in a 100% technical success rate ($p < 0.001$) (Table 2).

The median pre-procedural serum creatinine level was 1.96 mg/dL (Q1–Q3: 1.67–2.52), which decreased to 1.48 mg/dL (Q1–Q3: 1.33–1.65) after the procedure. This reduction in serum creatinine levels was statistically significant ($p < 0.001$). Similarly, the median VAS pain score decreased significantly from 5.0 (Q1–Q3: 4.0–6.0) pre-procedure to 1.0 (Q1–Q3: 1.0–2.0) post-procedure ($p < 0.001$) (Table 3).

The mean hemoglobin level was 12.89 ± 1.39 g/dL before the procedure and 12.74 ± 1.44 g/dL after the procedure, with no statistically significant difference observed. Post-procedural hematuria resolving within six hours occurred in three patients (7.5%). All complications were classified as minor according to the SIR classification system and were managed conservatively. No major complications were observed.

DISCUSSION

Retrograde ureteral stenting has long been considered a reliable method for relieving ureteral obstruction. However, retrograde access may fail in patients with pelvic malignancies or in the presence of severely tortuous ureteral anatomy. In such cases, percutaneous nephrostomy represents an alternative option for achieving urinary drainage (9,10).

Table 1. Patient Demographics and Clinical Characteristics

Parameter	Value
Age ± SD (years)	65.5 ± 11.4
Male sex, n (%)	27 (67.5%)
Female sex, n (%)	13 (32.5%)
Benign indication, n (%)	18 (45.0%)
Ureteral stone	2 (5.0%)
Benign prostatic hyperplasia	2 (5.0%)
Chronic cystitis	1 (2.5%)
Tortuous ureteral anatomy	1 (2.5%)
Retroperitoneal fibrosis	1 (2.5%)
Urinary diversion	5 (12.5%)
Renal transplant ureterovesical anastomotic stricture	6 (15.0%)
Malignant indication, n (%)	22 (55.0%)
Bladder cancer	11 (27.5%)
Prostate cancer	5 (12.5%)
Uterine cancer	4 (10.0%)
Colorectal cancer	2 (5.0%)
Single-stage procedure, n (%)	33 (82.5%)

Table 2. Procedural Characteristics and Technical Outcomes

Parameter	Value
Procedure time ± SD (min)	30.0 ± 9.4
Fluoroscopy time ± SD (min)	6.2 ± 2.3
Technical success, n (%)	40 (100.0)

Table 3. Pre- and Post-procedural Clinical Outcomes

Parameter	Pre-procedure	Post-procedure	p-value
Serum creatinine (mg/dL)	1.96 (1.67–2.52)	1.48 (1.33–1.65)	<0.001
VAS score	5.0 (4.0–6.0)	1.0 (1.0–2.0)	<0.001

Percutaneous nephrostomy is a minimally invasive and generally safe procedure with low complication rates (11,12). Nevertheless, the need for long-term external drainage constitutes a major drawback that may negatively affect patient comfort and quality of life. Consequently, antegrade DJ stent placement has emerged as a valuable alternative in patients with failed retrograde access, offering internal drainage and improved patient comfort (13). The antegrade approach allows direct access to the renal collecting system, facilitating more controlled advancement of guidewires and catheters across the obstruction site (14). In patients with distorted lower urinary tract anatomy, pelvic masses, or post-surgical fibrotic changes, this technique provides a significant advantage by eliminating the need for prolonged nephrostomy and enabling effective internal drainage (15,16). Patients who have undergone urinary

diversion or renal transplantation often develop complex anatomical alterations, and strictures at the anastomotic site represent an important source of morbidity in this population (17). The incidence of ureteral strictures following renal transplantation has been reported to range from approximately 1% to 4.5% (18). Our findings demonstrate that antegrade DJ stent placement can be safely and effectively applied in these patients when retrograde access is unsuccessful.

In the literature, common causes of failed retrograde stenting include distortion of the bladder trigone, tumor involvement of the ureteral orifice, and inability to traverse the distal ureter (10,19). In such scenarios, antegrade stenting has been shown to provide a clear technical advantage. Reported technical success rates for antegrade ureteral stenting are approximately 95%, with overall complication rates around 8% and major complication rates generally below 5% (20). In the present study, technical success was achieved in all cases, and the complication rate was lower than those reported in previous series. This favorable outcome may be attributed to institutional experience with antegrade DJ stent placement, careful patient selection, and the individualized choice between single-stage and 2-stage procedures. Furthermore, close collaboration between urology and interventional radiology in determining appropriate indications likely contributed to these results.

One of the distinguishing features of this study is the inclusion of anatomically complex and relatively uncommon indications, such as ureterovesical anastomotic strictures following renal transplantation and obstructive pathologies after urinary diversion, in addition to more common benign and malignant causes of ureteral obstruction. Most published series on antegrade ureteral stenting primarily focus on urological or gynecological malignancies, whereas data addressing these special patient populations within a single cohort remain limited. Despite the broad and heterogeneous range of indications, technical success was achieved in all patients in our series, supporting the consistent efficacy and safety of antegrade DJ stent placement across diverse clinical scenarios (21).

Retrograde access may also be limited in patients with bladder tumors involving the ureteral orifice or following transurethral resection (TUR) of early-stage (Ta-T1) bladder tumors, where optimal visualization of the ureteral orifice may be compromised. In such cases, antegrade DJ stenting represents an effective alternative for achieving internal urinary drainage (19). In our study, bladder cancer constituted the most frequent malignant indication, with many cases involving early-stage tumors associated with ureteral orifice involvement. Successful internal drainage was achieved in these patients using the antegrade approach, suggesting that this technique may be particularly useful in obstructions related to post-TUR anatomical distortion rather than extrinsic compression from advanced tumors.

The overall complication rate observed in our study was low, and all complications were classified as minor according to the SIR criteria and resolved with conservative management. These findings further support the favorable safety profile of antegrade DJ stent placement.

Several limitations of this study should be acknowledged. The retrospective, single-center design and the heterogeneous patient population may limit the generalizability of the results. Furthermore, selection bias may have occurred because only patients referred for antegrade intervention after failed retrograde stenting attempts were included in the study. Baseline serum creatinine levels prior to the development of ureteral obstruction were not consistently available; therefore, the extent to which post-procedural renal function returned to each patient's baseline status could not be determined. Nevertheless, the significant reduction in serum creatinine levels observed after the procedure supports the clinical effectiveness of antegrade DJ stent placement in relieving urinary obstruction. In patients who underwent a 2-stage approach, the independent contributions of initial percutaneous nephrostomy and subsequent antegrade DJ stent placement to the observed clinical improvement could not be evaluated separately. In addition, long-term complications such as stent migration or bladder irritation may have been underreported due to the retrospective nature of the analysis. Long-term follow-up data regarding stent patency, functional outcomes,

and quality of life remain limited in the existing literature (22). Future multicenter, prospective studies involving different patient subgroups—including benign versus malignant strictures, solitary kidney patients, and pediatric populations—are warranted to establish standardized protocols for antegrade ureteral stenting. Despite these limitations, our study stands out as having the broadest spectrum of indications reported in the literature regarding antegrade DJ stent applications.

In conclusion, when considered alongside existing evidence, the present study demonstrates that antegrade DJ stent placement is a safe and effective treatment option for both benign and malignant ureteral obstruction in patients with failed retrograde access. The combination of high technical success, low complication rates, and improved patient comfort highlights the value of this approach. A multidisciplinary strategy involving close collaboration between urology and interventional radiology is essential for optimizing clinical outcomes.

CONCLUSION

Antegrade DJ stent placement is a safe and effective treatment option for selected patients with failed retrograde ureteral stenting, providing high technical and clinical success rates in both benign and malignant ureteral obstruction. Owing to its low complication profile and ability to achieve adequate internal drainage, the antegrade approach represents a reliable alternative, particularly in patients with urinary diversion or renal transplantation. Implementation of this technique within a multidisciplinary framework involving urology and interventional radiology contributes significantly to improved clinical outcomes.

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

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

Ethical Approval: The Ethics Committee of the Ataturk University Faculty of Medicine approved (Approval No: B.30.2.ATA.0.01.00/898) the presented study.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Author Contributions: Conception: FA,MY; Design: ŞOD; Supervision: FA,ŞOD; Data Collection: FA,ŞOD ; Analysis: MY,Eİ; Literature Review: FA,Eİ,ŞOD; Writer: FA,MY,ŞOD; Critical Review: ŞOD

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):160–175. doi: 10.54233/endourolbull-1898671

Association Between Comorbidity Burden and Tissue-Adjusted Enucleation Time During HoLEP: A Retrospective Cohort Study

HoLEP Sırasında Komorbidite Yükü ile Doku Yüküne Göre Düzeltilmiş Enükleasyon Süresi Arasındaki İlişki: Retrospektif Kohort Çalışması

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ABSTRACT

Objective: To quantify phase-specific operative performance during holmium laser enucleation of the prostate (HoLEP) and evaluate the association between comorbidity burden and tissue-adjusted enucleation performance.

Materials and Methods: This single-center retrospective cohort screened 574 HoLEP procedures performed between January 2023 and June 2025 and included 349 patients. Enucleation efficiency (g/min), morcellation efficiency, and overall extraction efficiency were calculated descriptively. To avoid mathematical coupling, the primary inferential analysis modeled natural log-transformed enucleation time and adjusted for age, log-transformed enucleated tissue weight, prostate-volume stratum, and antithrombotic use. Heteroscedasticity-consistent HC3 standard errors were used.

Results: Median age was 67 years, and 67.9% had at least one comorbidity. Unadjusted enucleation time was similar in patients without and with comorbidity (41.5 vs 42.0 min; $p = 0.337$), whereas enucleation efficiency was lower in those with comorbidity (0.93 vs 1.75 g/min; $p < 0.001$). In the adjusted model, each additional comorbidity was associated with a 9.9% longer enucleation time for a given tissue burden (95% CI: 4.8%-15.2%; $p < 0.001$; adjusted R^2=0.167). The association persisted after additional adjustment for operative technique category (8.0%; 95% CI: 4.5%-11.6%; $p < 0.001$). Antithrombotic use was not independently associated with enucleation time.

Conclusion: Comorbidity burden was associated with slower tissue-adjusted enucleation performance despite similar unadjusted enucleation times. Total operating-room occupancy was not assessed. These hypothesis-generating findings require multicenter validation with operator-level, anesthetic, and intraoperative bleeding data before use in scheduling or benchmarking.

Keywords: comorbidity, enucleation, holmium laser enucleation of the prostate, operative time, prostatic hyperplasia

Cite As: *Kayali Y, Aydogan TB, Torun A, Bicaklioglu F, Cetin B, Erdemoglu O, Yilmaz U, Eryildirim B. Association Between Comorbidity Burden and Tissue-Adjusted Enucleation Time During HoLEP: A Retrospective Cohort Study. Endourol Bull. 2026;18(3):160–175.* https://doi.org/10.54233/endourolbull-1898671

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Received : February 27, 2026 ***Accepted*** : August 21, 2026

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ÖZET

Amaç: Holmium lazer prostat enükleasyonunda (HoLEP) faza özgü cerrahi verimliliği tanımlamak ve komorbidite yükünün dokuya göre düzeltilmiş enükleasyon performansı ile ilişkisini değerlendirmek.

Gereç ve Yöntemler: Bu tek merkezli retrospektif kohortta Ocak 2023-Haziran 2025 arasında uygulanan 574 HoLEP olgusu tarandı ve 349 hasta analize alındı. Enükleasyon verimliliği (g/dk), morselasyon verimliliği ve toplam ekstraksiyon verimliliği tanımlayıcı olarak hesaplandı. Matematiksel eşleşmeyi önlemek amacıyla birincil çıkarımsal analizde doğal logaritması alınmış enükleasyon süresi sonuç değişkeni olarak modellendi; analiz yaş, logaritmik enükle edilen doku ağırlığı, prostat hacmi kategorisi ve antitrombotik kullanımına göre düzeltildi. Heteroskedastisiteye dayanıklı HC3 standart hataları kullanıldı.

Bulgular: Medyan yaş 67 yıl olup hastaların %67.9'unda en az bir komorbidite vardı. Ham enükleasyon süresi komorbiditesi olmayan ve olan hastalarda benzerdi (41.5 ve 42.0 dk; $p = 0.337$), ancak enükleasyon verimliliği komorbiditesi olanlarda daha düşüktü (0.93 ve 1.75 g/dk; $p < 0.001$). Düzeltilmiş modelde her ek komorbidite, aynı doku yükü için enükleasyon süresinde %9.9 artışla ilişkiliydi (%95 GA: %4.8-%15.2; $p < 0.001$; düzeltilmiş R^2=0.167). Cerrahi teknik kategorisini de içeren duyarlılık analizinde ilişki devam etti (%8.0; %95 GA: %4.5-%11.6; $p < 0.001$). Antitrombotik kullanım bağımsız olarak enükleasyon süresiyle ilişkili değildi.

Sonuçlar: Komorbidite yükü, benzer ham enükleasyon sürelerine karşın, doku yüküne göre düzeltilmiş daha yavaş enükleasyon performansıyla ilişkiliydi. Toplam ameliyathane kullanım süresi değerlendirilmedi. Bulguların planlama veya karşılaştırma amacıyla kullanılmasından önce operatör, anestezi ve intraoperatif kanama değişkenlerini içeren çok merkezli çalışmalarla doğrulanması gerekir.

Anahtar Kelimeler: benign prostat hiperplazisi, cerrahi süre, enükleasyon, holmium lazer prostat enükleasyonu, komorbidite

INTRODUCTION

Benign prostatic hyperplasia (BPH) is highly prevalent among aging men and remains a major cause of lower urinary tract symptoms (LUTS) and bladder outlet obstruction. As a guideline-endorsed intervention, endoscopic enucleation offers durable outcomes across a broad spectrum of prostate volumes, with holmium laser enucleation of the prostate (HoLEP) serving as a widely adopted reference technique (1).

Operative efficiency is commonly expressed as tissue removed per unit time during enucleation or morcellation. These metrics are useful for describing technical performance, learning-curve progression, and phase-specific procedural bottlenecks; however, they are also influenced by gland size, tissue characteristics, operative technique, surgeon experience, laser platform and power settings, and morcellator design (2,3).

Although HoLEP is safe and effective in patients with substantial medical comorbidity (4), the contribution of patient-level comorbidity to phase-specific operative performance is less well characterized than anatomical and technical determinants. Medical complexity may coexist with factors that alter operative flow, but observational associations cannot establish mechanisms such as bleeding, impaired visibility, tissue fibrosis, or anesthetic instability unless those variables are directly measured.

We therefore evaluated consecutive HoLEP procedures to quantify phase-specific efficiency metrics and to examine whether cumulative comorbidity burden was associated with tissue-adjusted enucleation performance. The study was designed as a hypothesis-generating analysis rather than a direct test of operating-room resource utilization.

MATERIALS AND METHODS

Study Design and Participants

All patients who underwent HoLEP at a tertiary referral center between January 2023 and June 2025 were screened for eligibility for this single-center retrospective cohort study (n = 574). Eligibility required reliable perioperative data for enucleated tissue weight and phase-specific time stamps. Exclusions were concomitant or staged procedures during the same anesthetic session (n = 97), prior prostate surgery that could alter dissection planes (n = 64), reoperation or salvage HoLEP (n = 11), and incomplete or unreliable perioperative documentation (n = 53). The final analytic cohort comprised 349 unique patients (Figure 1).

Surgical Team, Technique, and Equipment

Procedures were performed by one of four endourologists. Before the study period, each surgeon had completed at least 50 HoLEP procedures and was considered to have passed the initial learning-curve phase. Operator identity and a reliable chronological case sequence were not retained in the de-identified analytic dataset; therefore, surgeon-level adjustment and formal learning-curve analyses were not possible. Three operative technique categories were documented, but technique selection was not protocolized and depended on prostate morphology and surgeon preference; technique category was therefore evaluated only in sensitivity analysis.

All procedures used a 28-Fr continuous-flow endoscopic resectoscope with isotonic saline irrigation. Enucleation and morcellation were performed using a single integrated holmium:yttrium aluminum garnet (Ho:YAG) platform (MultiPulse HoPLUS 150; Jena Surgical, Jena, Germany) with a built-in morcellation module; no standalone morcellator was used. A 550-µm laser fiber was used in all cases. Laser settings were standardized at 2.0 J and 40 Hz (80 W) in short-pulse mode for enucleation and 2.0 J and 35 Hz (70 W) in long-pulse mode for coagulation. Morcellation was performed at high aspiration, 2,000 rpm rotation speed, and 3.0 Hz oscillation frequency.

Perioperative Antithrombotic Management

In the analytic cohort, antiplatelet and anticoagulant medications were discontinued five days before surgery following preoperative consultation with the relevant specialty. When bridging was considered clinically necessary, enoxaparin was administered at the dose recommended by the consulting physician.

Data Collection and Definitions

Clinical variables were retrieved from electronic medical records and operative reports and included age, prostate-specific antigen (PSA), estimated prostate volume (PV), antiplatelet use, anticoagulant use, transrectal ultrasound-guided biopsy history, preoperative urethral catheterization, and medical therapy for BPH. PSA density was calculated as PSA divided by PV. Prostate volume was categorized a priori as <80 g, 80–120 g, or >120 g.

Comorbidity burden was defined as the unweighted count of eight prespecified conditions: hypertension, diabetes mellitus, coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease (COPD) or asthma, prior prostate cancer, non-urologic malignancy, and neurovascular or neurodegenerative disease. Rather than utilizing a validated anesthetic risk score, a simple comorbidity count was employed as an intuitive metric to reflect cumulative documented disease burden. Notably, established risk stratifiers and operative parameters—such as the American Society of Anesthesiologists (ASA) physical status classification, Charlson Comorbidity Index, intraoperative blood pressure, irrigation pressure, and tissue consistency—could not be evaluated due to their absence in the analytic dataset.

Operative Outcomes

Enucleation time was defined as the interval from initiation of laser enucleation to completion of adenoma enucleation. Morcellation time was defined as the interval from morcellator activation to completion of tissue retrieval. Total

extraction time was the sum of enucleation and morcellation times and should not be interpreted as anesthesia time or total operating-room occupancy. Enucleated tissue weight was obtained from the specimen weight documented for histopathology. Descriptive efficiency metrics were calculated as enucleated tissue weight divided by enucleation time, morcellation time, or total extraction time.

The descriptive primary performance metric was enucleation efficiency. Because including tissue weight as both a component of an efficiency ratio and a regression predictor creates mathematical coupling, the primary inferential outcome was natural log-transformed enucleation time modeled conditional on tissue burden. Morcellation time and total extraction time were secondary inferential outcomes.

Statistical Analysis

Continuous variables are presented as median and interquartile range (IQR), and categorical variables as number and percentage. Comparisons between two groups used the Mann-Whitney *U* test, with rank-biserial correlation reported as an effect-size measure. Comparisons across PV strata used the Kruskal-Wallis test followed, when significant, by Dunn tests with Bonferroni adjustment. No clinically meaningful threshold for phase time or efficiency was prespecified; therefore, absolute median differences and effect sizes were interpreted alongside p values.

Multivariable ordinary least-squares models used natural log-transformed phase times. The primary model included cumulative comorbidity count, age, log-transformed enucleated tissue weight, PV stratum, and any preoperative antithrombotic use. Heteroscedasticity-consistent HC3 standard errors were used. Coefficients were converted to percentage change as $(e^{\beta}-1)\times100$ and are reported with 95% confidence intervals. Model R^2 and adjusted R^2 are provided. Sensitivity analyses replaced any antithrombotic use with separate antiplatelet and anticoagulant indicators and additionally adjusted for operative technique category.

Individual comorbidities were evaluated in separate exploratory models that also included the number of other comorbidities. Benjamini-Hochberg false-discovery-rate adjustment was applied across the eight condition-specific tests for each outcome. For subgroups with fewer than 10 patients, 5,000 nonparametric bootstrap resamples were used as a sparse-data sensitivity analysis. Condition-specific morcellation findings were treated as exploratory regardless of nominal significance.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA), with additional syntax-based procedures used for heteroscedasticity-consistent standard errors, false-discovery-rate adjustment, and bootstrap analyses.

Ethics Approval

The study protocol was approved by the Local Ethics Committee of Dr. Lütfi Kırdar Kartal City Hospital (Decision No. 2025/010.99/23/21; December 30, 2025). The study was conducted in accordance with the principles of the Declaration of Helsinki. Since the study was retrospective and based on anonymized data, the requirement for informed consent was waived.

RESULTS

Cohort Characteristics

Of 574 screened procedures, 349 unique patients were included (Figure 1). The median age was 67 years (IQR: 62–73), and median preoperative PV was 84 g (IQR: 60–127). Any antithrombotic medication was recorded in 104 patients (29.8%): 66 received antiplatelet therapy, 42 received anticoagulant therapy, and 4 received both. Detailed baseline characteristics are shown in Table 1.

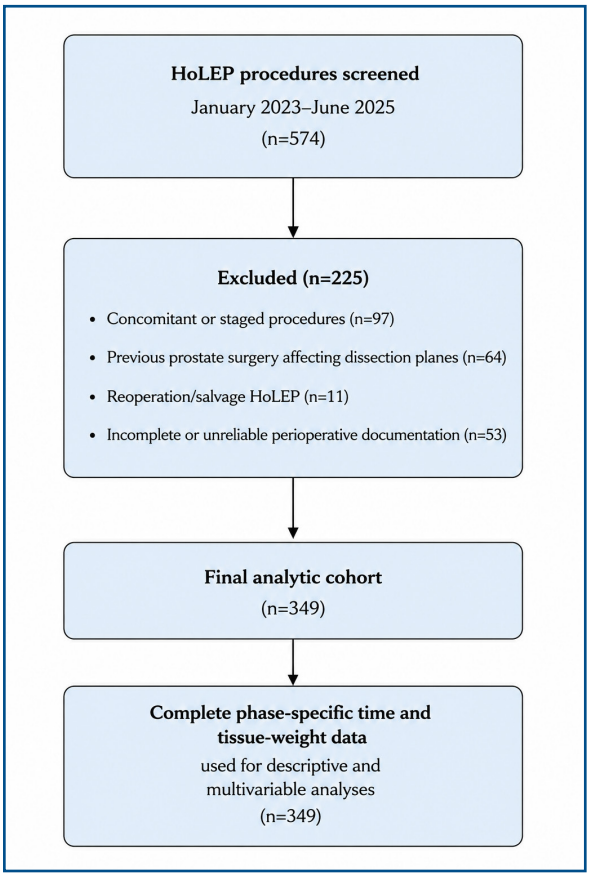


Figure 1. Patient flow through screening, exclusion, and final analysis.
Flow diagram showing 574 screened HoLEP procedures, the four recorded exclusion categories totaling 225 procedures, and the final analytic cohort of 349 unique patients.

At least one comorbidity was documented in 237 patients (67.9%). Comorbidity counts were 0 in 112 patients (32.1%), 1 in 117 (33.5%), 2 in 100 (28.7%), 3 in 16 (4.6%), and 4 in 4 (1.1%). Hypertension was the most common condition (47.6%), followed by coronary artery disease (22.6%) and diabetes mellitus (15.5%).

Operative and Efficiency Outcomes

Median enucleated tissue weight was 53.0 g (IQR: 32.0–70.0). Median enucleation, morcellation, and total extraction times were 42.0, 9.0, and 51.0 minutes, respectively. Median enucleation efficiency was 1.12 g/min, morcellation efficiency was 7.00 g/min, and overall extraction efficiency was 0.96 g/min (Table 2).

Effect of Prostate Volume

Enucleation time did not differ across PV strata ($p = 0.386$), whereas enucleation efficiency increased from 0.86 g/min in prostates <80 g to 1.75 g/min in prostates >120 g ($p < 0.001$). Morcellation time differed statistically across strata (9, 7, and 9 min; $p = 0.001$), but the pattern was non-linear and the absolute median differences were small. Detailed post hoc comparisons are presented in Table 3.

Unadjusted Comparisons by Comorbidity Status

Unadjusted enucleation time was similar in patients without and with at least one comorbidity (41.5 vs 42.0 min; absolute median difference, 0.5 min; $p = 0.337$; rank-biserial correlation=0.064). Morcellation time was 9.0 vs 8.0 minutes (absolute difference, −1.0 min; $p = 0.013$; rank-biserial correlation=−0.164), a statistically significant but small difference. Total extraction time did not differ (51.5 vs 49.0 min; $p = 0.480$). In contrast, enucleation efficiency was lower among patients with comorbidity (0.93 vs 1.75 g/min; $p < 0.001$; rank-biserial correlation=−0.498) (Table 4).

Table 1. Baseline demographic and clinical characteristics and comorbidity profile (n=349).

Variable	Category	Value
Age, years		67 (62-73)
Preoperative PSA, ng/mL		3.26 (2.00-4.90)
Preoperative prostate volume, g		84 (60-127)
PSA density, ng/mL/g		0.037 (0.023-0.072)
TRUS-guided biopsy history		144 (41.3)
Preoperative urethral catheter		88 (25.2)
Antithrombotic therapy	Any antithrombotic	104 (29.8)
	Antiplatelet	66 (18.9)
	Anticoagulant	42 (12.0)
	Both	4 (1.1)
Preoperative medical therapy	None	20 (5.7)
	Alpha-blocker	138 (39.5)
	Combination (alpha-blocker + 5-ARI)	191 (54.7)
Prostate-volume stratum	<80 g	157 (45.0)
	80-120 g	98 (28.1)
	>120 g	94 (26.9)
Comorbidity count	0	112 (32.1)
	1	117 (33.5)
	2	100 (28.7)
	3	16 (4.6)
	4	4 (1.1)
Comorbidity	Any comorbidity	237 (67.9)
	Hypertension	166 (47.6)
	Diabetes mellitus	54 (15.5)
	Coronary artery disease	79 (22.6)
	Chronic kidney disease	26 (7.4)
	COPD or asthma	32 (9.2)
	Prior prostate cancer	8 (2.3)
	Non-urologic malignancy	8 (2.3)
	Neurovascular or neurodegenerative disease*	8 (2.3)

Data are median (IQR) or n (%). *Includes cerebrovascular disease, Alzheimer disease, and other dementias.
IQR: interquartile range; COPD: chronic obstructive pulmonary disease; TRUS: transrectal ultrasound; 5-ARI: 5-alpha-reductase inhibitor.

Adjusted Association Between Cumulative Comorbidity Burden and Phase Time

In the primary log-time model, each additional comorbidity was associated with a 9.9% longer enucleation time conditional on tissue weight, age, PV stratum, and antithrombotic use (95% CI: 4.8%-15.2%; $p < 0.001$; R^2=0.181; adjusted R^2=0.167) (Table 5). Any antithrombotic use was not independently associated with enucleation time (–6.1%; 95% CI: –15.2% to 4.1%; $p = 0.232$).

Table 2. Operative time components and efficiency outcomes (n=349).

Operative metric	Median (IQR)
Enucleated tissue weight, g	53.0 (32.0-70.0)
Enucleation time, min	42.0 (32.0-63.0)
Morcellation time, min	9.0 (5.0-10.0)
Total extraction time, min	51.0 (41.0-76.0)
Enucleation efficiency, g/min	1.12 (0.68-1.81)
Morcellation efficiency, g/min	7.00 (4.00-9.57)
Overall extraction efficiency, g/min	0.96 (0.57-1.43)

Data are presented as median (interquartile range, IQR).

Table 3. Operative outcomes stratified by prostate volume (n=349).

Outcome	PV <80 g (n=157)	PV 80-120 g (n=98)	PV >120 g (n=94)	p
Enucleation time, min	40.0 (35.0-55.0)	44.0 (25.0-57.0)	45.0 (35.0-65.0)	0.386
Enucleation efficiency, g/min	0.86[a] (0.50-1.22)	1.03[b] (0.80-1.84)	1.75[c] (1.25-2.30)	**<0.001**
Morcellation time, min	9.0[ab] (5.0-10.0)	7.0[a] (5.0-10.0)	9.0[b] (6.5-10.8)	**0.001**
Morcellation efficiency, g/min	5.91[a] (3.00-8.12)	7.14[b] (4.56-9.57)	7.60[b] (5.62-11.67)	**<0.001**
Overall extraction efficiency, g/min	0.75[a] (0.43-1.14)	0.93[b] (0.71-1.36)	1.40[c] (1.07-1.75)	**<0.001**

Data are median (IQR). Overall comparisons used the Kruskal-Wallis test; significant tests were followed by Dunn-Bonferroni pairwise comparisons. Values sharing a superscript letter are not significantly different.
PV: prostate volume.

Table 4. Unadjusted operative outcomes by comorbidity status (n=349).

Outcome	No comorbidity (n=112)	Any comorbidity (n=237)	Absolute median difference	p	Rank-biserial correlation
Enucleation time, min	41.5 (30.0-56.0)	42.0 (33.0-66.0)	0.5	0.337	0.064
Morcellation time, min	9.0 (5.0-12.0)	8.0 (5.0-10.0)	-1.0	0.013	-0.164
Total extraction time, min	51.5 (39.0-68.5)	49.0 (42.0-80.0)	-2.5	0.480	0.047
Enucleation efficiency, g/min	1.75 (1.19-2.18)	0.93 (0.60-1.37)	-0.82	<0.001	-0.498
Morcellation efficiency, g/min	8.00 (5.20-11.67)	6.00 (3.33-8.83)	-2.00	<0.001	-0.247
Overall extraction efficiency, g/min	1.38 (0.95-1.73)	0.79 (0.50-1.17)	-0.59	<0.001	-0.491

Data are median (IQR). The absolute median difference is any comorbidity minus no comorbidity. Rank-biserial correlation values farther from zero indicate larger distributional separation.

Table 5. Primary multivariable associations between cumulative comorbidity burden and phase-specific time outcomes.

Outcome	Adjusted % change per additional comorbidity	95% CI	p	R^2	Adjusted R^2
Enucleation time	9.9	4.8 to 15.2	<0.001	0.181	0.167
Morcellation time	-8.3	-15.2 to -0.8	0.031	0.197	0.183
Total extraction time	7.2	2.6 to 12.1	0.002	0.232	0.219

Outcomes were natural log-transformed. Models were adjusted for age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use and used HC3 robust standard errors. Positive values indicate longer phase time; negative values indicate shorter phase time. Total extraction time is enucleation plus morcellation time and is not total operating-room occupancy.

Each additional comorbidity was associated with an 8.3% shorter morcellation time (95% CI: −15.2% to −0.8%; p = 0.031) and a 7.2% longer total extraction time (95% CI: 2.6%-12.1%; p = 0.002). The morcellation association was considered exploratory and should not be interpreted as a beneficial biological effect. Total extraction time represents only enucleation plus morcellation and not total operating-room occupancy.

The association with enucleation time was materially unchanged when antiplatelet and anticoagulant use were entered separately (9.7%; 95% CI: 4.6%-15.1%; $p < 0.001$) and when operative technique category was additionally included (8.0%; 95% CI: 4.5%-11.6%; $p < 0.001$; adjusted $R^2 = 0.523$) (Supplementary Table S1). Standardized predictions increased from 43.0 minutes at zero comorbidities to 62.7 minutes at four comorbidities, with wider uncertainty in the highest-burden category because only four patients had four conditions (Figure 2).

Table 6. Exploratory condition-specific associations with enucleation time.

Condition	n	Adjusted % change	95% CI	p	FDR-adjusted q value
Hypertension	166	28.1	18.0 to 39.0	<0.001	<0.001
Diabetes mellitus	54	-6.4	-16.3 to 4.6	0.244	0.390
Coronary artery disease	79	1.7	-8.3 to 12.9	0.743	0.743
Chronic kidney disease	26	2.9	-12.7 to 21.4	0.731	0.743
COPD or asthma	32	-2.6	-14.4 to 10.9	0.695	0.743
Prior prostate cancer*	8	84.1	64.3 to 106.3	<0.001	<0.001
Non-urologic malignancy*	8	32.0	11.6 to 56.2	0.001	0.003
Neurovascular/ neurodegenerative disease*	8	42.6	0.3 to 102.9	0.048	0.096

Each model included the condition of interest, number of other comorbidities, age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use, with HC3 robust standard errors.

*Sparse subgroups; 5,000-resample bootstrap 95% CIs were 64.3%-105.9%, 13.4%-57.8%, and 2.2%-105.6%, respectively. These estimates are exploratory.

FDR: false discovery rate.

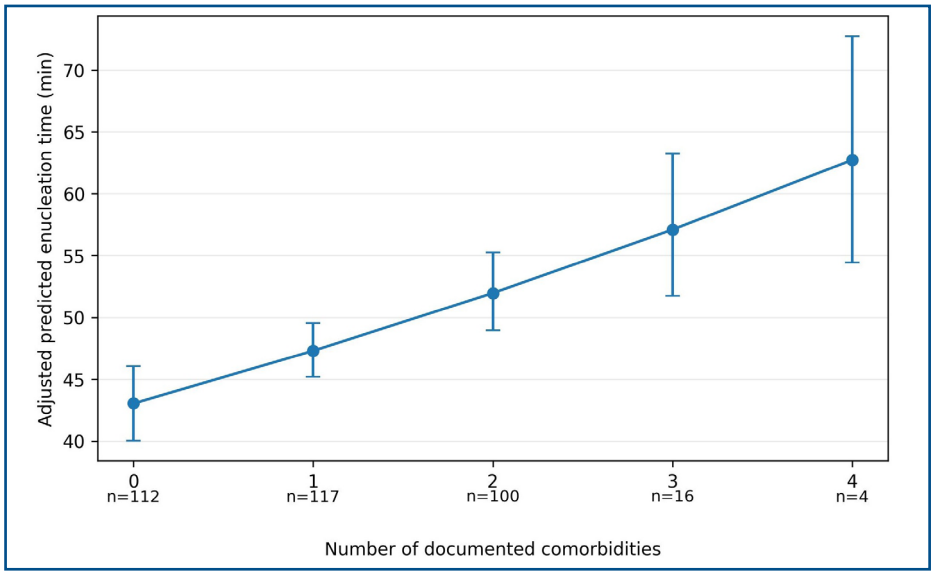


Figure 2. Adjusted predicted enucleation time according to cumulative comorbidity burden.

Average marginal predictions were derived from the primary log-time model and standardized over the observed covariate distribution. Error bars represent 5,000-resample bootstrap 95% confidence intervals. The number of patients with 0, 1, 2, 3, and 4 comorbidities was 112, 117, 100, 16, and 4, respectively.

Exploratory Condition-Specific Analyses

After adjustment for the number of other comorbidities and false-discovery-rate correction, hypertension was associated with 28.1% longer enucleation time (95% CI: 18.0%-39.0%; q<0.001), whereas coronary artery disease was not associated with enucleation time (1.7%; 95% CI: -8.3% to 12.9%; q=0.743). Condition-specific estimates are summarized in Table 6 and visualized in Supplementary Figure S1. Prior prostate cancer and non-urologic malignancy were associated with longer enucleation time, but each subgroup included only eight patients; these estimates remained similar in 5,000-resample bootstrap analyses and are considered exploratory because of sparse data (Supplementary Table S2). Condition-specific morcellation results were inconsistent in direction and are reported only in Supplementary Table S3.

DISCUSSION

In this contemporary single-center HoLEP cohort of 349 patients, phase-specific operative performance was evaluated using both conventional efficiency metrics and tissue-adjusted time models. Three principal findings emerged. First, median enucleation and morcellation efficiencies were 1.12 g/min and 7.00 g/min, respectively, with substantial interpatient variability despite the use of a standardized laser platform and institutional workflow (Table 2). Second, enucleation efficiency increased across prostate-volume strata, whereas the relationship between prostate volume and morcellation time was non-linear and characterized by relatively small absolute differences (Table 3). Third, and most importantly, the presence of comorbidity was associated with a lower unadjusted tissue-removal rate, although raw enucleation time was nearly identical in patients without and with comorbidity. After accounting for tissue burden and relevant covariates, each additional comorbidity was associated with a 9.9% longer enucleation time for a given amount of enucleated tissue (Table 5). Accordingly, the principal finding should be interpreted as an association between comorbidity burden and slower tissue-adjusted enucleation performance, rather than evidence that patients with comorbidity necessarily require longer unadjusted enucleation or total operative time.

Operative efficiency in HoLEP has increasingly been used as a pragmatic descriptor of technical performance, learning-curve progression, and phase-specific procedural throughput. Early comparative work reported enucleation efficiencies of approximately 0.6–0.7 g/min and morcellation efficiencies of approximately 3–4 g/min, while also demonstrating considerable variation between institutions and across prostate sizes (5). Subsequent high-volume experience showed that cumulative case exposure and refinement of operative technique can produce substantial gains in enucleation efficiency, particularly in larger glands (6). Randomized comparisons with transurethral resection of the prostate (TURP) in patients with large prostates further demonstrated that operative duration alone may not adequately represent procedural performance, because HoLEP can remove a greater tissue volume while providing durable functional outcomes and shorter catheterization and hospitalization (7). Previous studies in medically complex populations have focused predominantly on perioperative safety, anesthetic risk, antithrombotic exposure, and conventional postoperative outcomes (8–11), whereas large contemporary series have supported the reproducibility and size-independent applicability of HoLEP across broad clinical case mixes (12–14). In the present cohort, procedures were performed by four endourologists, each of whom had completed at least 50 HoLEP cases before the study period and was considered to have passed the initial learning-curve phase. This reduces the likelihood that the findings were driven solely by novice performance; nevertheless, operator identity and chronological case sequence were unavailable for model-level adjustment, and residual variation related to individual technique, case selection, or continued refinement cannot be excluded.

Comorbidity was common in the present cohort, with 67.9% of patients having at least one documented condition and hypertension being the most prevalent diagnosis. In the unadjusted comparison, median enucleation time differed by only 0.5 minutes between patients without and with comorbidity—41.5 and 42.0 minutes, respectively—and this difference was not statistically significant (p = 0.337) (Table 4). By contrast, median enucleation efficiency was substantially lower in patients with comorbidity, at 0.93 versus 1.75 g/min. These apparently divergent findings

reflect the influence of tissue burden on ratio-based efficiency measures and underline the need to distinguish raw procedural time from tissue-adjusted performance. In the primary inferential model, each additional comorbidity was associated with a 9.9% longer enucleation time conditional on enucleated tissue weight, age, prostate-volume stratum, and antithrombotic use. The association remained present after additional adjustment for operative technique category, with an estimated 8.0% increase per additional comorbidity. Standardized model predictions increased from approximately 43.0 minutes in patients with no comorbidity to 62.7 minutes in those with four conditions; however, this upper estimate was based on only four patients and had correspondingly greater uncertainty (Figure 2). These findings demonstrate a graded statistical association, but they do not establish a causal effect of comorbidity or define a clinically validated threshold for scheduling or performance benchmarking.

Condition-specific analyses also require cautious interpretation. Hypertension was associated with a 28.1% longer tissue-adjusted enucleation time, whereas coronary artery disease was not independently associated with the outcome (Table 6). This discordance argues against interpreting the findings as a simple consequence of generalized "poor vascular health." Hypertension should not be considered a direct surrogate for intraoperative bleeding, impaired visibility, or increased hemostatic requirements because treated hypertensive patients may be normotensive during surgery, and intraoperative blood pressure is actively managed by the anesthesia team. In addition, anesthetic technique, hypertensive or hypotensive episodes, irrigation pressure, hemostasis time, and the frequency of coagulation maneuvers were not recorded. Coronary artery disease was also captured as a heterogeneous binary diagnosis without distinction among stable coronary disease, previous myocardial infarction, coronary stenting, heart failure, disease severity, or associated antithrombotic exposure. Prior HoLEP literature has primarily examined perioperative risk, predictors of enucleation time, and the safety of surgery in patients receiving antiplatelet or anticoagulant therapy rather than the independent relationship between these diagnoses and tissue-adjusted enucleation performance (8–11). In the present analysis, antithrombotic use was not independently associated with enucleation time. However, in the analytic cohort, antiplatelet and anticoagulant agents were discontinued five days before surgery, and selective enoxaparin bridging was used when recommended by the relevant specialty. Therefore, the absence of an independent association should be interpreted within this perioperative management strategy and should not be extrapolated to HoLEP performed under uninterrupted antithrombotic therapy. Prior prostate cancer and non-urologic malignancy were also associated with longer enucleation time, but each subgroup included only eight patients. Although bootstrap sensitivity analyses produced similar estimates, these findings remain exploratory and may reflect sparse-data instability, unmeasured tissue characteristics, previous diagnostic interventions, or other clinical factors rather than reproducible condition-specific effects.

The morcellation phase demonstrated a less coherent relationship with comorbidity burden. Patients with comorbidity had a median morcellation time of 8 minutes compared with 9 minutes in those without comorbidity, representing an absolute difference of only one minute and a small rank-biserial effect size despite statistical significance (Table 4). Similarly, median morcellation times across prostate-volume strata were 9, 7, and 9 minutes, which does not suggest a simple linear or clinically intuitive size-dependent pattern (Table 3). In the adjusted analysis, each additional comorbidity was associated with an 8.3% shorter morcellation time; however, this direction is not biologically persuasive and should not be interpreted as evidence that comorbidity improves morcellation performance. Condition-specific morcellation estimates were also inconsistent and were particularly pronounced in some small subgroups. Morcellation efficiency is likely to be determined more directly by adenoma consistency, tissue fragmentation, intravesical visibility, blade engagement, morcellator performance, and operator technique than by systemic comorbidity itself. Comparative evidence indicates that morcellator design can substantially affect tissue retrieval speed (15), while predictor analyses have emphasized the roles of tissue burden, procedural characteristics, and surgeon experience in determining morcellation time and efficiency (16). The relationship between prostate size and morcellation performance may also become non-linear at different gland-size thresholds, further limiting

simple between-group interpretation (17). For these reasons, the morcellation findings in the present study should be regarded as secondary, exploratory observations rather than confirmatory evidence of a comorbidity-related effect.

From an implementation perspective, separating enucleation and morcellation outcomes remains useful for identifying where procedural variation occurs; however, the present findings do not establish that comorbidity-based scheduling or risk-adjusted benchmarking is ready for direct clinical application. Total extraction time in this study represented only enucleation plus morcellation time and did not include anesthesia induction, positioning, endoscopic access, hemostasis outside the recorded phase, emergence from anesthesia, turnover time, or total operating-room occupancy. Similarly, American Society of Anesthesiologists (ASA) physical status classification, Charlson Comorbidity Index, postoperative complications, intensive care requirement, length of hospital stay, and perioperative resource utilization were not analyzed. Consequently, the observed association with tissue-adjusted enucleation performance cannot be assumed to translate into longer operating-room occupancy, greater complication risk, or increased hospital resource use. Phase-specific metrics may nevertheless provide a useful research framework for distinguishing enucleation-related bottlenecks from morcellation-related limitations, particularly when interpreted alongside device and technique characteristics (15,16). Laser power and energy source must also be considered when comparing operative performance. Both high-power and low-power HoLEP approaches have been reported to provide acceptable safety and functional outcomes, although perioperative parameters and efficiency benchmarks may vary according to the equipment and settings used (18,19). In a prospective multicenter randomized trial, HoLEP and thulium laser enucleation of the prostate showed similar operative time, enucleated tissue weight, catheterization time, hospital stay, and follow-up functional outcomes, whereas thulium laser enucleation was associated with a smaller postoperative hemoglobin decrease and fewer early episodes of acute urinary retention and stress urinary incontinence (20). Because all procedures in the present cohort were performed using a single high-power Ho:YAG platform with standardized fiber and laser settings, the observed performance estimates should be interpreted within this specific technological context and should not be directly generalized to other laser systems.

Several methodological features strengthen the interpretability of the present findings. Phase-specific time stamps and tissue weights were available for all included patients, equipment and laser parameters were standardized, all participating surgeons had completed the initial HoLEP learning curve, and absolute time differences and effect-size measures were considered alongside p values. The primary inferential model used enucleation time conditional on tissue weight rather than entering tissue weight as a predictor of an outcome ratio containing the same variable, thereby avoiding mathematical coupling. Heteroscedasticity-consistent standard errors, model-fit statistics, false-discovery-rate correction, bootstrap sensitivity analyses for rare subgroups, and additional adjustment for operative technique were also incorporated.

Limitations

Nevertheless, several limitations remain. The retrospective single-center design limits causal inference and external validity. Of the 574 screened procedures, 225 were excluded, and detailed baseline comparisons between included and excluded patients could not be performed because complete analytic variables were not available for all excluded cases; selection bias therefore remains possible. Although the four surgeons had each performed at least 50 HoLEP procedures before the study period, surgeon identity, calendar period, and chronological case number were not retained, precluding operator-level or learning-curve adjustment. Detailed intraoperative measurements of blood loss, visibility, hemostasis time, blood-pressure variability, anesthesia type, irrigation pressure, tissue consistency, fibrosis, and capsular-plane difficulty were unavailable. Comorbidity burden was represented by an unweighted count in which conditions with different clinical severity and perioperative implications contributed equally; ASA physical status classification and the Charlson Comorbidity Index were not available for comparison. Several condition-specific subgroups were small, and multiplicity adjustment and bootstrap analyses cannot completely eliminate sparse-data

bias or false-positive findings. Finally, the adjusted R^2 of the primary model was 0.167, indicating that most variation in enucleation time remained unexplained by the measured variables.

In summary, the present study extends the HoLEP efficiency literature by showing that cumulative comorbidity burden was associated with slower tissue-adjusted enucleation performance after accounting for tissue weight, prostate-volume stratum, age, and antithrombotic use. This association should not be interpreted as evidence that patients with comorbidity necessarily have longer raw enucleation time, longer total operating-room occupancy, or greater perioperative resource requirements. The condition-specific findings, particularly those obtained from rare subgroups, remain exploratory, and the underlying mechanisms cannot be determined from the available data. These results should therefore be regarded as hypothesis-generating and require validation in multicenter cohorts incorporating operator identity, chronological case sequence, validated comorbidity indices, anesthesia variables, intraoperative bleeding and visibility measures, and complete operating-room utilization data before being applied to scheduling or benchmarking.

CONCLUSION

Higher comorbidity burden was associated with longer enucleation time after accounting for tissue burden, age, prostate-volume stratum, and perioperative antithrombotic use. This association reflects slower tissue-adjusted enucleation performance rather than a demonstrated increase in unadjusted operative time or total operating-room occupancy. The findings are hypothesis-generating and should be validated in multicenter cohorts with operator-level, anesthetic, hemostatic, and perioperative resource data.

Funding: The authors received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors for this study.

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

Informed Consent: Informed consent was waived due to the retrospective design of the study.

Ethics Approval: The study protocol was approved by the local ethics committee (Decision No: 2025/010.99/23/21; 30 December 2025) and was conducted in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee because of the retrospective and de-identified nature of the study.

Author Contributions: Concept and design: Yunus Kayalı. Data acquisition: Yunus Kayalı, Tahsin Batuhan Aydoğan, Alpcan Torun, Uğur Yılmaz. Data analysis and interpretation: Yunus Kayalı, Tahsin Batuhan Aydoğan, Alpcan Torun, Uğur Yılmaz. Drafting of the manuscript: Yunus Kayalı, Fatih Bıçaklıoğlu. Critical revision of the manuscript for important intellectual content: Yunus Kayalı, Bilal Çetin. Other intellectual contribution listed in the signed authorship form: Yunus Kayalı, Onur Erdemoğlu. Statistical analysis: Yunus Kayalı. Supervision/other: Yunus Kayalı, Bilal Eryıldırım. All authors read and approved the final manuscript.

Availability of Data and Materials: The datasets generated and analyzed during the current study are not publicly available because they contain clinical information subject to institutional and ethical restrictions. De-identified data may be made available by the corresponding author upon reasonable request and subject to approval by the relevant institution and ethics committee.

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SUPPLEMENTARY TABLES

Supplementary Table S1. Sensitivity analyses for cumulative comorbidity burden and enucleation time

Model	Antithrombotic adjustment	Additional adjustment	Adjusted % change per additional comorbidity	95% CI	p value	R^2	Adjusted R^2
Primary model	Any antithrombotic use	None	9.9	4.8 to 15.2	<0.001	0.181	0.167
Sensitivity model 1	Antiplatelet and anticoagulant entered separately	None	9.7	4.6 to 15.1	<0.001	0.182	0.166
Sensitivity model 2	Antiplatelet and anticoagulant entered separately	Operative technique category	8.0	4.5 to 11.6	<0.001	0.535	0.523

All outcomes were natural log-transformed enucleation time. All models adjusted for age, log-transformed enucleated tissue weight, and prostate-volume stratum and used HC3 robust standard errors.

Supplementary Table S2. Sparse-subgroup bootstrap sensitivity analyses for enucleation time

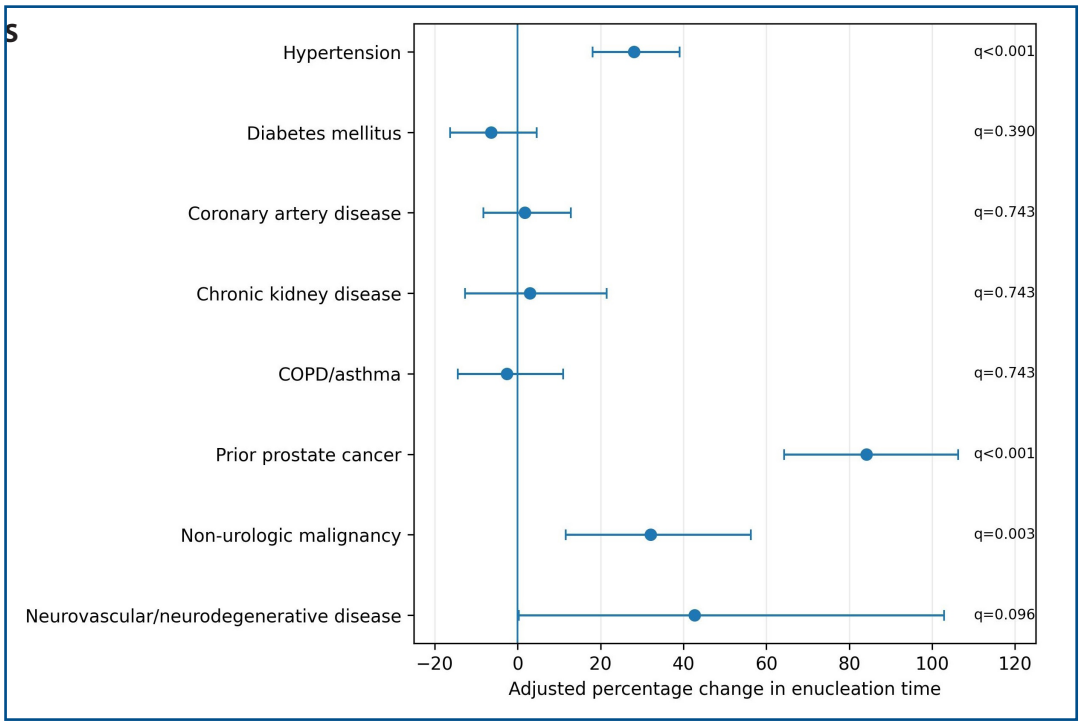
Condition	n	Adjusted % change	HC3 robust 95% CI	5,000-resample bootstrap 95% CI	Interpretive status
Prior prostate cancer	8	84.1	64.3 to 106.3	64.3 to 105.9	Exploratory
Non-urologic malignancy	8	32.0	11.6 to 56.2	13.4 to 57.8	Exploratory
Neurovascular/neurodegenerative disease	8	42.6	0.3 to 102.9	2.2 to 105.6	Exploratory

Bootstrap analyses resampled patients with replacement and refitted the same adjusted condition-specific model. Wide intervals and small subgroup sizes preclude confirmatory interpretation.

Supplementary Table S3. Exploratory condition-specific associations with morcellation time

Condition	n	Adjusted % change	95% CI	p value	FDR-adjusted q value	Interpretation
Hypertension	166	8.8	-7.1 to 27.5	0.296	0.395	Not significant
Diabetes mellitus	54	12.6	-7.2 to 36.7	0.230	0.368	Not significant
Coronary artery disease	79	-3.2	-19.0 to 15.7	0.721	0.721	Not significant
Chronic kidney disease	26	-37.3	-52.5 to -17.1	0.001	0.006	Exploratory shorter time
COPD or asthma	32	-35.8	-51.1 to -15.6	0.001	0.006	Exploratory shorter time
Prior prostate cancer	8	-17.4	-31.5 to -0.4	0.046	0.122	Not FDR-significant
Non-urologic malignancy	8	11.2	-19.0 to 52.8	0.512	0.585	Not significant
Neurovascular/ neurodegenerative disease	8	-39.3	-71.7 to 30.1	0.199	0.368	Not significant

Each model included the condition of interest, number of other comorbidities, age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use, with HC3 robust standard errors. Negative values indicate shorter morcellation time. These analyses are exploratory because morcellation is strongly influenced by unmeasured tissue, visibility, device, and technical factors. FDR: false discovery rate.



Supplementary Figure S1. Adjusted condition-specific associations with enucleation time

Forest plot showing percentage change in enucleation time with 95% confidence intervals from exploratory condition-specific log-time models. Each model adjusted for the number of other comorbidities, age, log-transformed enucleated tissue weight, prostate-volume stratum, and any antithrombotic use, with HC3 robust standard errors. Positive values indicate longer enucleation time. False-discovery-rate-adjusted q values are reported in Table 6. Rare-subgroup findings are exploratory.

Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):176–186. doi: 10.54233/endourolbull-1911968

Beyond Statistical Accuracy: Decision Curve Analysis and Single-Center Independent Validation of the SHA.LIN Score for PCNL Outcomes

İstatistiksel Doğruluğun Ötesinde: PCNL Sonuçlarında SHA.LIN Skorunun Karar Eğrisi Analizi ve Tek Merkezli Bağımsız Validasyonu

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ABSTRACT

Objective: To perform a single-center independent validation of the SHA.LIN score and compare its predictive accuracy and clinical net benefit with the Guy's Stone Score (GSS), S.T.O.N.E. score, and CROES nomogram in a large cohort of patients undergoing percutaneous nephrolithotomy (PCNL).

Materials and Methods: We retrospectively analyzed 271 adult patients undergoing PCNL between 2020 and 2025. Stone-free status (SFS) was defined as the absence of stones or asymptomatic fragments <4 mm on non-contrast computed tomography at 1 month. Predictive performance was assessed using area under the curve (AUC), calibration plots, and Decision Curve Analysis (DCA).

Results: The SFS rate was 73.1%. The CROES nomogram demonstrated the highest predictive accuracy (AUC: 0.802, 95% CI: 0.765–0.839), followed by the SHA.LIN score (AUC: 0.756, 95% CI: 0.715–0.797). The SHA.LIN score significantly outperformed both GSS (AUC: 0.719, p=0.023) and S.T.O.N.E. (AUC: 0.690, p<0.0001). In both univariate and multivariable analyses, the CROES nomogram and SHA.LIN score emerged as significant independent predictors of stone-free status, whereas Guy and STONE scores failed to retain significance after multivariable adjustment. In DCA, the SHA.LIN score showed superior net clinical benefit compared with GSS and S.T.O.N.E. across threshold probabilities between 40% and 80%.

Conclusion: The SHA.LIN score is a reliable, independently validated single-center tool for predicting PCNL outcomes. Although the CROES nomogram demonstrates high statistical accuracy, the SHA.LIN score provides superior clinical utility and net benefit in decision curve analysis. Furthermore, CROES and SHA.LIN scores remained independent predictors of stone-free status, whereas Guy and STONE scores failed to demonstrate independent predictive value in multivariable analyses. Further prospective studies with larger cohorts are warranted to validate these findings.

Keywords: percutaneous nephrolithotomy, nephrolithometry, SHA.LIN score, stone-free status, predictive models

Cite As: *Hacibey I, Sezgin V, Akdag A, Sevik C, Yilmaz E, Keskin ET, Canat HL. Beyond Statistical Accuracy: Decision Curve Analysis and External Validation of the SHA.LIN Score for PCNL Outcomes. Endourol Bull. 2026;18(3):176–186.* https://doi.org/10.54233/endourolbull-1911968

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Received : March 18, 2026 ***Accepted*** : July 21, 2026

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ÖZET

Amaç: Bu çalışmada, perkütan nefrolitotomi (PCNL) uygulanan geniş bir hasta kohortunda SHA.LIN skorunun tek merkezli bağımsız doğrulamasının yapılması ve Guy's Stone Score (GSS), S.T.O.N.E. skoru ve CROES nomogramı ile öngörü doğruluğu ve klinik net fayda açısından karşılaştırılması amaçlandı.

Gereç ve Yöntemler: 2020 ile 2025 yılları arasında PCNL uygulanan 271 erişkin hasta retrospektif olarak analiz edildi. Taşsızlık durumu, ameliyat sonrası 1. ayda yapılan kontrastsız bilgisayarlı tomografide taş saptanmaması veya 4 mm'den küçük asemptomatik fragman varlığı olarak katı biçimde tanımlandı. Prediktif performans, eğri altında kalan alan (AUC), kalibrasyon grafikleri ve Karar Eğrisi Analizi (Decision Curve Analysis) kullanılarak değerlendirildi.

Bulgular: Taşsızlık oranı %73,1 olarak bulundu. En yüksek prediktif doğruluk CROES nomogramında saptandı (AUC: 0,802; %95 GA: 0,765–0,839); bunu SHA.LIN skoru izledi (AUC: 0,756; %95 GA: 0,715–0,797). SHA.LIN skoru, hem GSS'ye (AUC: 0,719; p=0,023) hem de S.T.O.N.E. skoruna (AUC: 0,690; p<0,0001) göre anlamlı derecede üstün performans gösterdi. Hem tek değişkenli hem de çok değişkenli analizlerde CROES nomogramı ve SHA.LIN skoru taşsızlık durumunun anlamlı bağımsız öngörücüleri olarak öne çıkarken; Guy ve STONE skorları çok değişkenli düzeltme sonrasında anlamlılıklarını koruyamamıştır. Karar eğrisi analizinde SHA.LIN, %40–80 eşik olasılığı aralığında GSS ve S.T.O.N.E.'a kıyasla daha yüksek net klinik fayda sağladı.

Sonuçlar: SHA.LIN skoru, PCNL sonuçlarını öngörmede güvenilir ve tek merkezli bağımsız validasyonu yapılmış bir araçtır. CROES nomogramı yüksek istatistiksel doğruluk gösterse de SHA.LIN skoru, karar eğrisi analizinde daha üstün klinik fayda sağlamaktadır. Dahası, çok değişkenli analizlerde CROES ve SHA.LIN skorları taşsızlık durumunun bağımsız öngörücüleri olarak kalırken, Guy ve STONE skorları bağımsız öngörü değeri gösterememiştir. Bu bulguları doğrulamak için daha geniş kohortlarla yapılacak ileriye yönelik çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: perkütan nefrolitotomi, nefrolitometri, SHA.LIN skoru, taşsızlık durumu, prediktif modeller

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) remains the gold standard treatment for large (>2 cm) and complex renal calculi due to its high stone-free rates (SFR) compared to other modalities (1, 2). Despite technical advancements, PCNL is associated with potential complications, including bleeding, organ injury, and sepsis. Therefore, accurate preoperative prediction of surgical outcomes is essential for patient counseling, surgical planning, and risk stratification (3).

To standardize the reporting of stone complexity and predict perioperative outcomes, several nephrolithometry scoring systems have been developed over the last decade. The most widely adopted systems include the Guy's Stone Score (GSS), the S.T.O.N.E. nephrolithometry score, and the Clinical Research Office of the Endourological Society (CROES) nomogram (4-6). While these tools have demonstrated validity in various cohorts, they differ in complexity, reproducibility, and predictive accuracy. Furthermore, deviations in their performance across different populations underscore that predictive performance may systematically vary across patient cohorts and distinct institutional settings, necessitating continuous geographic validation (7).

Traditional nephrolithometry scoring systems often face limitations in daily practice. While GSS relies on subjective criteria and S.T.O.N.E. demands time-consuming measurements, the CROES nomogram requires complex calculator-based modeling that limits rapid bedside screening. To address these limitations and balance clinical simplicity with prognostic power, the SHA.LIN score was developed. By integrating key tomographic metrics such as stone burden, hydronephrosis, and stone density into a straightforward categorical framework, this novel system captures complex stone morphology without losing practical bedside utility (8). Initial reports suggest that the SHA.LIN score offers a balance between simplicity and prognostic power. However, external validation studies comparing its performance head-to-head with established nomograms are limited, and its calibration, specifically its reliability in predicting stone-free failure at the boundaries of the lowest and highest risk spectrums, remains to be fully elucidated.

The primary aim of this study is to perform a single-center independent validation of the SHA.LIN score and evaluate its predictive capability with the GSS, S.T.O.N.E., and CROES nomograms. As a secondary objective, we evaluated the postoperative outcomes of these scoring systems regarding specific perioperative safety outcomes, including hemoglobin drop and complications.

MATERIALS AND METHODS

Study Design and Patient Selection

This retrospective study was approved by the Institutional Review Board (IRB No: 2026/76, Date: October 15, 2025) and the requirement for written informed consent was waived due to the retrospective design and use of de-identified data. Data were analyzed from patients who underwent PCNL for renal calculi at our tertiary referral center between April 2020 and December 2025. A total of 271 adult patients (>18 years) with available preoperative non-contrast computed tomography (NCCT) images were included in the study. Exclusion criteria were skeletal anomalies preventing standard positioning, active urinary tract infection, coagulation disorders, renal anomalies (e.g., horseshoe kidney), and patients with incomplete data. None of the patients included in this cohort were part of the original SHA.LIN development dataset, and the present study represents a fully independent retrospective single-center validation cohort. Between April 2020 and December 2025, a total of 306 patients underwent percutaneous nephrolithotomy at our institution. Of these, 35 patients were excluded due to skeletal anomalies preventing standard positioning (n = 4), renal anomalies (n = 17), coagulation disorders (n = 3), and incomplete clinical data (n = 11). The remaining 271 patients with complete preoperative imaging and outcome data constituted the final study cohort.

Preoperative Assessment and Scoring Systems

All patients underwent detailed preoperative evaluation, including serum biochemistry, coagulation profile, urine culture, and NCCT. Stone burden was calculated as the cumulative surface area in square millimeters based on the maximal length and width measurements of each individual stone. For patients presenting with multiple renal calculi, the surface areas of all separate stones were calculated independently and subsequently summed to determine the total definitive stone burden. The complexity of renal stones was graded preoperatively using four nephrolithometry scoring systems:

SHA.LIN Score: The SHA.LIN score was calculated using six preoperative parameters assessed on non-contrast computed tomography. Stone size was calculated as stone surface area (mm^2) using maximal length and width measurements and categorized as 0–399 mm^2, 400–799 mm^2, 800–1,599 mm^2, and ≥1,600 mm^2, corresponding to increasing score levels. Hydronephrosis was graded as none or mild, moderate, or severe. Stone anatomical distribution was classified as pelvis or mid/lower calyx, upper calyx, calyceal diverticulum or partial staghorn stone, and complete staghorn stone. The length of the percutaneous tract was measured as the skin-to-stone distance and categorized as ≤100 mm or >100 mm. Stone density was assessed using mean Hounsfield unit values and categorized as ≤950 HU or >950 HU. The number of involved calyces was classified as 0–2 or ≥3. The total SHA.LIN score was calculated by summing all component scores, with higher scores indicating greater stone complexity (8).

Guy's Stone Score (GSS): Graded I to IV based on stone size, location and anatomy (4).

S.T.O.N.E. Nephrolithometry Score: Based on five variables: Size, Tract length (mm), Obstruction, Number of calyces with calculi, and Essence (stone density in Hounsfield units) [5].

CROES Nomogram: Calculated based on variables such as stone burden, location, prior treatment, presence of staghorn, number of stone and case volume [6]. The CROES nomogram was mathematically inverted by subtracting each calculated score from its maximum possible value to ensure that higher scores uniformly represented a greater probability of surgical failure across all evaluated systems.

All nephrolithometry scores were independently calculated by two experienced endourologists who underwent prior standardized training on stone scoring systems. Interobserver reliability for these evaluations was objectively assessed using the intraclass correlation coefficient (ICC) and any rare scoring discrepancies were resolved through mutual consensus prior to final data analysis.

Surgical Technique

All procedures were performed under general anesthesia by two experienced endourologists (A.A and E.T.K) with more than ten years of experience using a standardized percutaneous nephrolithotomy technique. Access to the collecting system was routinely achieved under fluoroscopic guidance in the prone position utilizing a single subcostal tract approach. The tract was subsequently dilated using Amplatz dilators to 26–30 Fr, depending on the stone burden and collecting system anatomy. Stone fragmentation was performed using pneumatic or ultrasonic lithotripsy. At the end of the procedure, a nephrostomy tube or double-J stent was placed at the surgeon's discretion

Outcome Definitions

The primary endpoint was stone-free status (SFS). SFS was defined as the complete absence of stones or the presence of asymptomatic residual fragments < 4 mm on postoperative NCCT performed at the 1-month follow-up.

Secondary endpoints included operative time, hemoglobin drop (calculated as the difference between preoperative and postoperative day 1 values), and complications. Complications were graded according to the Clavien–Dindo classification system.

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R software (version 4.0.3). Although a formal post hoc power analysis was not performed due to the retrospective and validation based nature of the study, our sample size adheres to the current prediction model validation guidelines. According to established methodological frameworks for external validation, a minimum of one hundred patients and at least ten to twenty events per outcome category are required to ensure statistical stability and our cohort provides adequate statistical power to evaluate the discrimination and calibration of the models. The normality of continuous variables was assessed using the Shapiro Wilk test. Because the data were normally distributed, continuous variables were presented as mean ± standard deviation (SD). Categorical variables were expressed as frequencies and percentages. Receiver Operating Characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was calculated to evaluate the predictive capability of each scoring system for SFS. The DeLong test was used to compare the AUC values of the different scoring systems pairwise. The Hosmer-Lemeshow test were used to assess the agreement between predicted probabilities and observed outcomes. Decision Curve Analysis (DCA) was conducted to determine the net clinical benefit of the scoring systems across a range of threshold probabilities. The threshold probability range of 40–80% was selected for DCA because it represents a clinically critical decision-making window where the likelihood of stone-free failure is substantial enough to warrant considering alternative approaches, such as staged procedures or multiple tracts, without overwhelming the patient with unnecessary upfront morbidity (9).

Numerical net benefit values along with their corresponding ninety five percent confidence intervals were calculated at specific clinical thresholds to evaluate the exact clinical utility of each model. Internal validation of the decision curve analysis models was rigorously performed using a bootstrap resampling approach involving two thousand repetitions to guarantee the stability and reproducibility of the net benefit estimations. Pearson correlation analysis was used to assess the relationship between scoring systems and perioperative safety outcomes (hemoglobin drop, complications). Furthermore, univariable logistic regression analysis was conducted to evaluate the association between the scoring systems and clinically significant complications (Clavien–Dindo grade ≥2). A two-sided p-value of <0.05 was considered statistically significant. Furthermore, univariable logistic regression analysis was conducted

to evaluate the association between the scoring systems and clinically significant complications (Clavien–Dindo grade ≥2). A two-sided p-value of <0.05 was considered statistically significant.

RESULTS

A total of 271 patients who underwent PCNL were included in the study. The mean age of the patients was 43.9 ± 11.5 years, and the mean stone size was 651 ± 464 mm^2. The overall stone-free rate (SFR) was 73.1%. (n = 198), and the rate of clinically significant postoperative complications (Clavien–Dindo grade ≥2) was 15.9% (n = 43). Among the forty three patients who experienced postoperative complications, fourteen required blood transfusions, ten developed urosepsis, twelve mandated double J stent insertions, six required angioembolization, and one underwent a salvage nephrectomy. The mean SHA.LIN score was 9.51 ± 2.67, while the mean Guy's Stone Score (GSS), S.T.O.N.E., and CROES scores were 2.21 ± 0.86, 7.86 ± 1.98, and 224.6 ± 58.9, respectively (Table 1). Interobserver reliability analysis demonstrated excellent agreement for all evaluated scoring systems. The intraclass correlation coefficient was 0.86 with a ninety five percent confidence interval of 0.82 to 0.89 for the SHA.LIN score. Similarly, the coefficients for the Guy's Stone Score, S.T.O.N.E. score, and CROES nomogram were 0.83, 0.81, and 0.88, respectively, indicating robust reproducibility across all scoring methodologies. Baseline characteristics stratified by the primary endpoint, stone-free status, are presented in Table 1. Among the evaluated variables, only the CROES score differed significantly between stone-free and non-stone-free patients (232.3 ± 58.1 vs 189.3 ± 47.1, p < 0.001), whereas age, sex, body mass index, stone size, SHA.LIN, Guy's Stone Score, and S.T.O.N.E. score were comparable between groups.

The predictive accuracy of the four scoring systems for stone-free status was evaluated using ROC curve analysis. The CROES nomogram demonstrated the highest predictive capability with an area under the curve (AUC) of 0.802 (95% CI: 0.765–0.839). The SHA.LIN score showed a ~~high~~ acceptable and moderate predictive value with an AUC of 0.756 (95% CI: 0.715–0.797), which was superior to both the Guy's Stone Score (AUC: 0.719, 95% CI: 0.677–0.758) and the S.T.O.N.E. score (AUC: 0.690, 95% CI: 0.642–0.737) (Figure 1). In addition to AUC values, optimal cut-off thresholds were determined for each scoring system using the Youden index. The optimal cut-off was ≥9 for the SHA.LIN score, yielding a sensitivity of 70.6% and a specificity of 37.8%. For Guy's Stone Score, the optimal threshold was ≥2, with a sensitivity of 74.6% and a specificity of 31.1%. For the S.T.O.N.E. score, the optimal cut-off was ≥6, corresponding to a sensitivity of 94.9% and a specificity of 83.1%. The CROES nomogram showed the best balance, with an optimal cut-off of ≥231, a sensitivity of 51.3%, and a specificity of 85.1% (Table 2).

Table 1. Baseline demographic, clinical, and perioperative characteristics according to stone-free status

Variable	Stone-free (n=198)	Not stone-free (n=73)	p
Age (years), mean ± SD	44.5 ± 11.9	42.2 ± 10.6	0.123
Male sex, n (%)	133 (67.5%)	57 (77.0%)	0.169
Female sex, n (%)	64 (32.5%)	17 (23.0%)	
Body mass index (kg/m^2), mean ± SD	27.8 ± 5.1	28.0 ± 5.0	0.782
Stone size (mm^2), mean ± SD	620.2 ± 430.6	609.4 ± 450.4	0.860
SHA.LIN score, mean ± SD	9.3 ± 2.6	10.3 ± 2.6	<0.001
Guy's Stone Score, mean ± SD	2.1 ± 0.9	2.0 ± 0.9	0.628
S.T.O.N.E. score, mean ± SD	7.7 ± 1.7	7.7 ± 1.7	0.903
CROES score, mean ± SD	232.3 ± 58.1	189.3 ± 47.1	<0.001
Hemoglobin drop (g/dL), mean ± SD	2.2 ± 1.2	2.3 ± 1.4	0.637

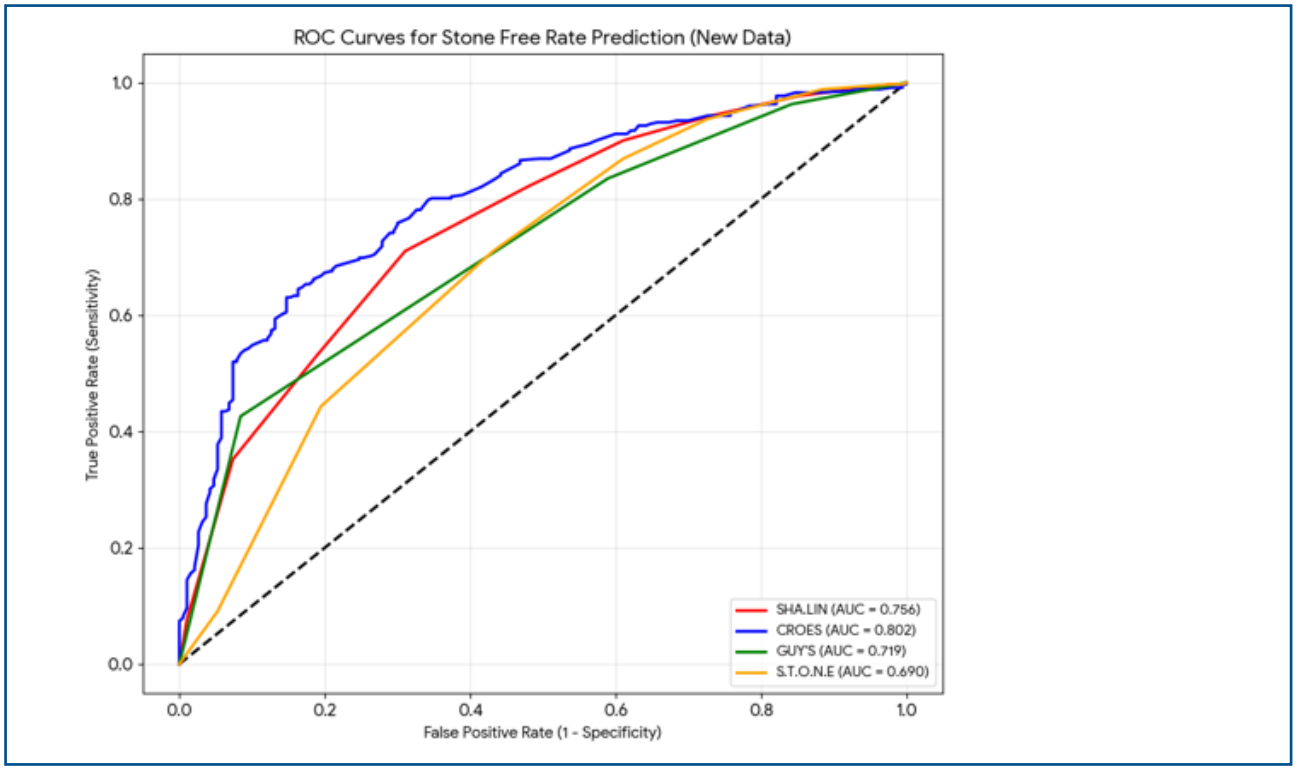


Figure 1. Receiver operating characteristic (ROC) curves comparing the predictive performance of the SHA.LIN score, Guy's Stone Score, S.T.O.N.E. score, and CROES nomogram (inverted) for predicting stone-free failure at 1 month after PCNL.

Table 2. Comparison of optimal cut-off values, sensitivity, and specificity across different renal stone scoring systems

Score	Optimal cut-off	Sensitivity	Specificity
SHA.LIN	≥ 9	70.6%	37.8%
Guy's Stone Score	≥ 2	74.6%	31.1%
S.T.O.N.E.	≥ 6	94.9%	83.1%
CROES	≥ 231	51.3%	85.1%

Pairwise comparison of ROC curves using the DeLong test revealed that the predictive accuracy of the SHA.LIN score was significantly higher than that of the S.T.O.N.E. score ($p < 0.0001$) and Guy's Stone Score ($p = 0.023$). Consistently, the CROES nomogram yielded the highest AUC and demonstrated superior discriminatory performance compared with SHA.LIN ($p = 0.0002$).

Multivariable logistic regression analysis adjusted for age, sex, BMI, and ASA score demonstrated that both CROES score (OR 1.014, 95% CI 1.009–1.020, $p < 0.001$) and SHA.LIN score (OR 1.18, 95% CI 1.05–1.33, $p = 0.004$) were independent predictors of stone-free status. In contrast, Guy Stone Score and STONE score were not independently associated with stone-free outcomes in the adjusted models.

In addition to stone-free prediction, correlation analyses were performed to evaluate the association between nephrolithometry scores and perioperative safety outcomes (Table 3). -A weak but statistically significant positive correlation was observed between the SHA.LIN score and hemoglobin drop ($r = 0.127$, $p = 0.003$). Similarly, a weak correlation was found between the CROES nomogram and hemoglobin drop ($r = -0.204$, $p < 0.001$). In contrast, univariable logistic regression analysis demonstrated that none of the nephrolithometry scoring systems were

significantly associated with clinically significant postoperative complications (Clavien–Dindo grade ≥2). The SHA.LIN score was not associated with complication risk (OR: 1.04, 95% CI: 0.97–1.11, p = 0.26). Similarly, no significant associations were observed for the Guy's Stone Score (OR: 1.18, 95% CI: 0.91–1.54, p = 0.21), the S.T.O.N.E. score (OR: 1.07, 95% CI: 0.95–1.20, p = 0.27), or the CROES nomogram (OR: 0.99, 95% CI: 0.98–1.01, p = 0.34).

The specific numerical net benefit values and their ninety five percent confidence intervals across the key threshold probabilities are comprehensively documented in Table 4, demonstrating that the SHA.LIN score maintains a consistently higher net benefit compared to the Guy's Stone Score and S.T.O.N.E. score within the critical decision window.

Calibration was objectively evaluated using the Hosmer–Lemeshow goodness-of-fit test. The analysis confirmed that the SHA.LIN score ($\chi^2 = 10.29$, p = 0.173) and the CROES nomogram ($\chi^2 = 6.83$, p = 0.555) demonstrated a good fit with no significant difference between predicted and observed outcomes. To supplement the non significant calibration testing metrics and ensure a robust validation model the calibration slope for the SHA.LIN score was calculated as zero point eighty nine indicating an acceptable proportional agreement between the predicted risks and the actual observed stone free outcomes. In contrast, Guy's Stone Score ($\chi^2 = 18.45$, p = 0.018) and S.T.O.N.E. ($\chi^2 = 22.10$, p = 0.005) showed a significant lack of fit, indicating that these models were less reliable in predicting stone-free failure in this cohort.

Decision Curve Analysis was utilized to evaluate the net clinical benefit of the scoring systems. At threshold probabilities ranging from 40% to 80%, the SHA.LIN score demonstrated a higher net benefit compared to the Guy's and S.T.O.N.E. scores, suggesting its superior clinical utility in decision-making processes for preventing unnecessary interventions or predicting complex cases (Figure 2). While the CROES nomogram provided the highest overall net benefit, the SHA.LIN score offered superior utility compared to other categorical scores (GSS, STONE) in the 40-80% threshold range.

Table 3. Correlation Between Nephrolithometry Scores and Perioperative Safety Outcomes

Score	Hb drop (r)	p	Clavien–Dindo severity (r)	p
SHA.LIN	0.127	**0.003**	0.042	**0.318**
CROES	−0.204	**<0.001**	−0.058	**0.184**
Guy's	0.097	**0.023**	0.031	**0.446**
S.T.O.N.E.	0.068	**0.105**	0.019	**0.672**

Table 4. Numerical Net Benefit Values for Predicting Stone Free Failure

Threshold Probability	SHA.LIN Score Net Benefit (CI %95)	CROES Nomogram Net Benefit (CI %95)	Guy's Stone Score Net Benefit (CI %95)	S.T.O.N.E. Score Net Benefit (CI %95)
0.40	0.11 (0.07 - 0.15)	0.13 (0.09 - 0.17)	0.08 (0.04 - 0.12)	0.08 (0.04 - 0.12)
0.45	0.09 (0.05 - 0.13)	0.12 (0.08 - 0.16)	0.06 (0.02 - 0.10)	0.07 (0.03 - 0.11)
0.50	0.08 (0.04 - 0.12)	0.10 (0.06 - 0.14)	0.05 (0.01 - 0.09)	0.06 (0.02 - 0.10)
0.55	0.06 (0.02 - 0.10)	0.07 (0.03 - 0.11)	0.01 (0.00 - 0.04)	0.04 (0.01 - 0.08)
0.60	0.04 (0.01 - 0.07)	0.05 (0.01 - 0.09)	0.02 (0.00 - 0.05)	0.03 (0.00 - 0.06)

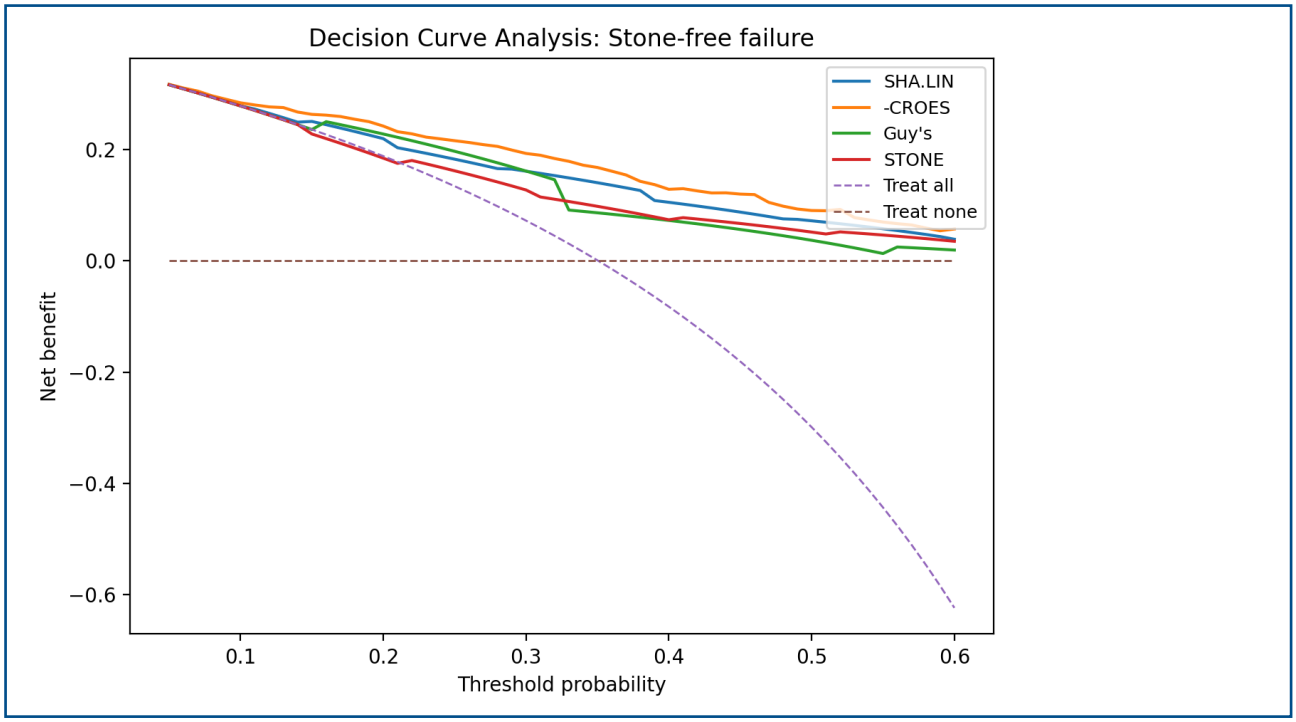


Figure 2. Decision curve analysis showing the net clinical benefit of the SHA.LIN score, Guy's Stone Score, S.T.O.N.E. score, and CROES nomogram (inverted) across a range of threshold probabilities for predicting stone-free failure.

DISCUSSION

Accurate preoperative prediction of SFS and perioperative morbidity remains a cornerstone of patient counseling, operative planning, and risk stratification in PCNL (1,3). In this independent retrospectively externally validated cohort, we compared the performance of the recently proposed SHA.LIN scoring system with three established nephrolithometry tools and demonstrated that, although the CROES nomogram achieved the highest overall discriminative accuracy, the SHA.LIN score provided acceptable predictive performance and clinically meaningful advantages over the widely used GSS and S.T.O.N.E. scores. In multivariable analyses adjusted for potential confounders, only CROES and SHA.LIN scores maintained independent predictive value for stone-free status. This finding suggests that these scoring systems may better reflect clinically relevant stone complexity parameters compared with Guy Stone Score and STONE score.

Consistent with previous validation studies, the CROES nomogram exhibited the strongest discrimination for SFS, which is largely attributable to its reliance on continuous variables and multivariable modeling approaches (6,7,10). However, despite its statistical superiority, the CROES nomogram requires calculator-based implementation and incorporates parameters that may limit its routine use in within high volume and time constrained clinical workflows. In contrast, categorical scoring systems remain attractive due to their simplicity and bedside applicability (11,12). Within this context, the SHA.LIN score represents an effective compromise between predictive accuracy and practical usability. The superior performance of the SHA.LIN score compared to GSS and S.T.O.N.E. in our cohort can be explained by its inclusion of morphologic and compositional parameters that directly influence stone clearance. Factors such as stone density , hydronephrosis grade, and the number of involved calyces capture elements of surgical complexity that extend beyond stone burden alone (8,13). These findings support and externally validate the original observations by Jia et al. (8), suggesting that more granular anatomical and radiological characterization improves outcome prediction in PCNL. In contrast, GSS and S.T.O.N.E., rely on broader categorical groupings that may insufficiently reflect intraoperative challenges (4,5,7). Although our overall stone-free rate (73.1%) may appear lower than those reported in some historical series, this discrepancy is largely attributable to our use of non-contrast CT rather than plain radiography (KUB) for postoperative evaluation. It is well established that KUB significantly

overestimates stone-free rates compared to CT; therefore, our adherence to CT-based criteria (< 4 mm) eliminates overestimation of residual stone clearance and ensures a more reliable assessment of surgical efficacy (14-16). An important strength of the present study is the incorporation of DCA, which evaluates the clinical consequences of prediction models beyond traditional discrimination metrics. DCA has been shown to better reflect real-world clinical decision-making than accuracy-based measures alone (9). In our analysis, the SHA.LIN score demonstrated superior net clinical benefit compared with GSS and S.T.O.N.E. across threshold probabilities between 40% and 80%. This range is particularly relevant in clinical practice, where surgeons must decide whether to pursue aggressive stone clearance strategies, plan for staged procedures, or anticipate auxiliary interventions in patients with intermediate-to-high procedural complexity. Calibration analysis further revealed acceptable agreement between predicted and observed outcomes for the SHA.LIN score, particularly in intermediate-risk groups, while deviations were noted at the extremes of risk distribution. Such behavior is commonly observed when prediction models are applied to independent external cohorts and reflects inherent limitations of risk stratification models rather than poor model performance (7,17). Importantly, these findings do not detract from the overall clinical utility of the SHA.LIN score but rather emphasize the complementary role of clinical judgment.

With respect to perioperative safety, we observed a weak yet statistically significant correlation between higher SHA.LIN scores and greater hemoglobin decline, a pattern also reported with the CROES nomogram in previous studies (6,11,13). However, given the low correlation coefficient obtained in our analysis, this statistical finding does not imply a definitive clinical causation or robust predictability regarding parenchymal blood loss. Conversely, the S.T.O.N.E. score did not demonstrate a significant association with hemoglobin drop in our cohort. None of the evaluated nephrolithometry systems were independently associated with clinically significant postoperative complications. Although this finding should be interpreted with caution due to the relatively low complication rate within our patient cohort which precluded the feasibility of performing a robust multivariate regression analysis, it remains consistent with prior evidence indicating that complications are multifactorial and heavily influenced by surgeon experience and patient-specific factors rather than stone complexity alone (4,5,7,18).

Although the present study provides a independent retrospective validation of the SHA.LIN score in a large, several considerations should be acknowledged when interpreting the findings. First, the single-center design may limit the generalizability of the results, as institutional factors such as surgical expertise, access techniques, and perioperative management protocols can influence PCNL outcomes. In particular, variations in patient positioning, tract size, energy sources for lithotripsy, and the adoption of miniaturized PCNL techniques may affect stone-free rates and complication profiles. Therefore, the predictive performance and calibration of the SHA.LIN score may differ across centers with heterogeneous surgical practices. Furthermore, while categorical systems like SHA.LIN offer pragmatic bedside utility, they lack the dynamic data integration capabilities of emerging artificial intelligence or machine learning models and remain susceptible to manual interobserver variations. Future multicenter studies involving diverse patient populations and alternative PCNL techniques are warranted to further assess the external validity and transportability of the SHA.LIN scoring system across different clinical settings.

CONCLUSION

CROES and SHA.LIN scores were independent predictors of stone-free status after adjustment for age, sex, BMI, and ASA score, whereas Guy Stone Score and STONE score did not retain significance in multivariable analyses. Further prospective studies with larger cohorts are warranted to validate these findings.

Acknowledgments: There are no acknowledgements to declare

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

Conflict of Interest: The authors declare that there is no conflict of interest

Informed Consent: This study was conducted in accordance with the Declaration of Helsinki. Due to the retrospective nature of the study, the requirement for informed consent was waived by the Institutional Ethics Committee.

Ethical Approval: This study was approved by the Ethics Committee of Başakşehir Çam and Sakura City Hospital (Approval No: 2026/76, Date: October 15, 2025).

Author Contributions:

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):187–197. doi: 10.54233/endourolbull-1917844

The Impact of Zero Ischemia Versus Standard Warm Ischemia on Long-Term Renal Function in Robotic Partial Nephrectomy: A Retrospective Cohort Study

Robotik Parsiyel Nefrektomide Zero Iskemi Ve Standart Sıcak Iskeminin Uzun Dönem Böbrek Fonksiyonları Üzerine Etkisi: Retrospektif Kohort Çalışması

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ABSTRACT

Objective: The aim of this study was to evaluate and compare the perioperative, oncological and long-term renal functional outcomes of the zero ischemia (off-clamp) and standard warm ischemia (on-clamp) approaches in patients undergoing robotic partial nephrectomy (RPN).

Materials and Methods: This retrospective cohort study examined 56 consecutive patients who underwent RPN for renal masses. The patients were divided into two groups: a zero ischemia group (n = 26) and a warm ischemia group (n = 30). Preoperative demographics, tumour characteristics (RENAL, PADUA and C-index) and perioperative data were recorded. Renal function was assessed using serum creatinine levels and estimated glomerular filtration rates (eGFR) before surgery, on the first day after surgery, and after one year.

Results: There were no differences in demographic variables or tumour complexity scores (RENAL, PADUA) between the groups. The C-index score was significantly higher in the zero ischemia group (median 3.1 vs. 1.86, $p = 0.001$), indicating a more peripheral tumour location. Although postoperative complication ($p = 0.494$) and positive surgical margin (PSM) ($p = 0.140$) rates were comparable, estimated blood loss (300 ml vs. 100 ml, $p < 0.001$) and hospital stay (4 days vs. 3 days, $p = 0.001$) were higher in the zero ischemia cohort. Both groups experienced an initial deterioration in renal function, but the zero ischemia group's eGFR and creatinine levels recovered to baseline within one year ($p = 0.970$). In contrast, the warm ischemia group experienced a significant decline in eGFR that persisted at one year ($p = 0.001$).

Conclusion: The zero ischemia approach in RPN may offer functional advantages, particularly in selected patients, in terms of complete long-term preservation of renal function compared to standard warm ischemia. Despite slightly increased intraoperative bleeding, this approach demonstrates comparable PSM rates, particularly for anatomically suitable, peripherally located tumours.

Keywords: robotic partial nephrectomy, zero ischemia, warm ischemia, c-index, renal cell carcinoma

Cite As: *Aktas Y, Durak HA, Yilmaz K, Kilic S, Sambel M, Ates M, Olcucu MT. The Impact of Zero Ischemia Versus Standard Warm Ischemia on Long-Term Renal Function in Robotic Partial Nephrectomy: A Retrospective Cohort Study. Endourol Bull. 2026;18(3):187–197.* https://doi.org/10.54233/endourolbull-1917844

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Received : March 28, 2026 ***Accepted*** : June 6, 2026

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ÖZET

Amaç: Bu çalışmanın amacı, robotik parsiyel nefrektomi (RPN) uygulanan hastalarda iskemisiz (klempsiz) ve standart sıcak iskemi (klempli) yaklaşımlarının perioperatif, onkolojik ve uzun dönem böbrek fonksiyonel sonuçlarını değerlendirmek ve karşılaştırmaktır.

Gereçler ve Yöntemler: Bu retrospektif kohort çalışmasında, böbrek kitleleri nedeniyle RPN uygulanan ardışık 56 hasta incelenmiştir. Hastalar iki gruba ayrıldı: iskemisiz yaklaşım grubu (n = 26) ve sıcak iskemi grubu (n = 30). Preoperatif demografik veriler, tümör özellikleri (RENAL, PADUA ve C-indeks) ve perioperatif veriler kaydedildi. Böbrek fonksiyonları; cerrahi öncesinde, postoperatif birinci günde ve birinci yılın sonunda serum kreatinin seviyeleri ile tahmini glomerüler filtrasyon hızları (eGFR) kullanılarak değerlendirildi.

Bulgular: Gruplar arasında demografik değişkenler veya tümör kompleksite skorları (RENAL, PADUA) açısından fark saptanmadı. C-indeks skoru iskemisiz yaklaşım grubunda anlamlı olarak daha yüksekti (medyan 3,1'e karşı 1,86, p = 0,001); bu da tümörlerin daha periferik yerleşimli olduğunu göstermektedir. Postoperatif komplikasyon (p = 0,494) ve pozitif cerrahi sınır oranları (p = 0,140) benzer bulunmasına rağmen, tahmini kan kaybı (300 ml'ye karşı 100 ml, p < 0,001) ve hastanede yatış süresi (4 güne karşı 3 gün, p = 0,001) iskemisiz yaklaşım kohortunda daha yüksekti. Her iki grupta da başlangıçta böbrek fonksiyonlarında bozulma görüldü; ancak iskemisiz yaklaşım grubunun eGFR ve kreatinin seviyeleri birinci yıl içinde preoperatif bazal seviyelerine döndü (p = 0,970). Buna karşılık, sıcak iskemi grubunda birinci yılda eGFR'de anlamlı bir düşüş saptandı (p = 0,001).

Sonuçlar: RPN'de iskemisiz yaklaşım, özellikle seçilmiş hastalarda, standart sıcak iskemiye kıyasla böbrek fonksiyonlarının uzun vadeli ve tam olarak korunması açısından potansiyel fonksiyonel avantajlar sunabilir. İntraoperatif kanamayı bir miktar artırmasına rağmen bu yaklaşım, özellikle anatomik olarak uygun, periferik yerleşimli tümörler için karşılaştırılabilir pozitif cerrahi sınır oranları göstermektedir.

Anahtar Kelimeler: robotik parsiyel nefrektomi, iskemisiz yaklaşım, sıcak iskemi, C-indeks, renal hücreli karsinom

INTRODUCTION

Renal cell carcinoma (RCC) accounts for approximately 2–4% of all cancers, and its incidence has increased markedly in recent decades (1). The primary reason for this increase is the widespread use of cross-sectional imaging techniques such as ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) (2). More than 45% of all newly diagnosed RCCs present as small renal masses (SRMs) of ≤4 cm (T1a), and this proportion is reported to be continuously rising (1). Current guidelines and large clinical series confirm that, when technically feasible, partial nephrectomy (PN) is the gold standard for T1 renal tumours, as it significantly better preserves renal function while maintaining comparable oncological outcomes (3). Due to technological advancements in minimally invasive surgery, robotic partial nephrectomy (RPN) has largely replaced open surgery, offering superior visualisation and enhanced manoeuvrability (4).

During partial nephrectomy, the renal artery or renal hilum is usually temporarily clamped in order to create a bloodless surgical field and facilitate comfortable renal reconstruction (5). However, the duration and extent of warm ischemia are the primary surgical factors that determine nephron loss (6). Large systematic reviews have demonstrated that a warm ischemia time (WIT) exceeding 25–30 minutes is associated with a postoperative decline in estimated glomerular filtration rate (eGFR) and poor short-term functional outcomes. Therefore, they advocate keeping the WIT below this threshold whenever possible (7).

The 'zero ischemia' (off-clamp) partial nephrectomy technique has been described as a means of minimising ischemic damage and preserving nephrons (8). Although the zero ischemia approach is theoretically ideal for preserving renal function, it presents technical challenges, including increased intraoperative blood loss, difficulty in tumour resection due to an obscured surgical field and an elevated risk of positive surgical margins (9). Therefore, the feasibility of this

technique depends largely on anatomical factors, such as the distance of the tumour from the centre of the kidney (C-index), as well as the surgeon's experience (10).

Currently, in the era of robotic surgery, it remains a matter of debate whether partial nephrectomy performed with zero ischemia provides a long-term functional advantage substantial enough to justify the increased bleeding risk when compared to the standard clamped ischemia approach (11,12). The aim of this study was to retrospectively evaluate and compare the perioperative, oncological, and long-term renal functional outcomes (via preoperative, first-day postoperative and first-year postoperative comparisons) of the zero ischemia and standard warm ischemia (on-clamp) approaches in patients who underwent robotic partial nephrectomy at our clinic.

MATERIALS AND METHODS

This retrospective cohort study was conducted following approval from the Clinical Research Ethics Committee of our institution (decision no. 20/11, date 22/12/2020), and in strict adherence to the principles of the World Medical Association's Declaration of Helsinki. Written informed consent for the surgical procedure and the anonymous use of clinical data for scientific research was obtained from all patients prior to the operation.

The medical records of 56 consecutive patients diagnosed with a renal mass and evaluated as anatomically and clinically suitable for partial nephrectomy were retrospectively reviewed. All patients underwent RPN by a single experienced surgical team in our clinic.

Baseline demographic characterisics (age, gender, and body mass index – BMI) and comorbidities (such as diabetes mellitus, hypertension, and coronary artery disease) were recorded during the patients' preoperative evaluation. The anatomical characteristics and surgical complexity of the tumours were evaluated using preoperative contrast-enhanced abdominal CT or MRI. Based on these images, we calculated the clinical tumour size and location, as well as the C-index (which reflects the distance of the tumour from the centre of the kidney) (13), and RENAL and PADUA nephrometry scores (14). Baseline renal function was determined using preoperative serum creatinine levels (mg/dL) and eGFR (ml/min/1.73 m^2), calculated using the abbreviated Modification of Diet in Renal Disease (MDRD) formula.

Patients were assigned to either the zero ischemia or standard warm ischemia approach based on the primary surgeon's preoperative anatomical assessment. A C-index threshold of 2.5 was used to stratify risk. The zero ischemia technique was prederred for predominantly peripheral tumours (C-index ≥ 2.5, classified as low risk of bleeding), as intraoperative bleeding could be more easily controlled without hilar clamping. Conversely, the standard on-clamp approach was favoured for more central and anatomically complex tumours (C-index <2.5, classified as high risk), to ensure a bloodless surgical field.

The patients were divided into two main groups based on the vascular clamping strategy applied during surgery:

The Zero Ischemia Group (n = 26): Patients in whom the renal artery or hilum was not clamped at any point during resection and whose renal blood flow was not interrupted. Surgical field vision and bleeding control in this group were achieved through adjusting the pneumoperitoneum pressure and using rapid, continuous renorrhaphy techniques.

Ischemia Group (n = 30): Patients in whom the renal artery and vein were temporarily clamped with a laparoscopic bulldog clamp during tumour resection and base suturing, with the procedure completed under standard warm ischemia.

All RPN procedures were performed using a transperitoneal approach with the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, California, USA).

We analysed perioperative data, including operation time, estimated blood loss (EBL), ischemia time, and length of hospital stay. Postoperative complications were evaluated using the Clavien-Dindo classification system. Oncological safety and efficacy were examined in terms of pathological tumour size, histological subtype, Fuhrman grade (for malignant cases), pathological stage, and surgical margin status.

To analyse perioperative and long-term changes in renal function, the serum creatinine and eGFR values of patients on the first postoperative day and at the postoperative first year were measured and compared with preoperative baseline values.

Statistical Analysis

The data obtained were analysed statistically using IBM SPSS Statistics software (version 25.0, Armonk, NY: IBM Corp.). Conformity to a normal distribution for the continuous variables was evaluated using visual methods (histograms and probability plots) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). As the data were not normally distributed, continuous variables were expressed as medians (minimum-maximum) and categorical variables as frequencies and percentages. The Mann-Whitney *U* test was used to compare continuous variables between the two independent groups (Zero Ischemia and Ischemia), and the Pearson Chi-square test or Fisher's exact test (when expected frequencies were low) was used to analyse categorical variables. The Wilcoxon signed-rank test was applied to examine sequential changes in preoperative, early postoperative, and first-year renal functions (creatinine and eGFR) within each group. A 2-sided $p < 0.05$ was considered statistically significant in all analyses.

RESULTS

A total of 56 patients who underwent RPN were included in the study. The patients were divided into two groups: zero ischemia (n = 26) and ischemia (n = 30). No significant differences were observed between the groups in terms of age, BMI, gender distribution, or comorbidities. However, a statistically significant difference was observed between the groups regarding tumour side ($p = 0.001$): right-sided tumours were more prevalent in the zero ischemia group (73%), whereas left-sided tumours predominated in the ischemia group (73%) (Table 1).

Clinical tumour size ($p = 0.308$), pathological tumour size ($p = 0.118$), malignant/benign tumour ratios ($p = 0.768$) and pathological stage distributions among malignant cases ($p = 0.159$) were similar in both groups. Furthermore, tumour complexity, as evaluated by RENAL ($p = 0.452$) and PADUA ($p = 0.230$) scores, showed no significant differences between the groups. However, the C-index score, which assesses the distance of the tumour from the centre of the kidney, was significantly higher in the zero ischemia group (median 3.1) than in the ischemia group (median 1.86) ($p = 0.001$). This finding indicates that tumours in the zero ischemia cohort were more peripherally located (Table 1).

In terms of perioperative data, the operation time was longer in the ischemia group (median 150 minutes) than in the zero ischemia group (median 130 minutes), but this difference was not statistically significant ($p = 0.062$). However, EBL was significantly higher in the zero ischemia group (median 300 ml) than in the ischemia group (median 100 ml) ($p < 0.001$). The length of hospital stay was also significantly longer in the zero ischemia cohort (median 4 days vs. 3 days, $p = 0.001$). Regarding oncological safety and surgical success, there were no significant differences between the two approaches in terms of positive surgical margin (PSM) rates ($p = 0.140$) or postoperative complication rates ($p = 0.494$). The two complications observed in the ischemia group were both classified as Clavien-Dindo Grade 2. Furthermore, direct comparison of the absolute change in eGFR (ΔeGFR) between the preoperative and first-year postoperative periods revealed a median decline of –1.25 ml/min/1.73m^2 in the zero ischemia group versus -4.75 ml/min/1.73m^2 in the warm ischemia group. However, this difference did not reach statistical significance ($p = 0.091$) (Table 1).

Preoperative creatinine ($p = 0.718$) and eGFR ($p = 0.980$) values were comparable between the groups. Within-group analyses evaluating changes in renal function over time revealed that both the zero ischemia and ischemia groups

demonstrated a statistically significant increase in creatinine levels in the early postoperative period compared to baseline values ($p = 0.005$ and $p = 0.001$, respectively) (Table 2).

Table 1. Comparison of the demographic, oncological and operative characteristics of patients undergoing robotic partial nephrectomy.

Variable	Zero Ischemia (n = 26)	Ischemia (>0 min) (n = 30)	p
Age (years)	56.5 (28 – 81)	53 (37 – 76)	0.444
Body Mass Index (BMI)	27.25 (21.5 – 34.2)	26.65 (20.5 – 41)	0.446
Gender - Male - Female	 17 (65.4%) 9 (34.6%)	 23 (76.7%) 7 (23.3%)	0.388
Comorbidities - DM - HT - CAD	 1 (3.8%) 9 (34.6%) 4 (15.4%)	 4 (13.3%) 10 (33.3%) 2 (6.7%)	 0.358 0.920 0.401
Ischemia time (min)	0	28 (14–31)	**<0.001**
Tumour Side - Left - Right	 7 (27%) 19 (73%)	 22 (73%) 8 (27%)	**0.001**
Clinical Tumour Size (cm)	3 (2 – 8.5)	4.05 (1.9 – 9)	0.308
Pathological Tumour Size (cm)	3 (1 – 10)	4.1 (2 – 7.2)	0.118
Tumour Type - Malignant - Benign	 19 (73.1%) 7 (26.9%)	 23 (76.7%) 7 (23.3%)	0.768
Tumour subtype - Clear - Papillary - Chromophobe - Benign	 12 (46.1%) 6 (23.1 %) 1 (3.8 %) 7 (27%)	 17 (56.7%) 6 (20%) 0 (0%) 7 (23.3%)	 0.474 0.284
Fuhrman grade - Grade 1 - Grade 2 - Grade 3	 4 (21.1%) 10 (52.6%) 5 (26.3%)	 6 (26.1%) 15 (65.2%) 2 (8.7 %)	 0.257
Pathological Stage (Malignant) - T1a - T1b - T2a - T3a	 18 (69.2%) 6 (23.2%) 2 (7.6%) 0 (0.0%)	 15 (50%) 13 (43.3%) 1 (3.3%) 1 (3.3%)	 0.159
RENAL Score	7 (4 – 10)	7 (4 – 10)	0.452
RENAL Risk Group - Low - Moderate - High	 12 (46.2%) 13 (50.0%) 1 (3.8%)	 11 (36.7%) 17 (56.7%) 2 (6.7%)	 0.731
PADUA Score	8 (6 – 11)	9 (6 – 12)	0.230
PADUA Risk Group - Low - Moderate - High	 9 (34.6%) 14 (53.8%) 3 (11.5%)	 9 (31.0%) 11 (37.9%) 9 (31.0%)	 0.201
C-index Score	3.1 (1.2 – 7.2)	1.86 (0.90 – 4.36)	**0.001**

C-index Risk Group - Low (≥2.5) - High (<2.5)	 17 (65.4%) 9 (34.6%)	 9 (30%) 21 (70%)	**0.015**
Operation Time (min)	130 (80 – 300)	150 (80 – 240)	0.062
Estimated Blood Loss (ml)	300 (30 – 1200)	100 (20 – 450)	**<0.001**
Surgical Margin - Negative - Positive	 19 (73.1%) 7 (26.9%)	 24 (80%) 6 (20%)	0.140
Complications	0 (0.0%)	2 (6.7%)	0.494
Hospitalisation (days)	4 (3 – 7)	3 (2 – 7)	**0.001**
Preoperative eGFR	82.05 (41.6 – 107.7)	81.5 (43 – 119)	0.980
First Year eGFR	83.5 (35.4 – 116.1)	76 (52 – 117)	0.275
eGFR Percent Change (%)	-1.70 (–28.4 – 27.5)	-4.90 (–25.7 – 23)	0.191
Absolute eGFR Change (ΔeGFR)	-1.25 (–26.1 – 24.3)	-4.75 (–19.8 – 9)	0.091
Preoperative Creatinine (mg/dL)	0.96 (0.61 – 1.69)	0.97 (0.67 – 1.88)	0.718
Postoperative Creatinine (mg/dL)	1.05 (0.66–1.83)	1.02 (0.88–1.67)	0.320
First Year Creatinine (mg/dL)	0.94 (0.60 – 1.94)	1.04 (0.68 – 1.51)	0.180

Note: Continuous variables are presented as the median (minimum-maximum) and categorical variables as frequencies (percentages). A *p*-value of less than 0.05 was considered statistically significant. The Mann-Whitney U test was used to compare continuous variables, while the Chi-square test or Fisher's exact test was used to compare categorical variables.
Abbreviations: BMI: Body Mass Index; DM: Diabetes Mellitus; HT: Hypertension; CAD: Coronary Artery Disease; eGFR: Estimated Glomerular Filtration Rate.

Table 2. Comparison of preoperative and postoperative renal functional outcomes within groups after robotic partial nephrectomy

Patient Group	Variable	Preoperative	Postoperative	p
Zero Ischemia (n = 26)	Preop. Cr. vs Postop. Cr.	0.96 (0.61 - 1.69)	1.06 (0.66 – 1.83)	**0.005**
	Preop. Cr. vs 1st Year Cr.	0.96 (0.61 - 1.69)	0.94 (0.60 – 1.94)	0.970
	Preop. eGFR vs 1st Year eGFR	82.05 (41.60 - 107.70)	83.50 (35.40 – 116.10)	0.970
Ischemia (>0 min) (n = 30)	Preop. Cr. vs Postop. Cr.	0.97 (0.67 - 1.88)	1.02 (0.88 – 1.67)	**0.001**
	Preop. Cr. vs 1st Year Cr.	0.97 (0.67 - 1.88)	1.04 (0.68 – 1.51)	**0.001**
	Preop. eGFR vs 1st Year eGFR	81.50 (43.0 - 119.0)	76.0 (52.0 – 117.0)	**0.001**

Note: Data are presented as median (minimum–maximum). The Wilcoxon signed-rank test was used to compare preoperative and postoperative measurements within each group. A *p*-value of less than 0.05 was considered statistically significant.
Abbreviations: Cr: Creatinine; eGFR: Estimated Glomerular Filtration Rate.

However, a critical distinction was observed between the two groups when long-term renal function (in the first year after surgery) was evaluated. In the zero ischemia group, first-year postoperative creatinine ($p = 0.970$) and first-year eGFR ($p = 0.970$) levels returned to preoperative baseline values, with no statistically significant loss in renal function. In contrast, in the ischemia group, the increase in creatinine ($p = 0.001$) and the decrease in eGFR ($p = 0.001$) were both statistically significant in the first postoperative year compared to the preoperative period, indicating deterioration in renal function persisting at one year (Figure 1).

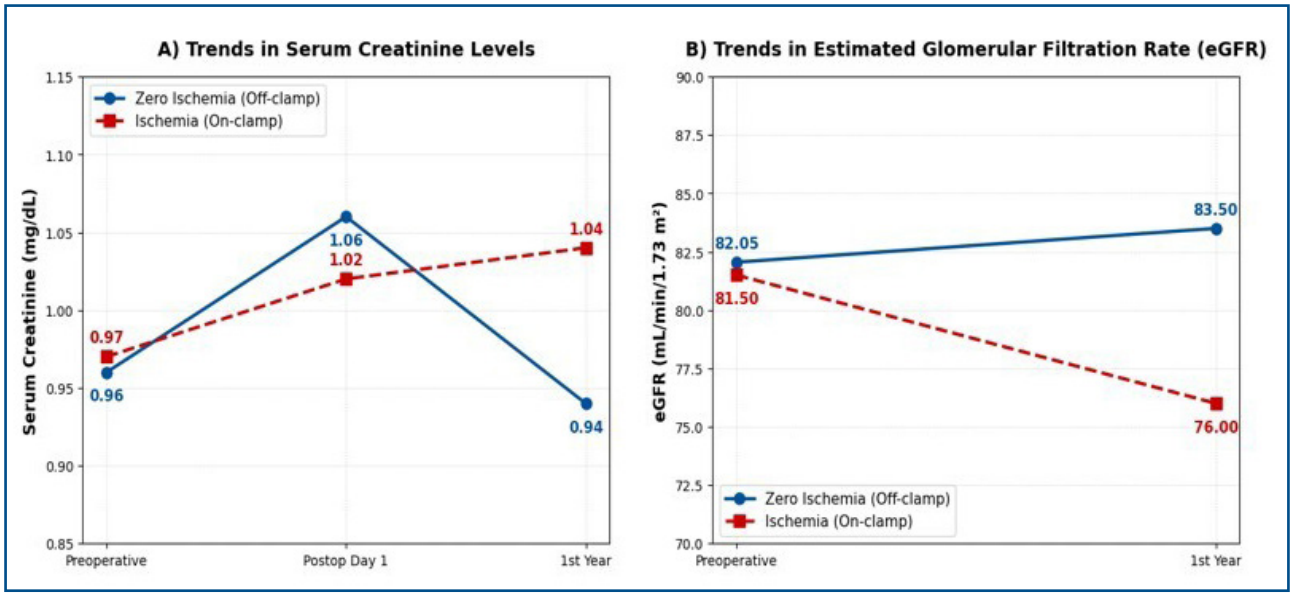


Figure 1. Trends in median serum creatinine and estimated glomerular filtration rate (eGFR) levels from the preoperative period to the first postoperative year. The zero ischemia group demonstrated a complete return to baseline function, whereas the ischemia group showed a persistent functional decline at one year.

DISCUSSION

In the present study, we compared the outcomes of zero and warm ischemia techniques (with the artery and vein clamped) in patients undergoing RPN. Our most significant finding is that, although renal function deteriorated in both groups during the early postoperative period, it recovered to preoperative baseline levels at the end of the first year in the zero ischemia group. In contrast, functional loss (a decline in eGFR and an increase in creatinine) persisting at one year was detected in the warm ischemia group. While the zero ischemia technique in RPN may offer short-term advantages, long-term evidence remains inconclusive, with most large-scale studies demonstrating no significant difference between limited warm ischemia and zero ischemia. Multicentre cohorts and systematic reviews report that, as warm ischemia time prolongs, the risk of early eGFR decline and acute kidney injury (AKI) increases. However, this difference largely disappears after 6–12 months (15–17). Although eGFR loss may be statistically lower in zero ischemia cases, it tends to diminish with extended follow-up and is generally clinically marginal (17,18). In patients with two functioning kidneys and good baseline renal function, no superior long-term functional advantage of zero ischemia has been established, particularly with a WIT of <20–25 minutes (15–17). Conversely, in patients with a solitary kidney or pre-existing chronic kidney disease (CKD), warm ischemia is more strongly associated with AKI, permanent eGFR decline and the development of new-onset CKD. Therefore, zero ischemia or a very short WIT is recommended wherever possible (19,20).

Systematic reviews have demonstrated that a WIT of more than 20–25 minutes (particularly more than 25–30 minutes) is associated with permanent functional loss (12,20,21). Rod et al. emphasised that, even when the amount of preserved parenchyma is controlled for, a WIT of >25 minutes correlates with the development of new-onset CKD and permanent eGFR decline (22). Furthermore, a 2025 meta-analysis reported that WIT exceeding 25–30 minutes can cause irreversible kidney damage and is associated with a significant decrease in eGFR (7). These findings may explain the eGFR decline that persisted at one year observed in our ischemia group in the first year (from 81.5 to 76.0). The median WIT in the on-clamp group was 28 minutes, slightly exceeding the widely accepted 20–25 minute safe threshold. Therefore, the observed renal functional decline is likely to be multifactorial, resulting from ischemia-reperfusion injury and the prolonged WIT. This longer WIT was unavoidable due to the higher anatomical complexity and central location of these tumours (lower C-index), which necessitated more demanding resection and

renorrhaphy. Although statistically significant, the magnitude of eGFR decline should be interpreted in the context of clinical relevance. The literature emphasises that zero ischemia PN protects nephrons from hypoxic ischemic and reperfusion injury, thereby minimising functional loss (20,21). This provides a robust biological and literature-based rationale for the recovery of renal function to baseline levels observed in the zero ischemia group in our study.

Furthermore, our study found that, while zero ischemia demonstrated comparable PSM rates, it slightly increased the EBL and length of hospital stay, as expected. However, this increase in EBL did not result in a significant difference in postoperative complication rates. Moreover, the bloody surgical field resulting from the absence of clamping makes the resection and renorrhaphy stages more technically challenging. Multicentre studies have found no significant differences between zero ischemia and warm ischemia RPN in terms of positive surgical margins, local recurrence and metastasis. Therefore, zero ischemia techniques are considered to be at least as oncologically safe as other methods (12,18,23). While some studies have reported increased bleeding, higher transfusion rates and longer hospital stays in the zero ischemia group (21,24), others have found no significant differences in EBL or length of stay (12,18,23). This heterogeneity in the literature may be attributed to variations in tumour complexity and surgeon experience. The PSM rates (26.9% in the zero ischemia and 20.0% in the ischemia group) were calculated for the whole cohort. Notably, only one benign case in each group had a PSM; the remainder were malignant. PSM was defined as tumour cells at the resected margin. These relatively high rates are primarily attributed to the surgical team's initial robotic learning curve and a deliberate nephron-sparing strategy that uses enucleation techniques.

The C-index quantifies the 'central-peripheral location' by calculating the ratio of the distance between the tumour centre and the kidney centre to the tumour radius. As the score increases, the tumour is located further from the kidney centre, indicating a more peripheral/superficial position (13). On the other hand, RENAL and PADUA are multivariate scoring systems that indicate overall tumour complexity by integrating multiple anatomical parameters, such as tumour size, exophytic/endophytic properties, proximity to the collecting system or renal sinus, and polar location (14). In our study, although tumour size and RENAL/PADUA scores did not differ between the groups, the significantly higher C-index score in the zero ischemia group (median 3.1 vs. 1.86) demonstrates that the tumours in this cohort were located closer to the renal periphery. Several studies have shown that bleeding management is less challenging for tumours situated farther from the sinus and that zero ischemia PN is more frequently preferred in these cases. The fact that the C-index reflects this distribution in our study is consistent with real-world surgical practice (14,25). Therefore, the C-index distribution, which supports a clamped approach for central tumours and an off-clamp approach for peripheral tumours, aligns with the current nephrometry literature and the original conceptual framework of the C-index. This demonstrates the rationale behind our surgical strategy (26,27).

Several limitations should be considered when evaluating the findings of our study. Firstly, the single-centre, retrospective design inherently limits the level of evidence, and the relatively small sample size may affect the generalizability of our results. Secondly, and most importantly, the lack of randomisation regarding the surgical approach introduces distinct selection bias. The significantly higher C-index in the zero ischemia group clearly shows that surgeons selected tumours that were located peripherally for the clampless approach, in order to minimise bleeding risks. This selection bias must be carefully considered when interpreting the functional outcomes, since the surgical difficulty and potential nephron loss were probably lower in the zero ischemia group. Thirdly, the evaluation of the protective effect on renal function is limited to one year after surgery. To fully elucidate the ultimate and permanent impact of this surgical strategy on renal reserve, prospective multicentre studies with larger cohorts and longer follow-up periods are required.

CONCLUSION

In conclusion, the zero ischemia approach to robotic partial nephrectomy may offer potential functional advantages, particularly in selected patients, in preserving renal function during the first year after surgery compared to the

standard warm-ischemia technique. Although clampless surgery may slightly increase intraoperative blood loss and lengthen the hospital stay, our findings suggest that this does not adversely affect the rates of perioperative complications and results in comparable positive surgical margin rates. For anatomically suitable, peripherally located small renal masses (high C-index), the zero ischemia technique could be considered a safe and effective alternative to prevent functional loss that persists at one year.

Acknowledgments: The authors would like to thank all the participants who contributed to this study.

Informed Consent: The requirement for study-specific informed consent was waived due to the retrospective design, but all patients provided standard written consent for surgery.

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

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

Ethical Approval: All procedures performed in this study were in accordance with the ethical standards of the institutional research committee (Approval No. 20/11; Date: December 22, 2020) and with the 1964 Helsinki Declaration.

Data Availability Statement: The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request.

Authorship Contributions: Concept and design: M.Ş., M.A.; Data Collection: M.T.O., Ş.K., H.A.D.; Data analysis and interpretation: Y.A., K.Y.; Manuscript writing and statistical analysis: Y.A.; Critical revision of the manuscript: Y.A., M.T.Ö.; Supervision: Y.A., M.T.Ö. All authors read and approved the final manuscript.

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):198–211. doi: 10.54233/endourolbull-1920320

Performing Extended Pelvic Lymph Node Dissection Before Prostatectomy was Associated with Lower Apical Positive Surgical Margin Rates During Robot-Assisted Radical Prostatectomy: A Single-Centre Retrospective Cohort Study

Robot Yardımlı Radikal Prostatektomi Sırasında Prostatektomi Öncesi Uygulanan Genişletilmiş Pelvik Lenf Nodu Diseksiyonu, Daha Düşük Apikal Pozitif Cerrahi Sınır Oranları Ile İlişkilidir: Tek Merkezli Retrospektif Kohort Çalışması

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ABSTRACT

Objective: Positive surgical margins remain clinically relevant after robot-assisted radical prostatectomy (RARP). Whether performing extended pelvic lymph node dissection (ePLND) before, rather than after, prostatectomy is associated with lower apical positive surgical margin (PSM) rates has not been evaluated with adjusted comparative data.

Materials and Methods: We performed a retrospective cohort study of 250 consecutive patients who underwent primary RARP with ePLND at a single tertiary centre. Patients were classified by operative sequence as ePLND-first (n = 121) or prostatectomy-first (n = 129). The primary multivariable analyses were conducted in the full 250-patient cohort with nerve-sparing intent coded as a 3-level categorical variable; a pre-specified subgroup analysis was conducted in the 188 patients undergoing any form of nerve-sparing surgery. The primary endpoint was apical PSM. Because apical PSM events were sparse, the adjusted analysis used Firth penalised logistic regression.

Results: Baseline characteristics were similar between groups. Apical PSM occurred in 6 of 121 patients (5.0%; 95% confidence interval [CI] 2.3% to 10.4%) in the ePLND-first group and 13 of 129 (10.1%; 95% CI 6.0% to 16.5%) in the prostatectomy-first group. In the primary multivariable analysis of the full 250-patient cohort, ePLND-first sequencing was associated with lower adjusted odds of apical PSM (adjusted OR 0.38; 95% CI 0.14 to 1.03; $p = 0.056$); in the pre-specified nerve-sparing subgroup (n = 188), the adjusted association was stronger (OR 0.19; 95% CI 0.04 to 0.97; $p = 0.046$; unadjusted 1.2% vs 8.8%, Fisher's exact $p = 0.023$). Total operative time was shorter in the ePLND-first group (195.2 vs 202.9 min; $p = 0.029$). Lymph node yield and major complication rates were similar between groups.

Conclusion: In this retrospective cohort, performing ePLND before prostatectomy was associated with directionally

Cite As: *Inkaya A, Gungor HS, Sisik NM, Topcu ME, Oksuz B, Sozen S, Beyatli M, Yurtseven CE, Esmeray A, Tahra A, Suçeken FY, Sobay R, Kucuk EV. Performing Extended Pelvic Lymph Node Dissection Before Prostatectomy was Associated with Lower Apical Positive Surgical Margin Rates During Robot-Assisted Radical Prostatectomy: A Single-Centre Retrospective Cohort Study. Endourol Bull. 2026;18(3):198–211.* https://doi.org/10.54233/endourolbull-1920320

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Received : April 1, 2026 ***Accepted*** : June 6, 2026

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lower adjusted odds of apical PSM during RARP in the full 250-patient cohort, with a stronger association in the pre-specified nerve-sparing subgroup analysis. For men undergoing nerve-sparing RARP with planned ePLND, sequence may represent a practical operative strategy associated with lower apical margin risk without an evident perioperative penalty.

Keywords: robot-assisted radical prostatectomy, extended pelvic lymph node dissection, positive apical surgical margin, prostate cancer

ÖZET

Amaç: Robot yardımlı radikal prostatektomi (RARP) sonrasında pozitif cerrahi sınırlar klinik önemini korumaktadır. Genişletilmiş pelvik lenf nodu diseksiyonunun (ePLND) prostatektomiden önce yapılmasının, daha düşük apikal pozitif cerrahi sınır oranları ile ilişkili olup olmadığı karşılaştırmalı verilerle değerlendirilmemiştir.

Gereç ve Yöntemler: Ocak 2022 ile Ocak 2025 tarihleri arasında tek bir üçüncü basamak merkezde primer RARP ve ePLND uygulanan ardışık 250 hastayı içeren retrospektif bir kohort çalışması yapıldı. Hastalar önce ePLND sonra prostatektomi (n = 121) ve önce prostatektomi sonra ePLND (n = 129) yapılanlar olmak üzere 2 gruba ayrıldı. Birincil çok değişkenli analizler tüm 250 hastalık kohortta, sinir koruma niyetinin üç düzeyli kategorik değişken (yok, tek taraflı, iki taraflı) olarak kodlandığı modelle gerçekleştirildi; herhangi bir sinir koruma uygulanan 188 hastada önceden belirlenmiş bir alt-grup analizi yapıldı. Birincil sonlanım noktası apikal pozitif cerrahi sınırdı. Apikal pozitif cerrahi sınır olayları az olduğu için düzeltilmiş analizde Firth cezalandırılmış lojistik regresyon kullanıldı.

Bulgular: Gruplar başlangıç özellikleri açısından benzerdi. Apikal pozitif cerrahi sınır, önce ePLND yapılan 121 hastanın 6'sında (%5,0; %95 güven aralığı [GA] %2,3-%10,4), önce prostatektomi yapılan 129 hastanın ise 13'ünde (%10,1; %95 GA %6.0-%16,5) saptandı. Tam 250 hastalık kohortta birincil çok değişkenli analizde ePLND'nin prostatektomiden önce yapılması yönsel olarak daha düşük apikal pozitif cerrahi sınır olasılığı ile ilişkili bulundu (OR 0,38; %95 GA 0,14–1,03; $p = 0,056$); önceden belirlenmiş sinir koruma alt-grup analizinde ilişki daha güçlüydü (OR 0,19; %95 GA 0,04–0,97; $p = 0,046$; düzeltilmemiş 1/86 vs 9/102 = %1,2 vs %8,8, Fisher kesin $p = 0,023$). Toplam ameliyat süresi önce ePLND yapılan grupta daha kısaydı (195,2'ye karşı 202,9 dakika; $p = 0,029$). Lenf nodu sayısı ve majör komplikasyon oranları gruplar arasında benzerdi.

Sonuçlar: Bu retrospektif kohortta, ePLND'nin prostatektomiden önce yapılması, RARP sırasında daha düşük apikal pozitif cerrahi sınır olasılığı ile yönsel olarak ilişkili bulundu; sinyal sinir koruma yapılan önceden belirlenmiş alt-grupta daha güçlüydü. Sinir koruma uygulanan ve ePLND planlanan RARP olgularında, lenf nodu diseksiyonunun prostatektomiden önce yapılması, belirgin bir perioperatif dezavantaj oluşturmadan daha düşük apikal cerrahi sınır riski ile birlikte pratik bir teknik tercih olabilir.

Anahtar Kelimeler: robot yardımlı radikal prostatektomi, genişletilmiş pelvik lenf nodu diseksiyonu, pozitif apikal cerrahi sınır, prostat kanseri

INTRODUCTION

Robot-assisted radical prostatectomy (RARP) is a standard surgical treatment for localised prostate cancer (1). Positive surgical margins remain clinically relevant after RARP because they are associated with biochemical recurrence and may alter the use of adjuvant or salvage therapy (2–6). Site-specific patterns vary across series, but the apex is repeatedly among the most common locations of margin positivity (2,4,5).

Extended pelvic lymph node dissection (ePLND) remains the recommended nodal template when lymph node dissection is undertaken at radical prostatectomy (7). Williams and colleagues described performing ePLND before the prostatectomy to improve exposure of the deep hypogastric planes during RARP (8). That rationale is plausible. Other technical modifications that improve visualisation of the apex, including the puboprostatic open-collar

technique and synchronous retro-apical urethral transection, have been associated with lower apical PSM rates (9,10). The same principle underlies detailed descriptions of apical dissection in robotic prostatectomy (11). However, published reports on ePLND sequencing have been primarily technical or descriptive, not adjusted comparisons of oncological margin outcomes (8,12).

It therefore remains unknown whether performing ePLND before rather than after prostatectomy during RARP is associated with lower apical PSM rates. We used data from 250 consecutive patients treated at a single tertiary centre to compare apical PSM rates between ePLND-first and prostatectomy-first sequencing, and to evaluate differences in overall PSM, operative efficiency, nodal yield, complications, and early biochemical recurrence.

MATERIALS AND METHODS

Study design and cohort

We conducted a retrospective cohort study at Umraniye Training and Research Hospital, Istanbul, Türkiye. Between January 2022 and January 2025, 932 patients underwent radical prostatectomy. After exclusion of 12 patients treated with an open approach, 920 patients who underwent RARP were screened. Of these, 323 underwent RARP with ePLND and were assessed for eligibility. We included patients who underwent primary RARP with ePLND during the study period. We excluded salvage RARP (n = 2), prior neoadjuvant androgen deprivation therapy (n = 10), clinically node-positive disease (cN1; n = 18), conversion to open surgery (n = 2), non-adenocarcinoma histology (n = 1), and cases with incomplete data (n = 40): 30 patients lacked postoperative follow-up data and 10 lacked preoperative biopsy results. The final analytic cohort comprised 250 patients (Figure 1). Of the 250 patients, 188 underwent some form of nerve-sparing surgery (unilateral or bilateral) and were analysed as a pre-specified subgroup in addition to the primary full-cohort analysis. The study was approved by the Scientific Research Ethic Committee of Umraniye Training and Research Hospital, Istanbul, Türkiye (IRB-2025-470, Date: December 18, 2025).

Exposure definition

Patients were classified according to operative sequence. In the ePLND-first group (n = 121), bilateral ePLND was completed before prostatectomy. In the prostatectomy-first group (n = 129), prostatectomy was completed before lymph node dissection. The sequence reflected surgeon preference during the study period. Five surgeons performed all procedures. The study was approved by the institutional review board of Umraniye Training and Research Hospital (approval number: IRB-2025–470).

Surgical technique

All procedures were performed using the da Vinci Xi robotic platform (Intuitive Surgical, Sunnyvale, CA, USA). The ePLND template included the obturator, external iliac, internal iliac, and common iliac nodal packets bilaterally, consistent with current guideline-based extended dissection (7). Surgical approach (Retzius-sparing or standard anterior) and nerve-sparing strategy were determined by the operating surgeon on the basis of disease characteristics and intraoperative findings.

Outcomes

The primary endpoint was apical PSM, defined as tumour cells extending to the inked apical margin on final pathology. Secondary endpoints were overall PSM, site-specific margin rates, total operative time, console time, ePLND time, estimated blood loss, length of stay, catheter duration, lymph node yield, major complications within 90 days (Clavien-Dindo grade III or higher), symptomatic lymphocele, 90-day readmission, and biochemical recurrence (BCR). BCR was defined as two consecutive postoperative prostate-specific antigen values of 0.2 ng/mL or higher. Pathological reporting followed the 2014 International Society of Urological Pathology consensus recommendations (13).

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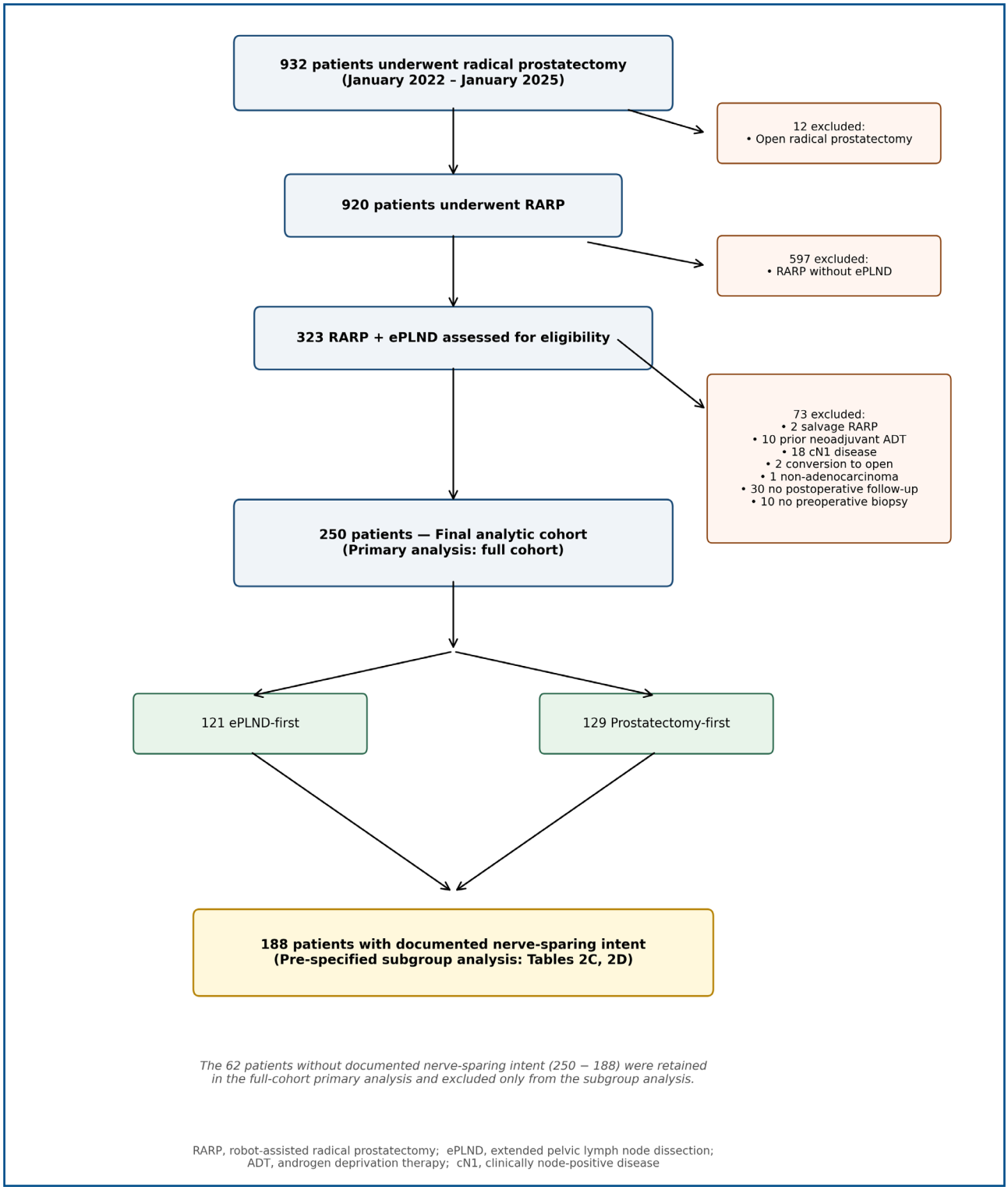


Figure 1. STROBE flow diagram of patient selection. Of 932 patients who underwent radical prostatectomy during the study period, 250 met all eligibility criteria and constituted the primary analytic cohort (full-cohort multivariable analysis: Tables 2A and 2B). Within this cohort, the 188 patients with documented bilateral or unilateral nerve-sparing intent comprised a pre-specified subgroup for the secondary analysis (Tables 2C and 2D); the 62 patients without nerve-sparing intent were retained in the full cohort and excluded only from the subgroup analysis. ePLND, extended pelvic lymph node dissection; RARP, robot-assisted radical prostatectomy; ADT, androgen deprivation therapy; PSM, positive surgical margin.

Statistical Analysis

Continuous variables are reported as mean standard deviation (SD) when approximately normally distributed and as median (interquartile range [IQR]) otherwise. Group comparisons used Welch's t-test or the Mann-Whitney *U* test for continuous variables, and the Chi-square test or Fisher's exact test for categorical variables. Proportions are reported with Wilson 95% confidence intervals (CIs), and absolute differences with Newcombe-Wilson 95% CIs.

All seven pre-specified covariates were entered simultaneously into a single multivariable model. Variable selection was specified a priori on clinical and anatomical grounds; no data-driven selection (e.g., stepwise or backward elimination) was applied. The univariable estimates presented alongside the multivariable results in Table 2 are reported for transparency, in line with STROBE recommendations, and were not used to select variables for the multivariable model. The primary adjusted analysis used Firth penalised logistic regression because apical PSM events were sparse relative to the number of candidate covariates. Firth penalisation reduces small-sample bias and addresses separation problems in logistic regression (14). Pre-specified covariates were operative sequence, cumulative surgeon experience, surgical approach, nerve sparing intent, prostate volume, biopsy Grade Group, and clinical T stage. We did not include postoperative pathological variables in the primary model because they may lie on the causal pathway between operative technique and margin status. For overall PSM, we used standard logistic regression with the same covariate set. A sensitivity analysis replaced clinical T stage with NCCN risk group to reduce concern about collinearity. The primary multivariable analyses were estimated in the full 250-patient cohort (19 apical PSM events; 44 overall PSM events) with nerve-sparing intent coded as a 3-level categorical variable (none, unilateral, bilateral; none as reference); the binary versus 3-level specification was compared by likelihood ratio testing, which favoured the 3-level coding ($p = 0.048$). A pre-specified subgroup analysis examined the 188 patients undergoing any form of nerve-sparing surgery (10 apical PSM events; 30 overall PSM events), motivated by the mechanistic basis of our hypothesis. All tests were 2-sided, and p values < 0.05 were considered statistically significant. Analyses were performed in Python 3.10 with NumPy 1.24 and custom routines implementing the Firth penalised likelihood with step-halving convergence control.

RESULTS

Baseline Characteristics

Baseline characteristics were generally similar between groups, with the exception of clinical T stage distribution (Table 1). Mean age was 65.5 ± 5.9 years in the ePLND-first group and 66.0 ± 5.8 years in the prostatectomy-first group ($p = 0.503$). Median preoperative PSA was 8.3 ng/mL (IQR 5.3–12.1) and 9.1 ng/mL (IQR 5.6–12.8), respectively ($p = 0.246$). Prostate volume, body mass index, Charlson comorbidity index, Briganti score, NCCN risk group, pathological T stage, and surgical approach were similar between groups. Clinical T stage distribution showed a borderline difference (overall $p = 0.055$): cT1c disease was more common in the ePLND-first group (46.3% vs 30.2%), whereas locally advanced disease was more common in the prostatectomy-first group (cT2c 19.4% vs 14.9%; cT3a 12.4% vs 8.3%; cT3b 7.0% vs 1.7%). Clinical T stage was included as an ordinal covariate in all multivariable models. The distribution of nerve-sparing intent (none, unilateral, bilateral) was similar between groups (overall $p = 0.265$; Table 1).

Apical Positive Surgical Margins

Apical PSM was less frequent in the ePLND-first group. The event rate was 6 of 121 patients (5.0%; 95% CI 2.3% to 10.4%) in the ePLND-first group and 13 of 129 (10.1%; 95% CI 6.0% to 16.5%) in the prostatectomy-first group ($p = 0.155$). The absolute risk difference was –5.1 percentage points (95% CI –12.1% to 1.7%).

In the primary multivariable analysis of the full 250-patient cohort, ePLND-first sequencing was associated with directionally lower adjusted odds of apical PSM (adjusted OR 0.38; 95% CI 0.14 to 1.03; $p = 0.056$; Table 2A and Figure 2). In the *p*re-specified subgroup analysis restricted to the 188 patients undergoing nerve-sparing surgery, apical

PSM occurred in 1 of 86 ePLND-first patients (1.2%) and 9 of 102 prostatectomy-first patients (8.8%; Fisher's exact p = 0.023), and the adjusted association was stronger (adjusted OR 0.19; 95% CI 0.04 to 0.97; $p = 0.046$; Table 2C). In a sensitivity analysis that replaced clinical T stage with NCCN risk group, the full-cohort point estimate was attenuated but directionally consistent (adjusted OR 0.44; 95% CI 0.17 to 1.16; $p = 0.098$). Within the nerve-sparing subgroup, the sensitivity estimate that replaced clinical T stage with NCCN risk group was similar to the primary subgroup result (adjusted OR 0.20; 95% CI 0.04 to 1.02; $p = 0.052$).

Table 1. Baseline Demographics and Clinical Characteristics

Variable	ePLND-first (n = 121)	Prostatectomy-first (n = 129)	p
Age, years, mean ± SD	65.5 ± 5.9	66.0 ± 5.8	0.503
BMI, kg/m^2, mean ± SD	28.2 ± 3.5	28.1 ± 3.4	0.751
PSA, ng/mL, median (IQR)	8.3 (5.3–12.1)	9.1 (5.6–12.8)	0.246
Prostate volume, mL, mean ± SD	44.5 ± 13.6	45.4 ± 12.3	0.612
Briganti score, %, mean ± SD	20.0 ± 9.3	20.6 ± 9.0	0.584
CCI, median (IQR)	1 (0–2)	1 (0–2)	0.196
Surgeon prior cases, median (IQR)	499 (228–829)	387 (210–715)	0.146
Clinical T stage, n (%)			0.055
cT1c	56 (46.3)	39 (30.2)	
cT2a	15 (12.4)	21 (16.3)	
cT2b	20 (16.5)	19 (14.7)	
cT2c	18 (14.9)	25 (19.4)	
cT3a	10 (8.3)	16 (12.4)	
cT3b	2 (1.7)	9 (7.0)	
Biopsy Grade Group, n (%)			0.563
1	12 (9.9)	10 (7.8)	
2	34 (28.1)	43 (33.3)	
3	31 (25.6)	39 (30.2)	
4	29 (24.0)	27 (20.9)	
5	15 (12.4)	10 (7.8)	
NCCN risk group, n (%)			0.759
Favorable intermediate	14 (11.6)	16 (12.4)	
Unfavorable intermediate	38 (31.4)	35 (27.1)	
High	69 (57.0)	78 (60.5)	
Approach, n (%)			0.570
Standard anterior	95 (78.5)	106 (82.2)	
Retzius-sparing	26 (21.5)	23 (17.8)	
Nerve-sparing intent, n (%)			0.265
None	35 (28.9)	27 (20.9)	
Unilateral	33 (27.3)	34 (26.4)	
Bilateral	53 (43.8)	68 (52.7)	
Pathological T stage, n (%)			0.926
pT2	74 (61.2)	77 (59.7)	
pT3a	33 (27.3)	35 (27.1)	
pT3b	14 (11.6)	17 (13.2)	

Abbreviations: BMI, body mass index; CCI, Charlson comorbidity index; IQR, interquartile range; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen; SD, standard deviation.

Table 2. Univariable and Multivariable Regression Analyses for Positive Surgical Margins

A. Primary analysis: Apical positive surgical margin in the full 250-patient cohort (19 events)

Variable	Univariable		Multivariable (Firth)	
	OR (95% CI)	p	OR (95% CI)	p
ePLND-first (vs Prostatectomy-first)	0.49 (0.18–1.29)	0.146	0.38 (0.14–1.03)	0.056
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.054	1.00 (1.00–1.00)	0.105
Retzius-sparing (vs Standard)	1.60 (0.56–4.53)	0.378	1.50 (0.53–4.27)	0.446
Unilateral nerve sparing (vs None)	0.55 (0.17–1.82)	0.329	0.33 (0.09–1.21)	0.094
Bilateral nerve sparing (vs None)	0.62 (0.24–1.58)	0.314	0.34 (0.12–0.99)	0.048
Prostate volume (per mL)	0.99 (0.96–1.03)	0.713	1.00 (0.97–1.04)	0.984
Biopsy Grade Group (per unit)	1.05 (0.70–1.58)	0.799	0.97 (0.65–1.46)	0.884
Clinical T stage (ordinal)	0.89 (0.65–1.20)	0.440	0.81 (0.59–1.11)	0.188

B. Primary analysis: Overall positive surgical margin in the full 250-patient cohort (44 events)

Variable	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
ePLND-first (vs Prostatectomy-first)	0.69 (0.36–1.34)	0.275	0.62 (0.31–1.23)	0.170
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.323	1.00 (1.00–1.00)	0.602
Retzius-sparing (vs Standard)	1.98 (0.94–4.15)	0.071	1.94 (0.91–4.17)	0.088
Unilateral nerve sparing (vs None)	1.03 (0.50–2.14)	0.938	0.75 (0.30–1.86)	0.528
Bilateral nerve sparing (vs None)	0.69 (0.36–1.34)	0.275	0.58 (0.25–1.35)	0.206
Prostate volume (per mL)	1.01 (0.98–1.03)	0.539	1.01 (0.98–1.04)	0.496
Biopsy Grade Group (per unit)	1.13 (0.85–1.50)	0.409	1.09 (0.80–1.47)	0.591
Clinical T stage (ordinal)	0.98 (0.80–1.21)	0.854	0.93 (0.75–1.16)	0.537

C. Pre-specified nerve-sparing subgroup analysis: Apical positive surgical margin (n = 188; 10 events)

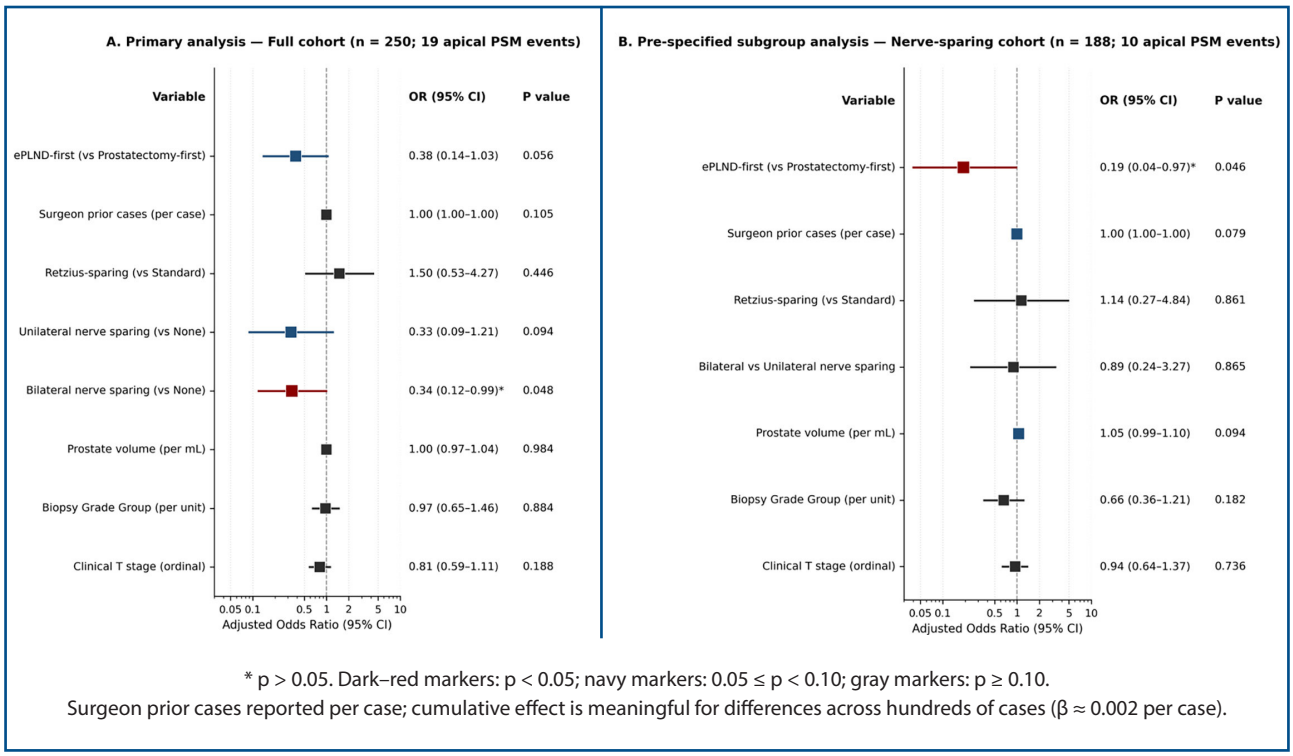
Variable	Univariable		Multivariable (Firth)	
	OR (95% CI)	P	OR (95% CI)	P
ePLND-first (vs Prostatectomy-first)	0.17 (0.03–1.00)	0.050	**0.19 (0.04–0.97)**	**0.046**
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.052	1.00 (1.00–1.00)	0.079
Retzius-sparing (vs Standard)	1.28 (0.29–5.59)	0.745	1.14 (0.27–4.84)	0.861
Bilateral vs Unilateral nerve sparing	1.21 (0.33–4.49)	0.779	0.89 (0.24–3.27)	0.865
Prostate volume (per mL)	1.04 (0.99–1.09)	0.143	1.05 (0.99–1.10)	0.094
Biopsy Grade Group (per unit)	0.69 (0.38–1.27)	0.236	0.66 (0.36–1.21)	0.182
Clinical T stage (ordinal)	1.00 (0.68–1.47)	0.985	0.94 (0.64–1.37)	0.736

D. Pre-specified nerve-sparing subgroup analysis: Overall positive surgical margin (n = 188; 30 events)

Variable	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
ePLND-first (vs Prostatectomy-first)	0.45 (0.19–1.05)	0.063	0.46 (0.19–1.10)	0.081
Surgeon prior cases (per case)	1.00 (1.00–1.00)	0.193	1.00 (1.00–1.00)	0.350
Retzius-sparing (vs Standard)	**2.66 (1.11–6.36)**	**0.028**	**2.60 (1.05–6.45)**	**0.040**
Bilateral vs Unilateral nerve sparing	0.80 (0.36–1.78)	0.587	0.72 (0.31–1.69)	0.454
Prostate volume (per mL)	1.02 (0.99–1.05)	0.296	1.01 (0.98–1.05)	0.461
Biopsy Grade Group (per unit)	1.00 (0.69–1.44)	0.986	0.94 (0.64–1.38)	0.749
Clinical T stage (ordinal)	1.05 (0.82–1.34)	0.692	0.99 (0.76–1.27)	0.922

Abbreviations: CI, confidence interval; ePLND, extended pelvic lymph node dissection; OR, odds ratio; PSM, positive surgical margin. Panels A and B report the primary analyses estimated on the full 250-patient cohort (19 apical and 44 overall PSM events).

Panels C and D report pre-specified subgroup analyses estimated on the 188 patients undergoing any form of nerve-sparing surgery (10 apical and 30 overall PSM events). The univariable column reports each variable's unadjusted association with the outcome. The multivariable column reports adjusted estimates from a single model in which all seven pre-specified covariates were entered simultaneously. In each panel, the apical PSM model used Firth penalised logistic regression because of sparse events; the overall PSM model used standard logistic regression. Bold indicates $p < 0.05$.



* p > 0.05. Dark–red markers: p < 0.05; navy markers: 0.05 ≤ p < 0.10; gray markers: p ≥ 0.10.
Surgeon prior cases reported per case; cumulative effect is meaningful for differences across hundreds of cases (β ≈ 0.002 per case).

Figure 2. Forest plot of multivariable regression analyses for variables associated with apical positive surgical margin. (A) Primary analysis in the full 250-patient cohort (19 apical PSM events) with nerve-sparing intent coded as a 3-level categorical variable (none, unilateral, bilateral; none as reference). (B) Pre-specified subgroup analysis in the 188 patients undergoing any form of nerve-sparing surgery (10 apical PSM events) with nerve sparing coded as bilateral versus unilateral. Square markers represent adjusted odds ratio point estimates; horizontal bars denote 95% confidence intervals. The vertical reference line indicates an odds ratio of 1.0. Dark-red markers: $p < 0.05$; navy markers: $0.05 \leq p < 0.10$; gray markers: $p \geq 0.10$. Both analyses used Firth penalised maximum likelihood estimation.

Overall Positive Surgical Margins

Overall PSM was numerically lower in the ePLND-first group, but the difference was imprecise. Overall PSM occurred in 18 of 121 patients (14.9%; 95% CI 9.6% to 22.3%) in the ePLND-first group and 26 of 129 (20.2%; 95% CI 14.1% to 27.9%) in the prostatectomy-first group ($p = 0.320$). The absolute difference was −5.3 percentage points (95% CI −14.6% to 4.3%).

In the primary multivariable analysis of the full 250-patient cohort, ePLND-first sequencing was directionally associated with lower overall PSM but did not reach statistical significance (adjusted OR 0.62; 95% CI 0.31 to 1.23; $p = 0.170$; Table 2B). Retzius-sparing approach was associated with borderline higher overall PSM (adjusted OR 1.94; 95% CI 0.91 to 4.17; $p = 0.088$). In the pre-specified nerve-sparing subgroup, ePLND-first sequencing showed a similar directional association (adjusted OR 0.46; 95% CI 0.19 to 1.10; $p = 0.081$; Table 2D), and Retzius-sparing was significantly associated with higher overall PSM (adjusted OR 2.60; 95% CI 1.05 to 6.45; $p = 0.040$). Site-specific PSM rates outside the apex were low and similar between groups (Figure 3).

Perioperative Outcomes

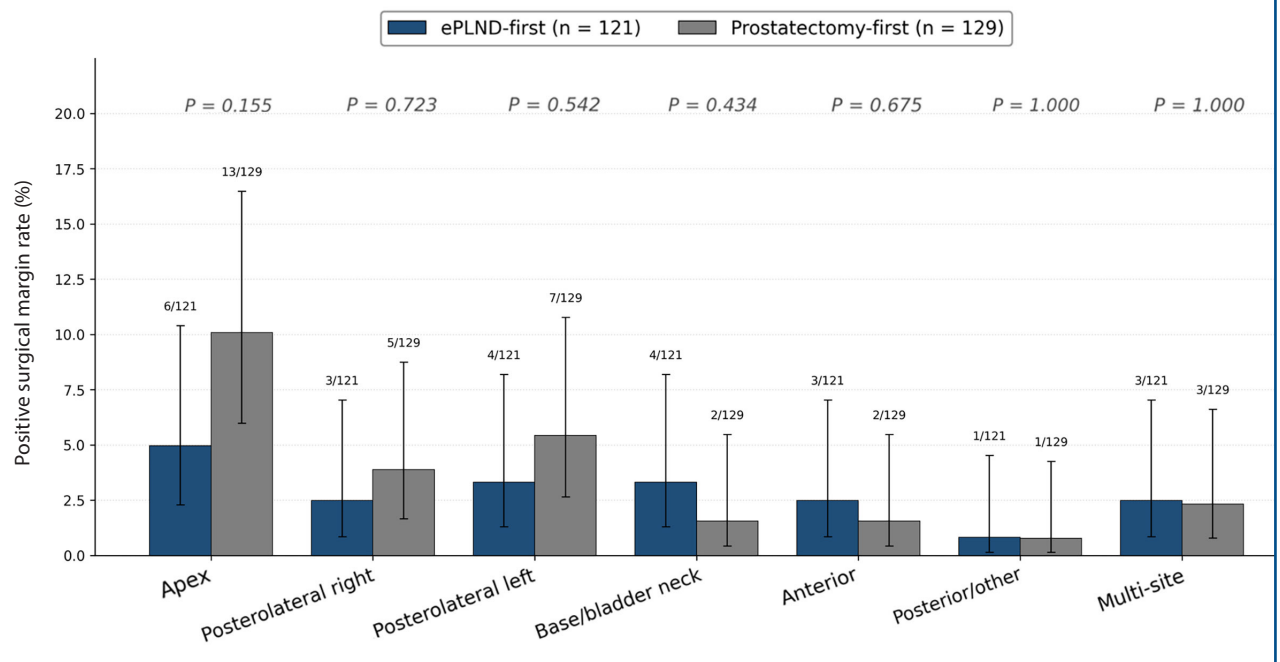
Operative efficiency favoured the ePLND-first sequence (Table 3). Mean total operative time was 195.2 +/- 27.4 minutes in the ePLND-first group and 202.9 +/- 28.2 minutes in the prostatectomy-first group, a mean difference of −7.7 minutes (95% CI −14.7 to −0.8; $p = 0.029$). Console time was also shorter (153.4 vs 161.4 minutes; $p = 0.024$). The ePLND component itself took less time when performed first (42.3 +/- 9.3 vs 46.5 +/- 9.2 minutes; $p < 0.001$).

Estimated blood loss, length of stay, and lymph node yield were similar between groups. Catheter duration differed by 0.4 days (8.5 +/- 1.3 vs 8.1 +/- 1.4 days; $p = 0.045$), a finding of marginal statistical significance and doubtful clinical importance.

Complications and Biochemical Recurrence

Complication rates were similar. Major complications within 90 days occurred in 4 of 121 patients (3.3%) in the ePLND-first group and 6 of 129 (4.7%) in the prostatectomy-first group ($p = 0.750$). Symptomatic lymphocele rates were nearly identical (7.4% vs 7.0%; $p = 1,000$), and 90-day readmission rates did not differ significantly (9.1% vs 5.4%; $p = 0.330$).

Biochemical recurrence was less frequent in the ePLND-first group in unadjusted analysis: 2 of 121 patients (1.7%; 95% CI 0.5% to 5.8%) versus 12 of 129 (9.3%; 95% CI 5.4% to 15.6%; $p = 0.011$). Mean follow-up was similar between groups (28.6 +/- 9.6 vs 27.1 +/- 10.2 months; $p = 0.219$).



Error bars represent Wilson 95% confidence intervals.
Number above bars are even counts (n/N). p-values from Fisher exact tests. * p < 0.05.

Figure 3. Site-specific positive surgical margin rates by surgical sequence group. Bars represent the proportion of patients with positive surgical margins at each anatomical site; error bars denote Wilson score 95% confidence intervals. Numbers above bars indicate event counts. The apex was the most common site of margin positivity in both groups, with a numerically lower rate in the ePLND-first group (5.0% vs 10.1%). Fisher's exact test P values: apex 0.155, posterolateral right 0.723, posterolateral left 0.542, base/bladder neck 0.434, anterior 0.675, posterior other 1,000, multi-site 1,000.

Table 3. Perioperative and Oncological Outcomes

Outcome	ePLND-first (n = 121)	Prostatectomy-first (n = 129)	p
Total operative time, min, mean ± SD	195.2 ± 27.4	202.9 ± 28.2	**0.029**
Console time, min, mean ± SD	153.4 ± 27.4	161.4 ± 28.2	**0.024**
ePLND time, min, mean ± SD	42.3 ± 9.3	46.5 ± 9.2	**<0.001**
EBL, mL, median (IQR)	161 (108–216)	166 (115–226)	0.345
LN yield, median (IQR)	22 (19–25)	22 (19–24)	0.363
LOS, days, median (IQR)	2 (2–3)	2 (2–3)	0.354
Catheter days, mean ± SD	8.5 ± 1.3	8.1 ± 1.4	**0.045**
Apical PSM, n (%)	6 (5.0)	13 (10.1)	0.155
Overall PSM, n (%)	18 (14.9)	26 (20.2)	0.320
EPE, n (%)	47 (38.8)	52 (40.3)	0.897
SVI, n (%)	14 (11.6)	17 (13.2)	0.848
Major complications, n (%)	4 (3.3)	6 (4.7)	0.750
Symptomatic lymphocele, n (%)	9 (7.4)	9 (7.0)	1.000
90-day readmission, n (%)	11 (9.1)	7 (5.4)	0.330
BCR, n (%)	2 (1.7)	12 (9.3)	**0.011**
Follow-up, months, mean ± SD	28.6 ± 9.6	27.1 ± 10.2	0.219

Abbreviations: BCR, biochemical recurrence; EBL, estimated blood loss; EPE, extraprostatic extension; ePLND, extended pelvic lymph node dissection; IQR, interquartile range; LN, lymph node; LOS, length of stay; PSM, positive surgical margin; SD, standard deviation; SVI, seminal vesicle invasion. Bold indicates $p < 0.05$.

DISCUSSION

In this cohort, performing ePLND before prostatectomy was associated with directionally lower adjusted odds of apical PSM during RARP (adjusted OR 0.38; 95% CI 0.14 to 1.03; $p = 0.056$ in the full 250-patient cohort), with a stronger signal in the pre-specified nerve-sparing subgroup (adjusted OR 0.19; 95% CI 0.04 to 0.97; $p = 0.046$; Fisher's exact 1/86 vs 9/102, $p = 0.023$). The ePLND-first sequence was also associated with shorter operative time, without an evident penalty in lymph node yield or perioperative safety.

Williams and colleagues described the ePLND-first sequence as a technical approach that clears the pelvic sidewall before the prostatectomy begins (8). Our findings extend that description by providing an adjusted comparison of sequence and apical margin status. Jarzemski and colleagues reported a combined laparoscopic approach to radical prostatectomy and lymphadenectomy, but did not compare sequence directly (12). The present study therefore addresses a specific question that, to our knowledge, had not previously been examined with multivariable adjustment.

The most plausible explanation is anatomical. Apical dissection is one of the most exacting steps in robotic prostatectomy (11). Prior technical modifications that improve exposure of the apical plane have been associated with lower apical margin rates. These include the puboprostatic open-collar technique and synchronous retro-apical urethral transection (9,10). ePLND-first sequencing may operate through the same principle. By removing the nodal packets before apical dissection, the surgeon may enter the deepest part of the operation with a cleaner field and less tissue crowding.

The association between operative sequence and apical PSM appeared to be concentrated in patients undergoing nerve-sparing surgery. Among the 188 patients with documented nerve-sparing intent, apical PSM occurred in 1

of 86 ePLND-first cases (1.2%) and 9 of 102 prostatectomy-first cases (8.8%; Fisher's exact p = 0.023). Among the 62 patients without nerve-sparing intent, apical PSM rates were nearly identical between sequence groups (5 of 35 versus 4 of 27; 14.3% versus 14.8%). This pattern is consistent with the proposed anatomical mechanism: in nerve-sparing cases, apical dissection follows a delicate plane where exposure quality may be most influential, whereas in non-nerve-sparing cases the apical dissection plane is intentionally wider for margin clearance and may be less dependent on pelvic sidewall exposure. The pattern may also reflect random variation given the sparse event count. Within the primary multivariable model, bilateral nerve sparing relative to no nerve sparing was itself independently associated with lower apical PSM (adjusted OR 0.34; 95% CI 0.12 to 0.99; $p = 0.048$; Table 2A). This pattern reflects disease selection in nerve-sparing cases: compared with patients undergoing nerve-sparing surgery, the non-nerve-sparing subgroup had a higher proportion of biopsy Grade Group ≥4 disease (45.2% vs 28.2%; $p = 0.020$), which ex*p*lains part of the higher absolute apical PSM rate in non-nerve-sparing patients (14.5% vs 5.3%; Fisher's exact p = 0.026). The multivariable model adjusts for biopsy Grade Group, clinical T stage, prostate volume, and surgeon cumulative experience, but residual confounding from unmeasured anatomic features that may inform the nerve-sparing decision (for example, MRI tumour location, capsular contact, or apical lesion proximity) cannot be excluded.

Surgical margin length carries independent prognostic weight for biochemical recurrence, with a recently described 3.5 mm cut-off from a cohort at our institution (15). Among the 19 patients with an apical positive margin in the present study, the mean apical margin length was similar between sequence groups (2.85 mm in the ePLND-first group versus 2.87 mm in the prostatectomy-first group); margin length above the 3.5 mm threshold was present in 1 of 6 apical PSMs in the ePLND-first group and 4 of 13 in the prostatectomy-first group. These data suggest that ePLND-first sequencing was associated with a lower incidence of apical PSM rather than with shorter margin length conditional on margin presence.

Not every outcome moved in the same direction. Overall PSM was numerically lower in the ePLND-first group, but the confidence interval was wide and included no clear difference. We therefore interpret the main signal as site-specific rather than global. The operative time difference favored ePLND-first, but the magnitude was modest. That finding is supportive, not central. In our data, Retzius-sparing RARP was associated with borderline higher overall PSM in the primary full-cohort analysis (adjusted OR 1.94; 95% CI 0.91 to 4.17; $p = 0.088$) and with significantly higher overall PSM within the nerve-sparing subgroup (adjusted OR 2.60; 95% CI 1.05 to 6.45; $p = 0.040$). The association did not extend to apical PSM specifically (adjusted OR 1.14; 95% CI 0.27 to 4.84). One anatomical interpretation is that the Retzius-sparing approach modifies the anterior and basal dissection planes while leaving the apical plane comparatively less perturbed, potentially shifting margin risk to non-apical sites; this interpretation is speculative and not directly tested by the present data. Published comparative evidence on margin outcomes with Retzius-sparing surgery remains mixed, and current systematic review data have not resolved the issue (16).

The ePLND component itself can be performed using different technical approaches, including antegrade and retrograde sequences of nodal packet dissection. In the present cohort the institutional standard approach was used across all five surgeons, and technique-level variation within ePLND was not analysed. Differences in ePLND technique may modify the operative time advantage observed in the ePLND-first group.

The lower BCR rate in the ePLND-first group should be interpreted with several reservations. The comparison was unadjusted; median follow-up of 26 months is short for definitive recurrence ascertainment; the distributions of pathological T stage, Grade Group, and overall PSM did not differ markedly between sequence groups; and the absolute number of events was small (2 events in the ePLND-first group versus 12 in the prostatectomy-first group). Plausible explanations include mediation through reduced apical PSM, chance aggregation given the sparse event count, or unmeasured biological factors. We do not infer a direct causal relationship between operative sequence and biochemical control.

This study has limitations. Operative sequence was determined by surgeon preference rather than randomisation, so residual confounding cannot be excluded; we adjusted for cumulative surgeon experience and ran a sensitivity analysis substituting NCCN risk group for clinical T stage, but unmeasured differences between groups may persist. Among measured baseline variables, clinical T stage distribution showed a borderline imbalance, with more locally advanced disease in the prostatectomy-first group (Table 1; overall $p = 0.055$); the multivariable model included clinical T stage as an ordinal covariate (Table 2A: adjusted OR 0.81; 95% CI 0.59 to 1.11; $p = 0.188$), and the sensitivity analysis substituting NCCN risk group for clinical T stage yielded a directionally consistent estimate (adjusted OR 0.44; 95% CI 0.17 to 1.16; $p = 0.098$), so the estimated effect of operative sequence was not driven by this imbalance. Apical PSM events were sparse, with 19 events in the full cohort and 10 in the nerve-sparing subgroup, yielding events-per-variable ratios of 2.7 and 1.4 respectively; Firth penalisation mitigates small-sample bias but does not eliminate wide confidence intervals, and the adjusted estimates are exploratory. Sequence assignment varied across the five participating surgeons (Supplementary Table S1), and surgeon-level clustering of operative practice could not be fully separated from the sequence-effect estimate. The nerve-sparing subgroup analysis examines the population in which our mechanistic hypothesis applies most directly; the weaker signal in the full cohort reflects attenuation by patients without nerve-sparing intent, in whom the apical dissection plane is intentionally wider. The study is retrospective and confined to a single centre; the 40 patients excluded for incomplete data (30 without follow-up, 10 without preoperative biopsy) reflect absence of essential outcome or covariate variables rather than selective dropout.

CONCLUSION

Performing extended pelvic lymph node dissection before prostatectomy was associated with directionally lower apical positive surgical margin rates in the full 250-patient cohort and significantly lower rates in the pre-specified nerve-sparing subgroup. The signal is consistent with the anatomical hypothesis that improved pelvic exposure facilitates the delicate apical dissection required for neurovascular bundle preservation. Where ePLND is planned during nerve-sparing radical prostatectomy, performing the lymph node dissection first is a practical operative strategy with no evident perioperative penalty.

Supplementary Table S1. Surgeon-level distribution of operative sequence and apical positive surgical margin events.

Surgeon	ePLND-first, n (apical PSM events)	Prostatectomy-first, n (apical PSM events)	Total cases
Surgeon 1	37 (1)	26 (1)	63
Surgeon 2	22 (1)	30 (2)	52
Surgeon 3	32 (1)	28 (1)	60
Surgeon 4	22 (3)	34 (6)	56
Surgeon 5	8 (0)	11 (3)	19
Total	**121 (6)**	**129 (13)**	**250**

Apical PSM event counts are shown in parentheses. No surgeon used exclusively one sequence.

Abbreviations

BCR, biochemical recurrence; BMI, body mass index; CCI, Charlson comorbidity index; CI, confidence interval; EBL, estimated blood loss; ePLND, extended pelvic lymph node dissection; IQR, interquartile range; ISUP, International Society of Urological Pathology; NCCN, National Comprehensive Cancer Network; OR, odds ratio; PSA, prostate-specific antigen; PSM, positive surgical margin; RARP, robot-assisted radical prostatectomy; SD, standard deviation.

Funding: This research received no external funding.

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

Informed Consent Statement: The requirement for informed consent was waived because of the retrospective design and the use of de-identified data.

Data Availability Statement: The data presented in this study are available from the corresponding author on reasonable request.

Ethical Approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Scientific Research Ethic Committee of Umraniye Training and Research Hospital, Istanbul, Türkiye (IRB-2025-470, Date: December 18, 2025).

Author Contributions

Conceptualization: A.İ., H.S.G., N.M.Ş.; Methodology: A.İ., H.S.G., A.T.; Data curation: A.İ., B.Ö., M.E.T., S.S.; Formal analysis: A.İ., H.S.G., A.E.; Investigation: A.İ., H.S.G., C.E.Y.; Writing - original draft: A.İ., N.M.Ş.; Writing - review and editing: R.S., E.V.K., H.S.G., F.Y.S., M.B. All authors read and approved the manuscript.

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):212–220. doi: 10.54233/endourolbull-1937415

Comparative Analysis of Avicenna Roboflex® and Conventional Ureteroscopy: A Porcine Model Study of Safety and Feasibility in Stone Management

Avicenna Roboflex® Ile Konvansiyonel Üreteroskopinin Karşılaştırılması: Taş Tedavisinde Güvenlik Ve Uygulanabilirliğin Domuz Modelinde Deneysel Analizi

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ABSTRACT

Objective: Robotic-assisted ureteroscopy is increasingly adopted in endourology. We aimed to evaluate the feasibility and safety of the Avicenna Roboflex® Urology system (Elmed, Ankara, Turkey) compared with conventional ureteroscopy in a porcine model.

Materials and Methods: The Avicenna Roboflex® platform was compared with conventional ureteroscopy in a live porcine model (n = 6) in the supine lithotomy position. Two experienced endourologists assessed task performance using Likert scales (1–4) for accuracy/workaround and ease of completion. Intraoperative events and ureteral injury were evaluated using the post-ureteroscopic lesion scale (PULS, 0–5). Histopathological assessment of tissue samples was performed by a blinded pathologist. Paired comparisons were performed using the 2-sided Wilcoxon signed-rank test, with $p < 0.05$ considered statistically significant.

Results: A total of 12 ureteroscopic procedures (6 conventional, 6 robotic) were completed without intraoperative complications. Histopathological analysis revealed no significant differences between groups, with minimal epithelial loss observed only in the proximal ureter. Task performance scores were comparable between groups; however, the robotic system showed a trend toward improved ease in flexible ureteroscope insertion and simulated stone removal. PULS scores were low and similar in both groups.

Conclusion: The Avicenna Roboflex® system demonstrated procedural feasibility and an acute tissue safety profile comparable to conventional ureteroscopy in this porcine model. Given the exploratory nature and small sample size of the study, these findings should be considered preliminary and require validation in adequately powered studies.

Keywords: kidney calculi, robotic surgical procedures, ureteroscopy

Cite As: *Ergul RB, Atar FA, Kabakci AS, Tokatli Z, Aydin AB, Celikbilek Erkasap P, Arun SS, Sofikerim M, Tefik T. Comparative Analysis of Avicenna Roboflex® and Conventional Ureteroscopy: A Porcine Model Study of Safety and Feasibility in Stone Management. Endourol Bull. 2026;18(3):212–220.* https://doi.org/10.54233/endourolbull-1937415

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Received *: March 17, 2026* ***Accepted*** *: September 28, 2026*

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ÖZET

Amaç: Robotik destekli üreteroskopi endoürolojide giderek daha fazla kullanılmaktadır. Bu çalışmada, Avicenna Roboflex® Üroloji sisteminin (Elmed, Ankara, Türkiye) uygulanabilirliği ve güvenliği, konvansiyonel üreteroskopi ile domuz modelinde karşılaştırıldı.

Gereç ve Yöntemler: Avicenna Roboflex® platformu, canlı domuz modelinde (n = 6) supin litotomi pozisyonunda konvansiyonel üreteroskopi ile karşılaştırıldı. İki deneyimli endoürolog, işlemlerin başarıyla tamamlanmasını doğruluk/alternatif çözüm ve görev tamamlama kolaylığı açısından Likert ölçeği (1–4) ile değerlendirdi. İntraoperatif olaylar ve üreter hasarı, post-üreteroskopik lezyon skoru (PULS, 0–5) ile değerlendirildi. Doku örnekleri kör bir patolog tarafından histopatolojik olarak incelendi. Eşleştirilmiş karşılaştırmalarda iki yönlü Wilcoxon işaretli sıralar testi kullanıldı ve $p < 0.05$ anlamlı kabul edildi.

Bulgular: Toplam 12 üreteroskopi işlemi (6 konvansiyonel, 6 robotik) komplikasyonsuz olarak tamamlandı. Histopatolojik değerlendirmede gruplar arasında anlamlı fark saptanmadı; epitel kaybı yalnızca proksimal üreterde minimal düzeyde gözlendi. Görev performans skorları benzerdi; ancak robotik sistem, fleksibl üreteroskopun yerleştirilmesi ve taş çıkarımını simüle eden işlemlerde daha iyi görev tamamlama kolaylığı eğilimi gösterdi. PULS skorları her iki grupta da düşük ve benzerdi.

Sonuçlar: Avicenna Roboflex® sistemi, bu domuz modelinde konvansiyonel üreteroskopi ile karşılaştırıldığında benzer prosedürel uygulanabilirlik ve akut doku güvenliği profili göstermiştir. Çalışmanın keşifsel niteliği ve küçük örneklem büyüklüğü göz önüne alındığında, bu bulgular öncül nitelikte değerlendirilmeli ve yeterli güce sahip ileri çalışmalarla doğrulanmalıdır.

Anahtar Kelimeler: böbrek taşları, robotik cerrahi prosedürler, üreteroskopi

INTRODUCTION

Urolithiasis remains a significant global health burden, with increasing incidence and recurrence rates worldwide (1). Over the past decades, ureteroscopy (URS) has evolved into a cornerstone modality for the management of urinary tract stones due to its minimally invasive nature, high stone-free rates, and favorable safety profile (2,3,4). In particular, flexible ureteroscopy (F-URS) has enabled access to all intrarenal calyces, making it an essential tool for the treatment of renal calculi, especially those <2 cm in size (5,6,7). Despite these advantages, conventional ureteroscopy presents several limitations. The procedure is associated with a steep learning curve, prolonged operative times in complex cases, and significant ergonomic strain for surgeons, including musculoskeletal fatigue and radiation exposure (8,9,10). These challenges have prompted the development of robotic-assisted platforms aimed at improving surgical precision, reducing operator fatigue, and enhancing overall procedural efficiency.

Robotic-assisted ureteroscopy has emerged as a promising innovation in endourology. The Avicenna Roboflex® Urology system (Elmed, Ankara, Turkey) is one of the first dedicated robotic platforms designed specifically for flexible ureteroscopy (11). This system allows the surgeon to control the ureteroscope remotely via a console, offering improved ergonomics, tremor filtration, and stable instrument manipulation (12). Early clinical and experimental studies suggest that robotic URS may reduce physical strain and provide comparable or even improved technical performance compared to conventional approaches (13,14).

However, despite growing interest, the current body of evidence on robotic ureteroscopy remains limited, particularly with respect to objective safety outcomes and tissue effects. Preclinical models, such as porcine studies, are critical for evaluating device performance, reproducibility, and potential tissue injury in a controlled environment prior to widespread clinical adoption (15). In this study, we aimed to compare the safety, feasibility, and usability of the Avicenna Roboflex® system with conventional ureteroscopy in a live porcine model. Specifically, we evaluated procedural performance, surgeon-reported outcomes, ureteral injury using the post-ureteroscopic lesion scale (PULS), and histopathological tissue effects.

MATERIALS AND METHODS

This experimental study was designed to evaluate the safety and feasibility of robotic-assisted ureteroscopy compared to conventional ureteroscopy using a live porcine model. As this was an exploratory pilot animal study evaluating the feasibility and safety of a novel robotic platform, no formal a priori sample size calculation was performed. The sample size was determined pragmatically while adhering to the principles of the 3Rs (Replacement, Reduction, and Refinement) in animal research, with the objective of generating preliminary data for future adequately powered studies. The study was designed, conducted, and reported in accordance with the Animal Research: Reporting of In Vivo Experiments (ARRIVE) 2.0 guidelines (16). A total of six female domestic pigs (Sus scrofa domesticus), weighing 41–55 kg (mean, 48.2 kg), were included in the study. Before inclusion in the experimental protocol, all animals underwent a preprocedural veterinary health assessment, including evaluation of vital signs, general physical condition, behavior, activity, breathing, and nutritional status. Only animals considered clinically healthy and suitable for the experimental study by the veterinarian were included; animals with abnormal findings on the preprocedural veterinary assessment were considered ineligible. All procedures were performed under general anesthesia in the supine lithotomy position. Each animal underwent bilateral ureteroscopy, with one ureter assigned to conventional ureteroscopy and the contralateral ureter to robotic-assisted ureteroscopy using the Avicenna Roboflex® system, thereby allowing each animal to serve as its own control. Treatment-side allocation and procedural order were determined using a sealed-envelope randomization method. This resulted in a total of 12 procedures, comprising six conventional and six robotic-assisted ureteroscopies. The porcine model was selected due to its anatomical and physiological similarity to the human urinary tract, allowing a realistic simulation of endourological interventions.

This study was conducted in accordance with institutional and national guidelines for the care and use of laboratory animals. Ethical approval was obtained from the Acıbadem Mehmet Ali Aydınlar University Animal Experiments Local Ethics Committee (Approval No: HDK-2024/33).

Flexible ureteroscopy was performed using a 7.5-Fr flexible ureteroscope (Hugemed). A 9.5/11.5-Fr ureteral access sheath (GUA1,138, Geotek) and a Roadrunner® Hydrophilic PC Wire Guide were used for ureteral access. Irrigation was provided with isotonic saline using a gravity-based system, with the irrigation fluid positioned 60 cm above the operative field. In the robotic group, the flexible ureteroscope was mounted onto the Avicenna Roboflex® Urology system (Elmed, Ankara, Turkey) and manipulated remotely using the dedicated surgeon console, whereas in the conventional group, the ureteroscope was manipulated manually. All procedures were performed by two experienced endourologists familiar with both conventional and robotic techniques.

All procedures followed a standardized protocol. Following induction of anesthesia, ureteral access was obtained over the guidewire, the ureteral access sheath was positioned, and the flexible ureteroscope was advanced into the renal collecting system. Ureteral navigation and manipulation within the upper and lower poles were then performed. Basket manipulation was performed using a Zero Tip™ Nitinol Stone Retrieval Basket (Boston Scientific) to simulate the procedural steps of stone retrieval; no actual stone extraction was performed. No laser lithotripsy was performed during the experimental procedures. The same procedural steps were performed in both groups, differing only in robotic versus manual manipulation of the flexible ureteroscope.

Procedural performance was assessed by the operating endourologists using a 4-point Likert scale for task accuracy and ease of task completion (1=poor, 2=fair, 3=good, and 4=excellent).

All intraoperative events were recorded. At the completion of each procedure, following withdrawal of the ureteroscope and removal of the ureteral access sheath, the ureter was inspected endoscopically for procedure-related injury. Ureteral injury was assessed using the Post-Ureteroscopic Lesion Scale (PULS), ranging from grade 0 to grade 5. The PULS score was assigned by the operating endourologist immediately after completion of the procedure.

Following completion of all experimental procedures, the animals were euthanized under general anesthesia by intravenous administration of 20 mL of 22.5% potassium chloride. Tissue samples were obtained and evaluated by an experienced veterinary pathologist who was blinded to the intervention groups (Figure 1). Histopathological assessment was performed on samples obtained from the renal pelvis, upper pole, lower pole, and proximal ureter. A total of 48 tissue samples were evaluated, with samples obtained from at least three different areas of each tissue. Specimens were fixed in 10% buffered formaldehyde, processed using standard histological procedures, embedded in paraffin, sectioned at a thickness of 4 µm, and stained with hematoxylin and eosin (H&E). Histomorphological findings were assessed according to the predefined scoring matrix specified in the animal study protocol.

Statistical analyses were performed using R software (Version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria). Owing to the small sample size and the ordinal nature of several study variables, non-parametric methods were used. Continuous and ordinal variables were summarized as median (range). Given the paired experimental design, with each animal serving as its own control, comparisons between robotic and conventional ureteroscopy were performed using the 2-sided Wilcoxon signed-rank test. Because the data contained ties and zero differences, *p*-values were calculated using the normal approximation with continuity correction; zero differences were excluded from the ranking procedure, and tied observations were assigned average ranks. A *p*-value <0.05 was considered statistically significant.

RESULTS

A total of 12 ureteroscopic procedures were successfully completed, including six conventional and six robotic-assisted interventions, without any intraoperative complications or technical failures. All predefined procedural steps were achieved in both groups. No statistically significant differences were observed between the conventional and robotic groups for any evaluated parameter (all $p > 0.05$).

Surgeon-based evaluation demonstrated comparable performance between conventional and robotic ureteroscopy. For insertion of the flexible ureteroscope into the renal pelvis, the robotic system showed a higher median accuracy/workaround score of 4 (3–4) compared to 3 (3–4) in the conventional group, while ease of task completion was

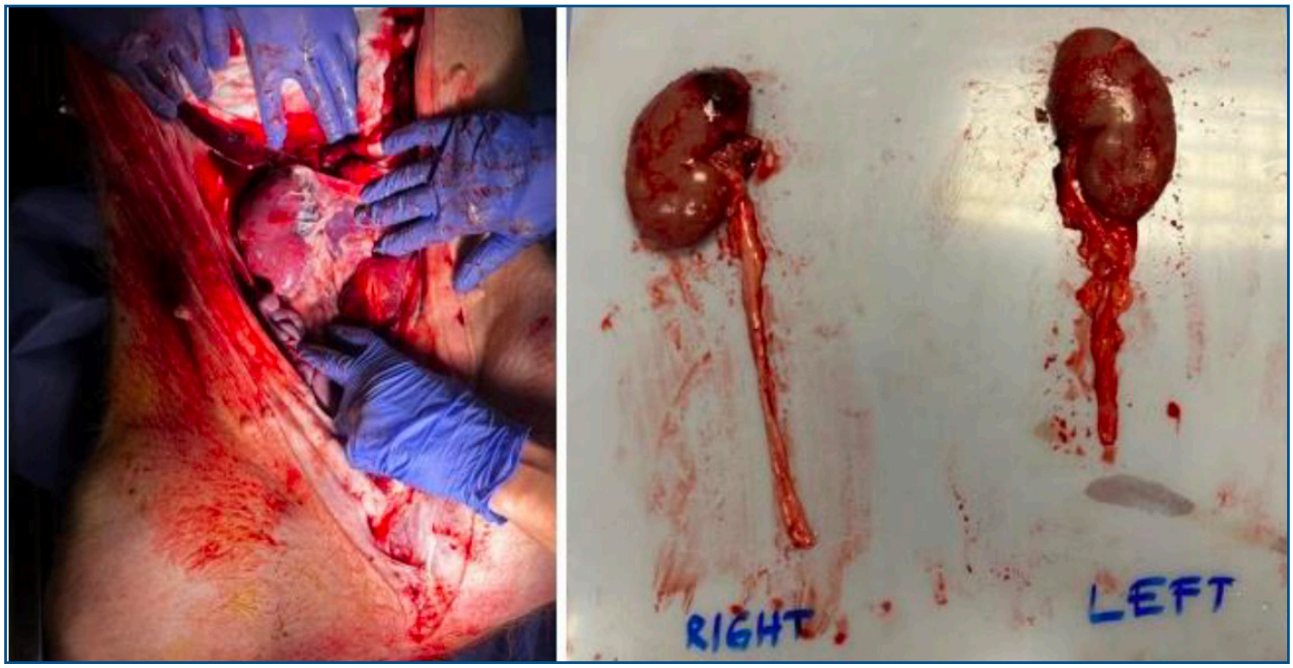


Figure 1. Intraoperative harvesting and macroscopic view of renal and ureteral specimens in the porcine model (right, conventional side; left, robotic-assisted side)

identical in both groups, with a median of 4 (3–4). During manipulation within the upper and lower poles, both approaches achieved maximal performance, with median accuracy/workaround scores of 4 (4–4) and ease of task completion scores of 4 (3–4) (Table 1).

In the simulated stone removal task, which involved retraction of the flexible ureteroscope into the ureteral access sheath followed by re-advancement, both groups demonstrated similar ease of task completion with a median score of 4 (3–4). However, the robotic system maintained a consistent maximal accuracy/workaround score of 4 (4–4), whereas the conventional approach showed a slightly wider range with a median of 4 (3–4).

Assessment of ureteral injury using the Post-Ureteroscopic Lesion Scale (PULS) revealed no clinically relevant differences between the groups, with both approaches demonstrating a median score of 0 (range 0–1), indicating minimal or no ureteral trauma.

Histopathological evaluation demonstrated minimal tissue alterations in both groups. Epithelial loss was confined to the proximal ureter and was focal, involving <25% of the ureteral mucosa (Figure 2). The median epithelial loss score was 1 (1–1) in the conventional group and 1 (0–1) in the robotic group, whereas no epithelial loss was observed in the renal pelvis, upper pole, or lower pole in either group. Focal inflammatory infiltrates consisting of lymphocytes and neutrophils were identified in selected renal specimens from both groups. Based on their histological characteristics, these findings were considered consistent with pre-existing focal nephritis rather than procedure-related acute injury. No pathological alterations were observed in the renal tubules or glomeruli. Overall, no substantial acute histopathological injury was identified in either group.

Table 1. Comparison of histopathological findings, task performance scores, and PULS outcomes between conventional and robotic ureteroscopy in a porcine model

	Control (Conventional)		Test (Avicenna Roboflex®)		p value	
Histopathology Assessment Category						
Epithelial Loss						
Proximal Ureter	1 (1-1)		1 (0-1)		1.000	
Upper Pole	0 (0-0)		0 (0-0)		1.000	
Renal Pelvis	0 (0-0)		0 (0-0)		1.000	
Lower Pole	0 (0-0)		0 (0-0)		1.000	
General Observation						
Proximal Ureter	0 (0-0)		0 (0-0)		1.000	
Upper Pole	0 (0-0)		0 (0-1)		0.500	
Renal Pelvis	0 (0-1)		0 (0-1)		1.000	
Lower Pole	0 (0-1)		0 (0-1)		1.000	
Task Completion Category	Accuracy/ Workaround	Ease of task completion	Accuracy/ Workaround	Ease of task completion	Accuracy/ Workaround	Ease of task completion
Insertion of F-URS in the renal pelvis	3 (3-4)	4 (3-4)	4 (3-4)	4 (3-4)	0.250	1.000
Manipulation within the upper pole with F-URS	4 (4-4)	4 (3-4)	4 (4-4)	4 (3-4)	1.000	1.000
Manipulation within the lower pole with F-URS	4 (4-4)	4 (3-4)	4 (4-4)	4 (3-4)	1.000	1.000
The F-URS is retracted from the renal pelvis into the UAS, then advanced back (simulating stone removal)	4 (3-4)	4 (3-4)	4 (4-4)	4 (3-4)	1.000	1.000
PULS Score	0 (0-1)		0 (0-1)		1.000	

Values: median (range)

Paired comparisons between conventional and robotic ureteroscopy were performed using the 2-sided Wilcoxon signed-rank test.

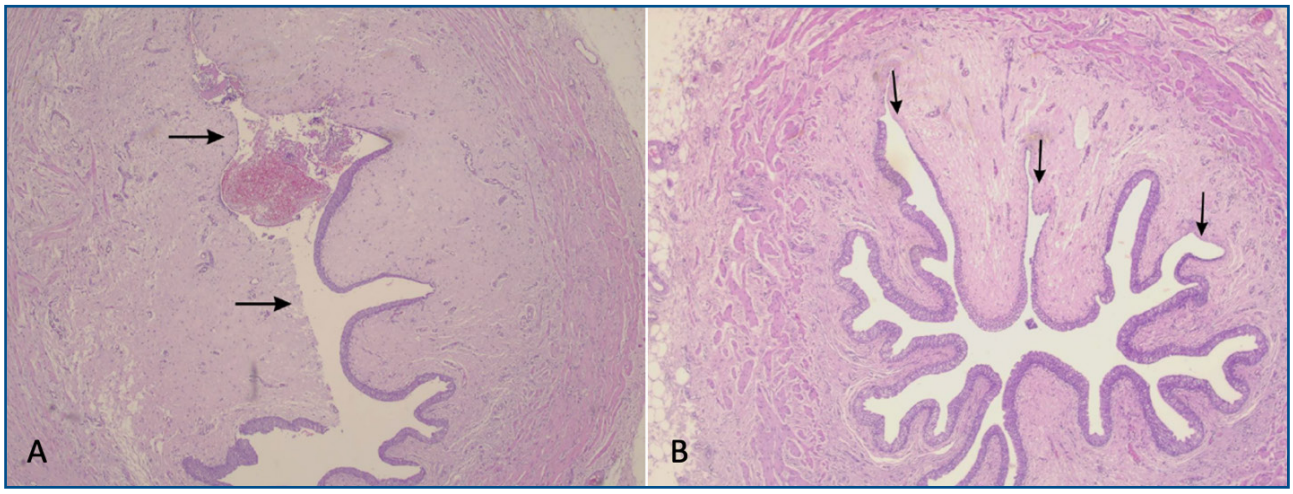


Figure 2. Representative histopathological findings of the proximal ureter following conventional and robotic-assisted ureteroscopy. (A) Conventional ureteroscopy showing focal epithelial loss involving <25% of the ureteral mucosa (arrows; H&E, ×4). (B) Robotic-assisted ureteroscopy showing similarly limited focal epithelial loss involving <25% of the ureteral mucosa (arrows; H&E, ×4).

DISCUSSION

In this experimental study, we evaluated the safety and feasibility of robotic-assisted ureteroscopy using the Avicenna Roboflex® system compared to conventional ureteroscopy in a live porcine model. Our findings demonstrated comparable procedural performance and safety outcomes between the two approaches, with no intraoperative complications, no clinically relevant ureteral injuries, and minimal histopathological alterations. These results are in line with previous studies demonstrating that ureteroscopy is a highly effective and safe modality for the management of urinary stone disease (17,18).

A key observation in this study is the comparable performance between robotic and conventional ureteroscopy across all evaluated tasks. Both techniques achieved high scores in accuracy and ease of task completion. Notably, the robotic platform showed a trend toward improved performance during ureteroscope insertion and simulated stone manipulation. Previous studies evaluating robotic flexible ureteroscopy have similarly reported enhanced instrument stability, improved dexterity, and better control of endoscope movements, which may contribute to improved technical performance (19,20).

Ergonomic challenges are well recognized in conventional ureteroscopy, particularly in prolonged or complex procedures. Surgeons are frequently exposed to awkward postures and repetitive movements, which may lead to musculoskeletal strain over time. Robotic systems have been proposed as a solution to these limitations by allowing console-based operation and reducing physical burden. Prior studies have demonstrated that robotic ureteroscopy may significantly improve surgeon ergonomics and reduce fatigue, potentially translating into improved procedural efficiency (21).

In line with our findings, a recent systematic review and meta-analysis reported that robotic ureteroscopy achieves high stone-free rates of approximately 86%, supporting its effectiveness as a minimally invasive treatment option (22). Although our study is preclinical, the comparable safety profile and procedural performance observed between robotic and conventional approaches are consistent with these clinical data, further supporting the feasibility of robotic-assisted ureteroscopy while highlighting the need for future standardized and comparative studies.

From a safety standpoint, our results are particularly reassuring. The absence of significant differences in PULS scores between groups indicates that robotic manipulation does not increase the risk of ureteral injury. Furthermore, histopathological analysis revealed only minimal epithelial changes without evidence of deeper tissue damage. These findings are consistent with existing literature showing that ureteroscopy, when performed under controlled conditions, is associated with low complication rates and minimal tissue trauma (14,23).

The use of a porcine model represents a major strength of this study, allowing controlled evaluation of both procedural performance and tissue effects in a setting that closely mimics human anatomy. However, several limitations should be acknowledged. This study should be interpreted as a hypothesis-generating pilot investigation rather than a definitive comparative study. The limited sample size, which was determined according to ethical principles governing animal experimentation, substantially restricts statistical power and increases the possibility of type II error. Consequently, the absence of statistically significant differences should not be interpreted as evidence of equivalence between the two approaches. Instead, these findings provide preliminary proof-of-concept data that may inform the design and sample size estimation of future adequately powered preclinical and clinical studies. Another limitation is the lack of objective measurement of radiation exposure and ergonomic parameters, which are increasingly recognized as important factors in endourological practice. In addition, task performance was subjectively assessed by the operating surgeons rather than by independent observers, introducing the possibility of observer and performance bias. Similarly, PULS assessment was performed by the operating surgeon and was therefore not blinded to the intervention, introducing the possibility of assessment bias. Furthermore, the experimental protocol simulated stone retrieval maneuvers rather than actual stone treatment, and no laser lithotripsy was performed; therefore, the findings may not fully reflect tissue effects occurring during clinical stone surgery. Finally, tissue harvesting and histopathological assessment were performed immediately after the procedures, allowing evaluation of acute tissue injury only. Consequently, delayed inflammatory responses, tissue remodeling, fibrosis, and subsequent ureteral stricture formation could not be assessed.

CONCLUSION

In this experimental porcine model, robotic-assisted ureteroscopy using the Avicenna Roboflex® system demonstrated procedural feasibility and an acute tissue safety profile comparable to conventional ureteroscopy. Both approaches were successfully completed without intraoperative complications or clinically relevant ureteral injury, and only minimal acute histopathological alterations were observed. Given the exploratory nature and small sample size of this study, these findings should be interpreted as preliminary preclinical evidence, and further adequately powered studies are required to evaluate the clinical performance and potential benefits of robotic-assisted ureteroscopy.

Acknowledgments: The authors would like to thank the veterinary staff and laboratory personnel who contributed to the animal care, procedural preparation, and histopathological assessments during this study.

Informed Consent: Not applicable. This study was conducted in an experimental animal model.

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

Funding: Elmed (Ankara, Turkey), the manufacturer of the Avicenna Roboflex® system, provided the robotic system and material support for the study by covering the procurement costs of the experimental animals. The manufacturer had no role in the study design, data collection, histopathological assessment, statistical analysis, interpretation of the results, manuscript preparation, or the decision to submit the manuscript for publication.

Ethical Approval: This study was approved by the Acıbadem Mehmet Ali Aydınlar University Local Ethics Committee

on Animal Experiments (Approval No: HDK-2024/33, Date: June 5, 2024).

Author Contributions:

RBE: Study conception and design, acquisition of data, data analysis and interpretation, drafting of the manuscript. FAA: Study design, acquisition of data, and critical revision of the manuscript. ASK: Study design, technical support, and critical revision of the manuscript. ZT: Acquisition of data, procedural support, and critical revision of the manuscript. ABA: Acquisition of data. PCE: Experimental study coordination, animal model preparation, and procedural support. SSA: Histopathological evaluation, interpretation of pathological findings, and critical revision of the manuscript. MS: Study conception and design, supervision, data interpretation, and critical revision of the manuscript. TT: Study conception and design, supervision, interpretation of results, and critical revision of the manuscript

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):221–238. doi: 10.54233/endourolbull-1954790

Association of the Preoperative Albumin-to-Globulin Ratio with Pathological Stage and Tumor Grade in Primary Bladder Tumor

Primer Mesane Tümörlerinde Ameliyat Öncesi Albumin-Globulin Oranının Patolojik Evre ve Tümör Derecesiyle İlişkisi

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ABSTRACT

Objective: This study aimed to investigate the association between the preoperative albumin-to-globulin ratio (AGR) and pathological stage and tumor grade in patients who underwent transurethral resection of bladder tumor (TURBT) for primary bladder tumors.

Materials and Methods: A total of 153 patients who underwent transurethral resection of bladder tumor (TURBT) for primary urothelial carcinoma between March 2017 and February 2020 were included in the study. AGR was calculated using preoperative serum albumin and total protein levels. Among the exclusion criteria were active infection, autoimmune disease, hepatic disease, and concomitant malignancy. The optimal AGR cut-off value was determined using receiver operating characteristic (ROC) curve analysis and the Youden index. Independent predictors of pathological stage (NMIBC/MIBC) and tumor grade (low/high Grade) were evaluated using logistic regression analysis.

Results: The median age of the patients was 68 years (IQR: 59–75), and 88.9% were male. The pathological stage distribution was Ta in 39.9%, T1 in 39.9%, and T2 in 20.3% of patients, while tumor grade distribution was low Grade in 54.2% and high Grade in 43.1%. The median AGR value of the cohort was 1.32 (IQR: 1.17–1.50). AGR was significantly lower in both the MIBC group (p = 0.003) and the high-grade group (p < 0.001) compared to their respective counterparts. ROC analysis identified an optimal cut-off value of 1.35 for both clinical outcomes (AUC=0.649, 95% CI: 0.542–0.755 for MIBC and AUC=0.656, 95% CI: 0.568–0.744 for high-grade disease). In multivariate logistic regression analysis, AGR was independently associated with both MIBC (OR=0.16, 95% CI: 0.03–0.97; p = 0.046) and high-grade disease (OR=0.18, 95% CI: 0.04–0.74; p = 0.018).

Conclusion: Preoperative AGR is independently associated with pathological stage and tumor grade in primary bladder tumors. The ability to calculate this parameter from routine biochemical tests without additional cost makes it clinically valuable for preoperative risk stratification. Further validation of these findings in larger patient cohorts is warranted.

Keywords: albumin-to-globulin ratio, neoplasm grading, neoplasm staging, transurethral resection of bladder tumor, urinary bladder neoplasms

Cite As: *Aydin ME, Basmaci I, Cesur G, Bozkurt I, Sefik E, Celik S, Bolat D, Aykac A, Degirmenci T. Association of the Preoperative Albumin-to-Globulin Ratio with Pathological Stage and Tumor Grade in Primary Bladder Tumor. Endourol Bull. 2026;18(3):221–238.* https://doi.org/10.54233/endourolbull-1954790

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Received : March 19, 2026 ***Accepted*** : September 28, 2026

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ÖZET

Amaç: Bu çalışma, primer mesane tümörü nedeniyle transüretral mesane tümörü rezeksiyonu (TURMT) geçiren hastalarda ameliyat öncesi albümin-globulin oranı (AGR) ile patolojik evre ve tümör derecesi arasındaki ilişkiyi araştırmayı amaçlamıştır.

Gereç ve Yöntemler: Mart 2017 ile Şubat 2020 tarihleri arasında primer ürotelyal karsinom nedeniyle transüretral mesane tümörü rezeksiyonu (TURMT) geçiren toplam 153 hasta çalışmaya dahil edilmiştir. AGR, ameliyat öncesi serum albümin ve toplam protein düzeyleri kullanılarak hesaplanmıştır. Dışlama kriterleri arasında aktif enfeksiyon, otoimmün hastalık, karaciğer hastalığı ve eşlik eden malignite yer almıştır. Optimal AGR eşik değeri, alıcı işletim karakteristik (ROC) eğrisi analizi ve Youden indeksi kullanılarak belirlenmiştir. Patolojik evre (NMIBC/MIBC) ve tümör derecesinin (düşük/yüksek derece) bağımsız prediktörleri lojistik regresyon analizi kullanılarak değerlendirilmiştir.

Bulgular: Hastaların medyan yaşı 68 yıl (IQR: 59–75) olup %88.9'u erkekti. Patolojik evre dağılımı hastaların %39.9'unda Ta, %39.9'unda T1 ve %20.3'ünde T2 iken, tümör derecesi dağılımı %54.2'sinde düşük dereceli ve %43.1'inde yüksek dereceliydi. Kohortun medyan AGR değeri 1.32 (IQR: 1.17–1.50) idi. AGR, hem MIBC grubunda ($p = 0.003$) hem de yüksek dereceli grupta ($p < 0.001$) ilgili karşıt gruplarına göre anlamlı derecede daha düşüktü. ROC analizi, her iki klinik sonuç için de 1.35'lik optimal bir kesme değeri belirledi (MIBC için AUC=0.649, %95 GA: 0.542–0.755 ve yüksek dereceli hastalık için AUC=0.656, %95 GA: 0.568–0.744). Çok değişkenli lojistik regresyon analizinde, AGR hem MIBC (OR=0.16, %95 GA: 0.03–0.97; $p = 0.046$) hem de yüksek dereceli hastalık (OR=0.18, %95 GA: 0.04–0.74; $p = 0.018$) ile bağımsız olarak ilişkili bulunmuştur.

Sonuçlar: Ameliyat öncesi AGR, primer mesane tümörlerinde patolojik evre ve tümör derecesi ile bağımsız olarak ilişkilidir. Bu parametrenin ek maliyet olmadan rutin biyokimyasal testlerden hesaplanabilmesi, ameliyat öncesi risk sınıflandırması için klinik olarak değerli kılmaktadır. Bu bulguların daha büyük hasta kohortlarında daha fazla doğrulanması gerekmektedir.

Anahtar Kelimeler: albümin-globülin oranı, mesane tümörü, transüretral mesane tümörü rezeksiyonu, tümör derecelendirmesi, tümör evrelendirmesi

INTRODUCTION

Bladder cancer is among the most common malignancies worldwide and represents one of the major challenges in urologic oncology (1). Approximately 70–80% of newly diagnosed bladder cancer cases are classified as non-muscle-invasive bladder cancer (NMIBC; Ta and T1), whereas muscle-invasive bladder cancer (MIBC; ≥T2) is detected in 20–25% of patients at diagnosis (2,3). Transurethral resection of bladder tumor (TURBT), the primary diagnostic procedure, is the fundamental surgical intervention that determines both diagnosis and treatment management by establishing the pathological stage and histological Grade of the tumor (4,5).

Pathological stage and tumor grade are the principal determinants of treatment selection and follow-up protocols in bladder cancer. The heterogeneous clinical course of NMIBC has necessitated the development of multivariable models, such as the European Association of Urology (EAU) risk classification; however, existing clinicopathological parameters may not always adequately reflect the individual patient risk profile (2,6). In this context, there is growing interest in novel biomarkers that can be obtained preoperatively, require no additional cost, and can be calculated from routine biochemical panels (7).

Systemic inflammation and nutritional status represent two fundamental physiological domains that directly influence tumor biology. The chronic inflammatory process accompanying tumor growth shapes the tumor microenvironment by promoting angiogenesis, tumor cell survival, invasion, and metastasis (8). In this process, proinflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) play key mediating roles. These cytokines suppress hepatic albumin synthesis while stimulating an increase in the globulin fraction, which includes acute-phase proteins (9). This mechanism establishes a direct relationship between inflammatory tumor burden and the serum protein profile, positioning the albumin-to-globulin ratio (AGR) as an integrated immunonutritional biomarker.

AGR is a simple biomarker calculated as the ratio of serum albumin to the difference between total protein and albumin [AGR = albumin / (total protein − albumin)] and reflects both nutritional status and systemic inflammatory

activity within a single parameter (4). A low AGR simultaneously reflects hypoalbuminemia, indicating poor nutritional reserves, and elevated globulin levels, indicating chronic inflammatory stimulation. Since total protein comprises both components, individual changes may offset and thereby mask each other when assessed alone; this has been proposed as a rationale for why AGR may provide additional discriminatory value compared with either component alone (4,9).

In recent years, the prognostic significance of AGR has been extensively investigated in various solid tumors. In the systematic review by Roberts et al. (7), which compiled data from 61 studies covering 18 different cancer types, AGR was shown to have a statistically significant association with at least one prognostic variable in multivariate analysis across all cancer types and can be calculated from routine preoperative biochemical panels without additional cost.

In the field of urologic oncology, the prognostic value of AGR has been investigated in both upper tract urothelial carcinoma (UTUC) and bladder cancer. Two meta-analyses by Xia et al. (10) one including 12 studies and 5,727 urothelial carcinoma (UC) patients, and another including 21 studies and 18,269 urologic cancer patients - consistently demonstrated that low pretreatment AGR was independently associated with worse overall survival, cancer-specific survival, and recurrence-free survival (11). In UTUC specifically, Xu et al. (n = 620), Otsuka et al. (n = 124), and Omura et al. (n = 179) each confirmed an independent association between low preoperative AGR and poor oncological outcomes after radical nephroureterectomy (9,12,13).

Regarding bladder cancer specifically, the majority of existing studies have focused on survival and recurrence outcomes. Niwa et al. (4) demonstrated that low pretreatment AGR (<1.60) was an independent risk factor for tumor recurrence in 364 patients with primary NMIBC, with a significant association with progression to muscle invasion also reported in univariate analysis. Quhal et al. (5) confirmed in a multicenter cohort of 1,096 patients that low AGR (<1.41) independently predicted progression from NMIBC to MIBC (HR=1.81, 95% CI: 1.22–2.68). Similarly, Schuettfort et al. (14) (n = 4,335) and Takada et al. (8) (n = 235) demonstrated independent associations between low preoperative AGR and adverse survival outcomes after radical cystectomy.

The common feature of all these studies is that they primarily focused on survival and recurrence outcomes as their main endpoints. To the best of our knowledge, no study in the current literature has specifically addressed the association between preoperative AGR and pathological stage and tumor grade obtained after TURBT as its primary hypothesis. However, pathological stage and Grade at diagnosis constitute the foundation of clinical decision-making. The distinction between NMIBC and MIBC fundamentally alters the treatment modality, while tumor grade directly shapes management across a broad spectrum, ranging from the selection of intravesical therapy to the intensity of follow-up (5,14).

In this study, we aimed to investigate the association between preoperative AGR and pathological stage (NMIBC/MIBC) and tumor grade (low grade/high Grade) in patients who underwent TURBT for primary bladder tumors. Determining the independent contribution of this parameter, which can be calculated from routine preoperative biochemical panels without additional cost, to conventional clinical variables may contribute to preoperative risk stratification and individualized patient management in bladder cancer.

MATERIALS AND METHODS

Study Design and Ethical Approval

This study was a single-center prospective cohort study conducted at the Department of Urology, University of Health Sciences İzmir Bozyaka Training and Research Hospital. Patients were prospectively enrolled at the time of TURBT between March 2017 and February 2020 and followed according to a pre-specified data collection protocol. Patient recruitment was terminated in February 2020 due to the COVID-19 pandemic, after which the prospectively

collected data were statistically analyzed. The study was approved by the Clinical Research Ethics Committee of the University of Health Sciences İzmir Bozyaka Training and Research Hospital (Decision No: 3; Date: March 15, 2017). Written informed consent was obtained from all patients before inclusion in the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Selection

The inclusion criteria were defined as follows: patients who underwent transurethral resection of bladder tumor (TURBT) and were diagnosed with primary urothelial carcinoma on pathological examination; patients who underwent complete TURBT; patients with available laboratory data on preoperative serum total protein and albumin levels; and patients with sufficient clinical, operative, and pathological data.

The exclusion criteria were defined as follows: recurrent bladder tumor; history of preoperative chemotherapy or radiotherapy; known systemic inflammatory or autoimmune disease, such as rheumatoid arthritis or systemic lupus erythematosus; active infection or urinary tract infection in the preoperative period; history of concomitant malignancy; liver cirrhosis, nephrotic syndrome, poorly controlled diabetes mellitus, chronic kidney disease, or any disease directly affecting albumin metabolism; use of corticosteroids or immunosuppressive drugs; biochemical values obtained more than 30 days before surgery; incomplete resection or insufficient/pathologically unevaluable specimens.

According to these criteria, a total of 153 patients were included in the final analysis. A flow diagram summarizing the patient selection process is presented in Figure 1.

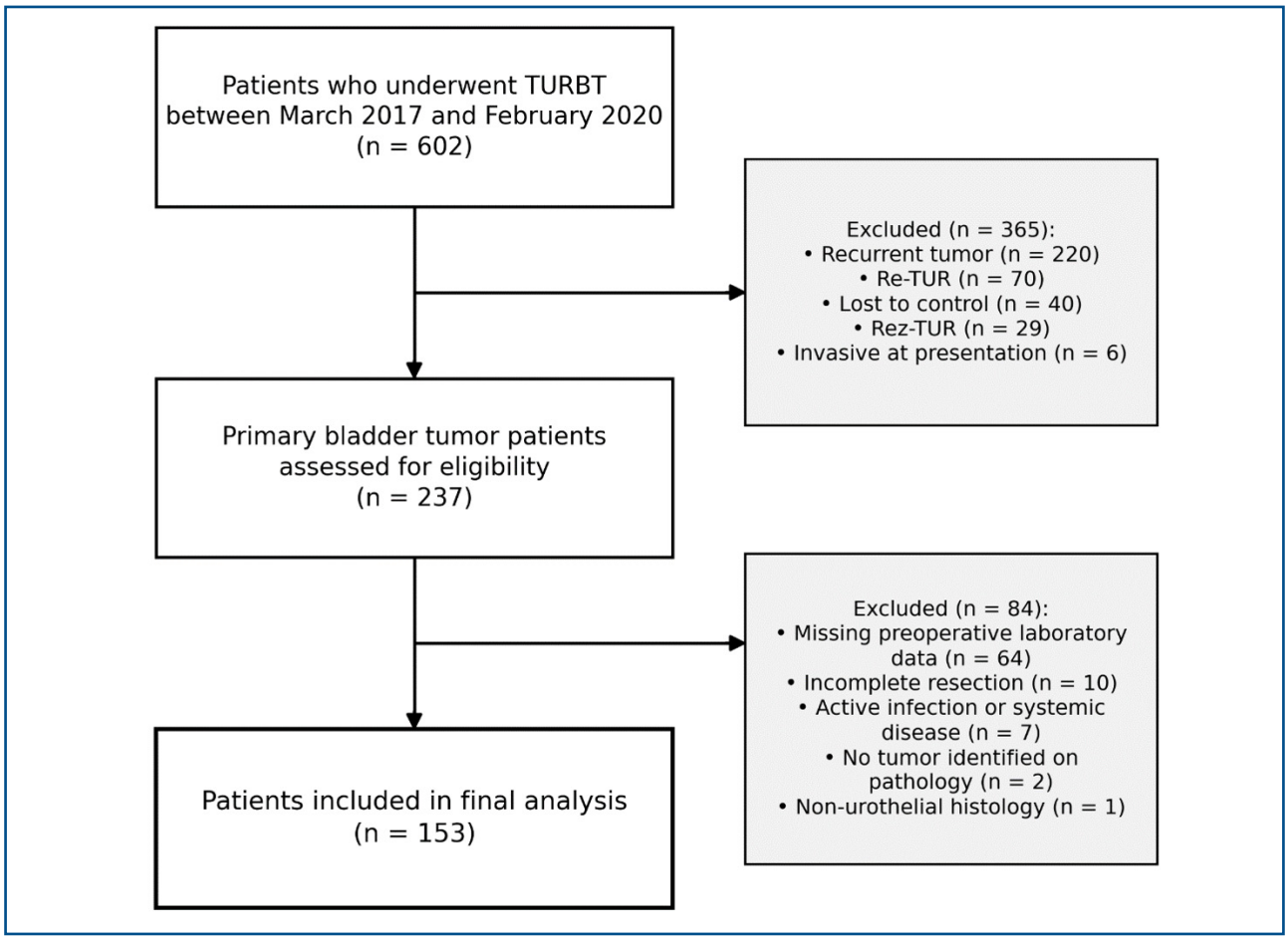


Figure 1. Flow diagram of patient selection

Surgical Procedure and Pathological Evaluation

All patients underwent macroscopically complete TURBT. Cases in which an incomplete resection was performed were not included in the study. Second look TURBT (re-TURBT) was routinely performed in patients with an indication in accordance with the recommendations of the EAU guidelines (15); the higher pathological result was considered for the determination of the final stage and Grade.

All resection specimens were evaluated in the institution's routine pathology laboratory. Pathological stage was determined according to the 2009 tumor-node-metastasis (TNM) classification system. Tumor grading was performed according to the World Health Organization/International Society of Urological Pathology (WHO/ISUP) 2004/2016 classification. The presence of concomitant carcinoma in situ (CIS) was also recorded separately (15).

Collection of Clinical and Pathological Data

The following data were prospectively recorded at the time of enrollment according to the study protocol, using a standardized data collection form, and subsequently verified against patient files and hospital information system records: age, sex, body mass index (BMI, kg/m^2), smoking status (absent/present), intraoperative total tumor size (cm) and number of tumors, transurethral resection (TUR) specimen volume (mL), and the presence of concomitant CIS.

Non-muscle-invasive bladder cancer (NMIBC) was defined as Ta and T1 disease, whereas muscle-invasive bladder cancer (MIBC) was defined as T2 disease. In terms of tumor grade, patients were dichotomized into low-grade and high-grade urothelial carcinoma groups. Cases diagnosed as papillary urothelial neoplasm of low malignant potential (PUNLMP) were included in the low-grade group.

Calculation of the Albumin-to-Globulin Ratio

Preoperative serum albumin and total protein levels were obtained from routine biochemical panels performed within 30 days before surgery. Globulin level was calculated as the difference between total protein and albumin [globulin (g/dL) = total protein (g/dL) – albumin (g/dL)]. The albumin-to-globulin ratio (AGR) was calculated using the following formula: AGR = albumin (g/dL) / [total protein (g/dL) – albumin (g/dL)].

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR), according to their distributional characteristics, whereas categorical variables were presented as frequencies and percentages (%). The normality of continuous variables was assessed for each group using the Shapiro-Wilk test. Variables with normal distribution were compared using the Student's t-test, while variables without normal distribution were compared using the Mann-Whitney U test. Categorical variables were analyzed using the Chi-square test; Fisher's exact test was applied when the expected cell frequency was less than 5.

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the discriminatory ability of AGR for pathological stage (NMIBC/MIBC) and tumor grade (low grade/high Grade). The area under the curve (AUC) and 95% confidence intervals (CIs) were calculated. AUC values and their 95% confidence intervals were obtained in SPSS. The shaded confidence band displayed around the ROC curve was estimated via bootstrap resampling (2,000 resamples) in Python (SciPy, scikit-learn). The optimal AGR cut-off value was determined using the Youden index [J = sensitivity + specificity – 1], which maximizes the sum of sensitivity and specificity. According to this cut-off value, patients were divided into low-AGR and high-AGR groups, and the distribution of stage and Grade between the groups was compared using the Chi-square test.

Logistic regression analysis was performed to determine the independent predictive value of AGR for MIBC and high-grade tumors. Variables showing statistical significance at a threshold of $p < 0.10$ in univariate analysis were included in the multivariate model. Candidate variables for the multivariate models — age, sex, body mass index (BMI), tumor size, tumor number, and the presence of CIS — were defined a priori based on clinical relevance. Age, sex, and BMI were retained in both multivariate models as standard demographic covariates regardless of their univariate statistical significance, consistent with established practice in clinical prediction modeling, whereas tumor size, tumor number, and CIS were included based on their univariate significance and their established relevance to tumor burden. Total protein, albumin, and globulin were not entered into the regression models together with AGR because of their direct mathematical relationship with this ratio. TUR specimen volume was excluded from the candidate variable pool because of its strong collinearity with tumor size and its intraoperative, rather than strictly preoperative, measurement. The CIS variable was excluded from the high-grade multivariate model because of complete separation, as no CIS cases were observed in the low-grade group. Univariate logistic regression results for all candidate variables are presented in Tables 4 and 6. Given the relatively small sample size — particularly within the MIBC subgroup (n = 31) — and the known instability of stepwise selection methods in such settings, all pre-specified variables were entered into the multivariate model simultaneously (Enter method) rather than through a stepwise selection procedure. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). A *p*-value of <0.05 was considered statistically significant in all analyses. The goodness-of-fit of each multivariable model was assessed using the Hosmer-Lemeshow test, and model discrimination was evaluated using the area under the receiver operating characteristic curve (AUC) with 95% confidence intervals, calculated from the predicted probabilities generated by each logistic regression model. To further explore an unexpected sign reversal observed for tumor number between univariable and multivariable analyses, a post hoc Spearman correlation analysis was performed to assess its association with tumor size and the presence of CIS. To evaluate whether AGR provided additional discriminatory value beyond its individual components, the AUC of AGR was compared with those of albumin, globulin, and total protein alone using DeLong's test for correlated ROC curves.

Given the early termination of patient recruitment due to the COVID-19 pandemic, a post hoc power analysis was performed (GPower 3.1, α=0.05) using the observed effect sizes as the basis for calculation (Cohen's d=0.594 for stage comparison and Cohen's d=0.582 for grade comparison). The existing sample of 153 patients was calculated to provide 84% statistical power for stage comparison and 94.6% statistical power for grade comparison, confirming that the 80% power threshold was exceeded for both analyses.

RESULTS

A total of 153 patients who underwent TURBT were included in the study. AGR was calculated from preoperative serum albumin and total protein values using the formula AGR = albumin / (total protein − albumin). The overall demographic, clinical, and biochemical characteristics of the cohort are summarized in Table 1.

The median age was 68 years (IQR: 59–75; mean ± SD: 67.3 ± 10.9). The majority of patients were male (n = 136, 88.9%). The median BMI was 26.6 kg/m^2 (IQR: 23.7–29.4), and active smoking was observed in 58.8% of patients. The median tumor size was 4.5 cm (IQR: 3.0–6.0), the median number of tumors was 2 (IQR: 1–4), and the median TUR specimen volume was 1.8 mL (IQR: 0.8–5.6). Concomitant carcinoma in situ (CIS) was present in 8 patients (5.2%).

Regarding pathological stage distribution, Ta, T1, and T2 disease were identified in 61 (39.9%), 61 (39.9%), and 31 (20.3%) patients, respectively. Tumor grade distribution was as follows: PUNLMP in 4 patients (2.6%), low-grade disease in 83 patients (54.2%), and high-grade disease in 66 patients (43.1%).

In the biochemical evaluation, the mean total protein level was 6.91 ± 0.66 g/dL, the mean albumin level was 3.91 ± 0.49 g/dL, and the mean globulin level was 3.00 ± 0.47 g/dL. The median AGR value of the cohort was 1.32 (IQR:

1.17–1.50; mean ± SD: 1.34 ± 0.28; minimum: 0.700, maximum: 2,294).

The NMIBC (Ta+T1, n = 122) and MIBC (T2, n = 31) groups were compared in terms of demographic and clinical characteristics. No statistically significant differences were observed between the two groups with respect to age, BMI, or smoking status ($p = 0.784$, $p = 0.538$, and $p = 0.781$, respectively). Sex distribution differed significantly between the groups, with a higher proportion of female patients in the MIBC group ($p = 0.048$). Tumor size and TUR specimen volume were significantly higher in the MIBC group ($p < 0.001$ for both). No statistically significant differences were observed in terms of tumor number or the presence of CIS ($p = 0.329$ and $p = 0.054$, respectively) (Table 2).

When biochemical parameters were evaluated, total protein and albumin levels alone did not reach statistical significance between the groups ($p = 0.806$ and $p = 0.076$, respectively). In contrast, globulin levels were significantly higher in the MIBC group (3.20 vs. 3.00 g/dL, $p = 0.041$). AGR was found to be markedly lower in the MIBC group compared with the NMIBC group (1.21 ± 0.24 vs. 1.37 ± 0.28; $p = 0.003$) (Table 2).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of AGR in predicting MIBC (Figure 2). According to the Youden index, the optimal AGR cut-off value was determined as 1.35 [AUC=0.649, 95% CI: 0.542–0.755; sensitivity 74.2%, specificity 50.8%]. When patients were divided into two groups according to this cut-off value, the rate of MIBC was 27.7% (23/83) in the low-AGR group (<1.35), whereas it was 11.4% (8/70) in the high-AGR group (≥1.35) ($p = 0.022$; Table 3).

Table 1. Overall Cohort Characteristics

	N = 153
Age (years), median (IQR); mean ± SD	68 (59–75); 67.3 ± 10.9
Sex, n (%) Male Female	 136 (88.9%) 17 (11.1%)
BMI (kg/m^2), median (IQR)	26.6 (23.7–29.4)
Smoking, Active, n (%)	90 (58.8%)
Tumor size (cm), median (IQR)	4.5 (3.0–6.0)
Number of tumors, median (IQR)	2 (1–4)
TUR specimen volume (mL), median (IQR)	1.8 (0.8–5.6)
CIS (+), n (%)	8 (5.2%)
Pathological stage, n (%) Ta T1 T2	 61 (39.9%) 61 (39.9%) 31 (20.3%)
Pathological Grade, n (%) PUNLMP Low Grade High Grade	 4 (2.6%) 83 (54.2%) 66 (43.1%)
Total protein (g/dL), mean ± SD	6.91 ± 0.66
Albumin (g/dL), mean ± SD	3.91 ± 0.49
Globulin (g/dL), median (IQR)	3.00 (2.60–3.30)
AGR, median (IQR); mean ± SD	1.32 (1.17–1.50); 1.34 ± 0.28

AGR: albumin-to-globulin ratio; BMI: body mass index; CIS: carcinoma in situ; IQR: interquartile range; PUNLMP: papillary urothelial neoplasm of low malignant potential; SD: standard deviation; TUR: transurethral resection.

Table 2. Comparison of the NMIBC (Ta+T1) and MIBC (T2) Groups

	NMIBC (Ta+T1) (n=122)	MIBC (T2) (n=31)	p
Age (years), mean ± SD	67.2 ± 10.6	67.8 ±12.0	0.784*
Gender, n (%) Male Female	 112 (%91.8) 10 (%8.2)	 24 (%77.4) 7 (%22.6)	 0.048**
BMI (kg/m^2), med (IQR)	26.4 (24.2–29.4)	27.0 (21.5–29.4)	0.538***
Smoking (Active), n (%)	73 (%59.8)	17 (%54.8)	0.781****
Tumor size (cm), med (IQR)	4.0 (2.5–6.8)	6.0 (5.0–8.0)	<0.001***
Number of tumors, med (IQR)	2 (1–3)	2 (1–3)	0.329***
TUR volume (mL), med (IQR)	1.6 (0.6–5.0)	6.8 (5.4–10.5)	<0.001***
CIS (+), n (%)	4 (%3.3)	4 (%12.9)	0.054**
Total protein (g/dL), mean ± SD	6.92 ± 0.64	6.89 ± 0.74	0.806*
Albumin (g/dL), mean ± SD	3.95 ± 0.45	3.75 ± 0.59	0.076*
Globulin (g/dL), med (IQR)	3.00 (2.60–3.30)	3.20 (2.85–3.50)	0.041***
AGR, mean ± SD	1.37 ± 0.28	1.21 ± 0.24	0.003*

AGR: albumin-to-globulin ratio; BMI: body mass index; CIS: carcinoma in situ; IQR: interquartile range; MIBC: muscle-invasive bladder cancer; NMIBC: non-muscle-invasive bladder cancer; SD: standard deviation; TUR: transurethral resection.
*Student's t-test, **Fisher's exact test, ***Mann-Whitney *U* test, ****Chi-square Test

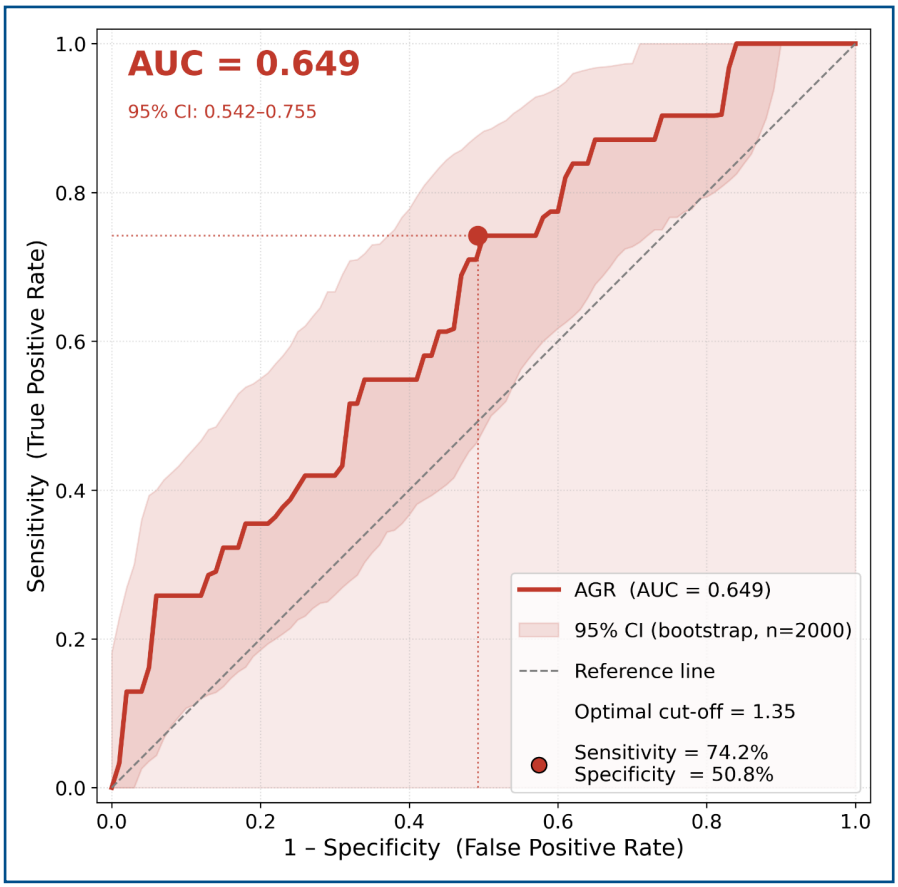


Figure 2. ROC curve of the albumin-to-globulin ratio (AGR) for predicting muscle-invasive bladder cancer. Optimal cut-off: 1.35 (AUC = 0.649, 95% CI: 0.542–0.755; sensitivity 74.2%, specificity 50.8%). Shaded area represents the 95% confidence band estimated by bootstrap resampling (2,000 resamples).

Table 3. Distribution of Stage and Grade According to AGR Groups (Cut-off: 1.35)

	Low AGR (<1.35) (n=83)	High AGR (≥1.35) (n=70)	p
NMIBC (Ta+T1), n (%) MIBC (T2), n (%)	60 (72.3%) 23 (27.7%)	62 (88.6%) 8 (11.4%)	0.022*
Low Grade, n (%) High Grade, n (%)	36 (43.4%) 47 (56.6%)	51 (72.9%) 19 (27.1%)	<0.001*

AGR: albumin-to-globulin ratio; MIBC: muscle-invasive bladder cancer; NMIBC: non-muscle-invasive bladder cancer.

* Chi-square Test

In the univariate logistic regression analysis, AGR was identified as a significant predictor of MIBC (OR=0.10, 95% CI: 0.02–0.52, $p = 0.007$). In the multivariate model including age, sex, BMI, tumor size, tumor number, and CIS, AGR remained independently associated with MIBC (OR=0.16, 95% CI: 0.03–0.97, $p = 0.046$). In the same model, tumor size (OR=1.34, 95% CI: 1.12–1.60, $p = 0.002$), tumor number (OR=0.79, 95% CI: 0.63–0.98, $p = 0.035$), the presence of CIS (OR=7.19, 95% CI: 1.34–38.56, $p = 0.021$), and female sex (OR=3.50, 95% CI: 1.02–12.06, $p = 0.047$) were also independently associated with MIBC (Table 4). The MIBC prediction model demonstrated adequate calibration (Hosmer-Lemeshow test: χ^2=6,085, df=8, $p = 0.638$) and acceptable discriminative ability (AUC=0.773, 95% CI: 0.682–0.865). In a post hoc exploratory analysis performed to investigate the sign reversal observed for tumor number, Spearman correlation analysis revealed a moderate positive correlation between tumor number and tumor size ($r = 0.522$, $p < 0.001$), and a weak positive correlation between tumor number and the presence of CIS ($r = 0.167$, $p = 0.039$).

For the purpose of grade-based comparisons, PUNLMP cases (n = 4) were included in the low-grade group, resulting in 87 low-grade and 66 high-grade patients. Low-grade (n = 87) and high-grade (n = 66) groups were compared. Patients in the high-grade group were significantly older ($p = 0.007$). No significant differences were observed between the groups in terms of BMI or smoking status ($p = 0.801$ and $p = 0.634$, respectively). Sex distribution did not differ significantly between the two groups ($p = 0.100$). Tumor size, tumor number, and TUR specimen volume were significantly higher in the high-grade group ($p < 0.001$, $p = 0.035$, and $p < 0.001$, respectively). CIS was observed only in the high-grade group ($p = 0.001$) (Table 5).

When biochemical parameters were evaluated, total protein levels did not differ significantly between the groups ($p = 0.559$). In contrast, albumin levels were significantly lower ($p = 0.022$), whereas globulin levels were significantly higher in the high-grade group ($p = 0.031$). AGR was markedly lower in the high-grade group ($p < 0.001$) (Table 5).

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of AGR in predicting high-grade tumors (Figure 3). According to the Youden index, the optimal AGR cut-off value was determined as 1.35 [AUC=0.656, 95% CI: 0.568–0.744; sensitivity 69.7%, specificity 60.9%]. The rate of high-grade tumors was 56.6% (47/83) in the low-AGR group (<1.35), whereas it was 27.1% (19/70) in the high-AGR group (≥1.35) ($p < 0.001$) (Table 3).

In the univariate logistic regression analysis, AGR was identified as a strong predictor of high-grade tumors (OR=0.10, 95% CI: 0.03–0.40, $p = 0.001$). Since the CIS variable resulted in complete separation in the high-grade group, as no CIS cases were present in the low-grade group, it was excluded from the multivariate model. In the multivariate model including age, sex, BMI, tumor size, and tumor number, AGR remained independently associated with high-grade disease (OR=0.18, 95% CI: 0.04–0.74, $p = 0.018$). Tumor size was also independently associated with high-grade disease in this model (OR=1.19, 95% CI: 1.02–1.37, $p = 0.023$; Table 6). The high-grade prediction model similarly demonstrated adequate calibration (Hosmer-Lemeshow test: χ^2=10,940, df=8, $p = 0.205$) and acceptable discriminative ability (AUC=0.736, 95% CI: 0.657–0.815).

Table 4. Logistic regression, MIBC (T2) predictors.

	Univariable OR (95%CI)	p	Multivariable OR (95%CI)	p
AGR	0.10 (0.02–0.52)	0.007	0.16 (0.03–0.97)	0.046
Tumor size (cm)	1.24 (1.08–1.42)	0.002	1.34 (1.12–1.60)	0.002
Number of tumors	1.01 (0.87–1.18)	0.879	0.79 (0.63–0.98)	0.035
Presence of CIS	4.37 (1.03–18.59)	0.046	7.19 (1.34–38.56)	0.021
Sex (female vs. male)	3.27 (1.13–9.45)	0.029	3.50 (1.02–12.06)	0.047
Age (years)	1.01 (0.97–1.04)	0.766	0.99 (0.95–1.03)	0.506
BMI (kg/m^2)	0.98 (0.90–1.07)	0.707	0.97 (0.89–1.07)	0.583

AGR: albumin-to-globulin ratio; BMI: body mass index; CI: confidence interval; CIS: carcinoma in situ; OR: odds ratio.

Table 5. Comparison of low-grade and high-grade groups.

	Low Grade (n=87)	High Grade (n=66)	p
Age (years), median (IQR)	64 (59–71)	71 (61–80)	0.007*
Gender, n (%) Male Female	 81 (%93.1) 6 (%6.9)	 55 (%83.3) 11 (%16.7)	 0.100**
BMI (kg/m^2), med (IQR)	26.3 (24.1–29.4)	27.2 (23.2–29.7)	0.801*
Smoking (Active), n (%)	53 (%60.9)	37 (%56.1)	0.634**
Tumor size (cm), med (IQR)	3.0 (2.0–5.5)	5.0 (4.0–8.0)	<0.001*
Number of tumors, med (IQR)	2 (1–3)	2 (1–4)	0.035*
TUR volume (mL), med (IQR)	1.3 (0.5–4.2)	5.1 (2.5–8.9)	<0.001*
CIS (+), n (%)	0 (%0.0)	8 (%12.1)	0.001***
Total protein (g/dL), mean ± SD	6.94 ± 0.65	6.88 ± 0.68	0.559****
Albumin (g/dL), med (IQR)	4.00 (3.80–4.30)	3.90 (3.43–4.28)	0.022*
Globulin (g/dL), med (IQR)	3.00 (2.60–3.20)	3.10 (2.80–3.48)	0.031*
AGR, mean ± SD	1.40 ± 0.28	1.25 ± 0.25	<0.001****

AGR: albumin-to-globulin ratio; BMI: body mass index; CIS: carcinoma in situ; IQR: interquartile range; PUNLMP: papillary urothelial neoplasm of low malignant potential; SD: standard deviation; TUR: transurethral resection.
PUNLMP cases (n = 4) were included in the low-grade group (total low-grade n = 87).
*Mann-Whitney *U* test, **Chi-square Test, ***Fisher's exact test, ****Student's t-test

ROC analyses performed for both clinical endpoints, namely MIBC and high-grade disease, yielded an AUC of 0.649 (95% CI: 0.542–0.755) for the prediction of MIBC and 0.656 (95% CI: 0.568–0.744) for the prediction of high-grade tumors. Notably, the optimal cut-off value determined by the Youden index overlapped at 1.35 in both analyses. Binary group comparisons according to the optimal cut-off value (AGR=1.35) are presented in Table 3.

DISCUSSION

In this study, preoperative AGR was shown to be independently associated with pathological stage (NMIBC/MIBC) and tumor grade (low grade/high Grade) in 153 patients who underwent TURBT for primary bladder tumor. AGR was significantly lower in the MIBC group (1.21 ± 0.24 vs. 1.37 ± 0.28; $p = 0.003$), and multivariate logistic regression analysis demonstrated that AGR was independently associated with MIBC (OR=0.16, 95% CI: 0.03–0.97; $p = 0.046$). Similarly, AGR was markedly lower in patients with high-grade tumors (1.25 ± 0.25 vs. 1.40 ± 0.28; $p < 0.001$), and AGR remained independently associated with high-grade disease (OR=0.18, 95% CI: 0.04–0.74; $p = 0.018$). The overlap of

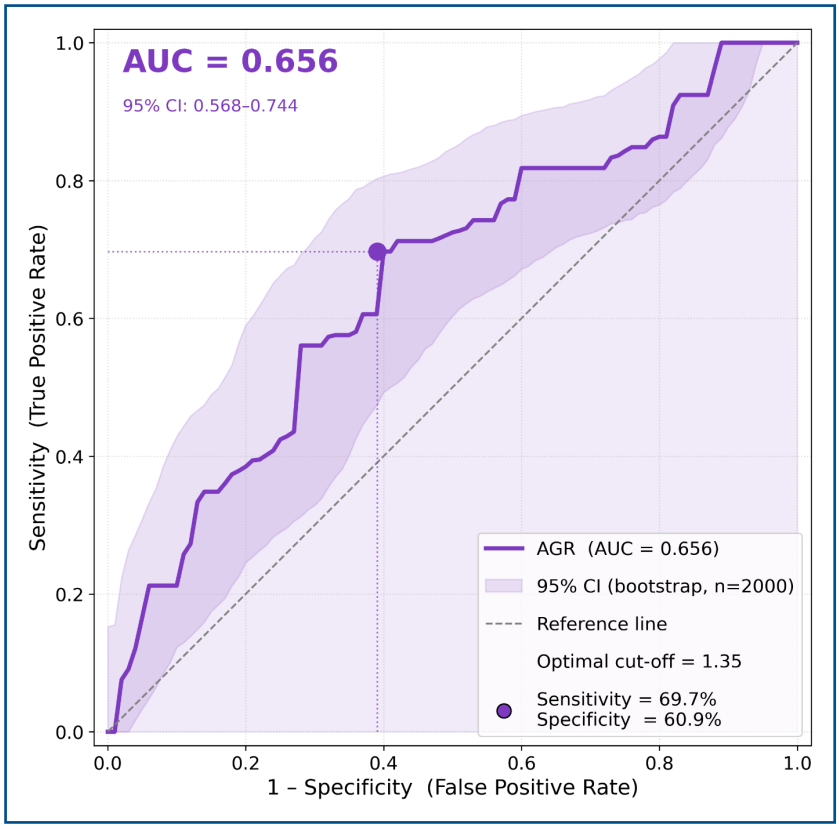


Figure 3. ROC curve of the albumin-to-globulin ratio (AGR) for predicting high-grade bladder tumor. Optimal cut-off: 1.35 (AUC = 0.656, 95% CI: 0.568–0.744; sensitivity 69.7%, specificity 60.9%). Shaded area represents the 95% confidence band estimated by bootstrap resampling (2,000 resamples).

Table 6. Logistic regression, high-grade predictors.

	Univariable OR (95%CI)	p	Multivariable OR (95%CI)	p
AGR	0.10 (0.03–0.40)	0.001	0.18 (0.04–0.74)	0.018
Tumor size (cm)	1.23 (1.09–1.38)	0.001	1.19 (1.02–1.37)	0.023
Number of tumors	1.14 (1.00–1.30)	0.050	1.00 (0.84–1.18)	0.959
Presence of CIS	Not estimable*	—	Excluded*	—
Sex (female vs. male)	2.70 (0.94–7.73)	0.064	2.87 (0.85–9.70)	0.091
Age (years)	1.04 (1.01–1.08)	0.009	1.03 (0.99–1.07)	0.098
BMI (kg/m^2)	1.01 (0.94–1.09)	0.714	1.03 (0.95–1.12)	0.456

AGR: albumin-to-globulin ratio; BMI: body mass index; CI: confidence interval; OR: odds ratio.

*CIS could not be estimated in the univariable analysis and was excluded from the multivariable model because no CIS cases were observed in the low-grade group (complete separation).

the optimal cut-off value at 1.35, as determined by the Youden index in both ROC analyses, provides clinicians with a single and practical threshold value.

Tumor size remained independently associated with both outcomes in the multivariate models, suggesting that AGR may provide a more meaningful predictive profile when used in combination with established clinical parameters rather than as a stand-alone marker. This finding also indicates that while AGR reflects systemic alterations associated with the biological aggressiveness of the tumor, it maintains an independent association with clinicopathological factors.

An additional statistical observation warrants comment: the number of tumors showed no significant association with MIBC in univariable analysis (OR=1.01, 95% CI: 0.87–1.18, $p = 0.879$), yet became significantly and independently associated with MIBC, with a reversed direction of effect. In this post hoc, exploratory analysis, the number of tumors was moderately correlated with tumor size (Spearman r = 0.52, $p < 0.001$) and, to a lesser extent, with the presence of CIS (r = 0.17, $p = 0.039$), both of which were themselves strong positive predictors of MIBC. In the unadjusted analysis, this positive confounding by tumor size and CIS masked the true negative partial association between tumor number and MIBC; once tumor size and CIS were accounted for in the multivariable model, this masked association became apparent. Given the relatively low events-per-variable ratio in the MIBC model (31 events for 7 covariates), this specific finding should nonetheless be interpreted with caution, as coefficient estimates for covariates with modest individual effect sizes may be sensitive to sample size constraints in addition to genuine suppression effects.

AGR is a biomarker whose prognostic significance has been extensively investigated in various malignancies. Roberts et al. (7) reviewed 61 studies including 18 different cancer types and reported that AGR showed a statistically significant association with at least one prognostic variable in multivariate analysis. In a meta-analysis conducted by Xia et al. (10) in patients with urothelial carcinoma, including 12 studies and 5,727 patients, low preoperative AGR was shown to have independent prognostic significance for overall survival (HR=1.99, 95% CI: 1.45–2.75), cancer-specific survival (HR=2.01, 95% CI: 1.50–2.69), and recurrence-free survival (HR=1.39, 95% CI: 1.12–1.72). These findings were further confirmed in a meta-analysis of urologic cancers, including 21 studies and 18,269 patients, in which low AGR was significantly associated with overall survival (HR=1.93, 95% CI: 1.56–2.39), cancer-specific survival (HR=2.22, 95% CI: 1.67–2.96), and recurrence-free survival (HR=1.69, 95% CI: 1.29–2.22) (11). However, survival and recurrence outcomes were the primary endpoints in all of these studies. To our knowledge, the present study is the first to evaluate pathological stage and tumor grade after TURBT as primary outcomes in relation to preoperative AGR.

The globulin fraction includes acute-phase proteins such as immunoglobulins, complement components, C-reactive protein, and fibrinogen. The chronic inflammatory process accompanying tumor growth increases the synthesis of these proteins, thereby elevating globulin levels. Moreover, tumor-related immunosuppression and inflammatory stimulation may also enhance immunoglobulin secretion from B lymphocytes, further contributing to increased globulin levels (9).

AGR is an integrated biomarker that reflects both nutritional reserve and the immunoinflammatory balance within a single parameter. Since total protein includes both components, individual changes may offset and thereby mask each other when total protein is evaluated alone. In the present study, total protein did not differ significantly in either the MIBC or high-grade groups ($p = 0.806$ and $p = 0.559$, respectively); however, globulin levels were significantly elevated in both groups (MIBC: $p = 0.041$; high Grade: $p = 0.031$), while albumin levels were significantly decreased in the high-grade group ($p = 0.022$). To formally test this, the ROC-AUC of AGR was compared against albumin, globulin, and total protein alone using DeLong's test. AGR showed a numerically higher AUC than each individual component for both MIBC (0.649 vs. 0.591, 0.619, and 0.509, respectively) and high-grade disease (0.656 vs. 0.608, 0.602, and 0.489, respectively); however, this difference reached statistical significance only when AGR was compared with total protein in the high-grade model ($p = 0.009$), while differences from albumin and globulin individually did not reach significance (all $p \geq 0.11$), likely reflecting the limited statistical power of this single-center cohort. These findings offer only partial support for the superiority of AGR as a ratio over its individual components and should be interpreted with appropriate caution.

Niwa et al. (4) suggested that combining albumin and globulin into a single ratio may reveal alterations that could be missed when each component is assessed separately. Takada et al. (8) emphasized that blood-based biomarkers such as AGR, neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein-to-albumin ratio (CAR) may provide complementary information regarding physiological reserve and biological tumor burden that cannot be captured

by imaging or conventional pathological staging, as they reflect both nutritional and inflammatory status. They also highlighted that chronic inflammation directly shapes the tumor microenvironment by promoting angiogenesis, tumor cell survival, invasion, and metastasis.

No study in the literature has investigated the association between AGR and pathological stage after TURBT in primary bladder tumor as a primary endpoint. Therefore, our findings were evaluated within the framework of studies that examined similar mechanisms but used different methodologies and outcome measures.

In their multicenter study including 1,096 patients with NMIBC, Quhal et al. (5) demonstrated that low preoperative AGR (<1.41) was an independent predictor of progression to MIBC (HR=1.81, 95% CI: 1.22–2.68; $p = 0.003$). Unlike the present study, pathological T-stage distribution and tumor grade did not differ between AGR groups at baseline in that cohort ($p = 0.77$ and $p = 0.21$, respectively), as its design evaluated progression risk during longitudinal follow-up rather than pathological stage at diagnosis.

Niwa et al. (4) evaluated 364 patients with primary NMIBC and found that low AGR (<1.6) was an independent predictor of tumor recurrence (multivariate HR=0.53, 95% CI: 0.36–0.78; $p < 0.01$). In the same study, low AGR was also reported to be significantly associated with progression to muscle invasion in univariate analysis (HR=0.24, 95% CI: 0.10–0.56; $p < 0.01$); however, multivariate analysis for progression was not performed. In that study, pathological T category and tumor grade did not differ significantly between AGR groups at baseline; however, the effect of AGR on the biological course of the disease was reflected in follow-up outcomes. In the present study, by contrast, this strong association was directly reflected in pathological staging at diagnosis, further emphasizing the predictive value of pre-TURBT AGR measurement for estimating pathological outcomes.

Schuettfort et al., (14) in a large multicenter series of 4,335 patients, reported a significant association between low AGR and pathological ≥pT3 disease after radical cystectomy (OR=1.15, 95% CI: 1.01–1.31; $p = 0.04$). However, pathological T-stage distribution did not differ significantly between AGR groups in that study ($p = 0.23$). This finding pertains to a radical cystectomy cohort and therefore has limited direct comparability with our TURBT-based results. In addition, the incorporation of AGR into existing clinical models was reported not to provide a meaningful improvement in AUC (ΔAUC <1%). In contrast, in the present study, AGR was independently associated with MIBC in multivariate analysis, together with tumor size, tumor number, the presence of CIS, and sex. This discrepancy may partly be attributable to differences in patient population heterogeneity, as patients undergoing radical cystectomy generally have more advanced tumors at baseline, and to the fact that the distinction between NMIBC and MIBC can be more clearly captured in the TURBT setting.

Omura et al. (13) evaluated 179 patients with UTUC and demonstrated, using the Chi-square test, that low preoperative AGR (<1.25) was significantly associated with pathological T stage ≥T3 ($p < 0.01$) and lymph node involvement N1–3 ($p < 0.01$). Despite differences in tumor location and treatment modality, namely radical nephroureterectomy, these findings are conceptually consistent with those of the present study. They suggest that the association between low AGR and more advanced pathological stage may not be limited to bladder cancer but may reflect a common biological pattern across urothelial carcinoma.

No study in the current literature has evaluated the association between AGR and pathological tumor grade in primary bladder tumor as a primary endpoint. In this context, the closest basis for comparison is provided by studies reporting the relationship between AGR and Grade as a secondary pathological finding in patients with UTUC.

Xu et al., (12) in their study including 620 patients with UTUC, investigated the association between low preoperative AGR (<1.45) and adverse pathological outcomes using multivariate logistic regression. They demonstrated that low

AGR was an independent predictor of high-grade tumor (OR=2.35, 95% CI: 1.62–3.42; $p < 0.001$), ≥pT2 stage (OR=1.34; $p < 0.001$), and lymphovascular invasion (OR=1.91; $p = 0.005$). This study provides one of the strongest pieces of evidence in the literature demonstrating the relationship between AGR and pathological Grade at the multivariate level. In the present study, a similar association was observed for high-grade disease, with an OR of 0.18. Despite the difference in tumor location, the consistency of the underlying biological mechanism is noteworthy.

In the study by Omura et al. (13), tumor grade alone was not significantly associated with AGR <1.25, whereas the dominant association was observed through pathological T stage. This finding suggests that the AGR-grade relationship may not have the same strength under all conditions and may vary according to patient population, cut-off value, and tumor characteristics.

The observation that CIS was present only in the high-grade group ($p = 0.001$), thereby causing complete separation in the multivariate grade model, should be considered an important methodological point. Since CIS is, by WHO/ISUP definition, classified as high-grade disease, this finding is an expected consequence of this classification rather than an independent biological validation, and should not be interpreted as additional evidence beyond what is already implied by the grading system itself.

In this study, the optimal AGR cut-off value determined by the Youden index was 1.35 for the prediction of both MIBC and high-grade disease. When the AGR cut-off values used in the literature are reviewed, they appear to range widely between 1.25 and 1.60: Xu et al. (12) reported 1.45, Otsuka et al. (9) 1.40, Schuettfort et al. (14) 1.42, Quhal et al. (5) 1.41, Omura et al. (13) 1.25, and Niwa et al. (4) 1.60. The cut-off value of 1.35 identified in the present study lies within the middle of this range. Notably, the cut-off of 1.35 identified in the present study closely approximates the mean AGR cut-off of 1,356 reported for overall survival across 61 studies in the systematic review by Roberts et al. (7), suggesting cross-methodological consistency.

The variation in cut-off values reported in the literature may be attributable to heterogeneity in patient populations, tumor location and biology, differences in statistical methods such as ROC-based approaches versus reference range-based thresholds, and interinstitutional variation in laboratory measurement conditions. Takada et al. (8) emphasized that ROC-based cut-off determination involves data-specific optimization and may therefore lead to optimism bias when applied to different cohorts; they further suggested that thresholds based on institutional reference ranges may be more reliable in terms of interinstitutional consistency and reproducibility. Establishing a universal AGR cut-off value specific to urothelial carcinoma requires large-scale prospective studies.

The considerable variability in the AGR cut-off values reported across the literature is noteworthy; values in existing studies range from 1.25 to 1.60. This variability can largely be attributed to differences in the patient populations studied: higher thresholds have generally been reported in NMIBC cohorts (4,5), whereas lower values have been observed in upper urinary tract urothelial carcinoma (9,16) and radical cystectomy series (17,18), with an intermediate value reported in a grade-specific cohort (19). Given this variability, it appears more realistic to regard AGR not as a fixed, binary cut-off but as a continuous risk indicator to be interpreted alongside established clinicopathological parameters. Indeed, in the present cohort, a low AGR value (particularly when accompanied by large tumor size, multiple tumors, or the presence of CIS) may raise preoperative suspicion for MIBC or high-grade disease, prompting closer intraoperative assessment during TURBT and, when warranted, earlier multidisciplinary discussion. On the other hand, given the modest sensitivity and specificity observed in our study, we wish to emphasize that a high AGR value alone should not be used to exclude the possibility of advanced-stage or high-grade disease. Until the cut-off value is validated in external cohorts and, ideally, institution-specific reference ranges are established, we suggest that AGR be used not as an independent decision-making tool, but as a supportive indicator contributing to existing preoperative risk assessment.

To date, no study has formally incorporated AGR into existing risk stratification tools (such as the EAU risk groups (15) or the EORTC (20) and CUETO (21) scoring systems) by adding it as a variable and recalibrating these nomograms accordingly. The closest evidence available comes from two sources. In a large NMIBC cohort, low AGR was not significantly associated with either recurrence-free survival ($p = 0.59$) or progression-free survival ($p = 0.22$) within any EAU risk group once patients were stratified accordingly (5). Along similar lines, a panel of systemic inflammatory biomarkers that included AGR was tested, using machine-learning methods, for predicting upstaging to MIBC, lymph node involvement, and advanced pathological stage in a radical cystectomy cohort, but was found to add only limited discriminative value beyond established clinicopathological variables (22). Together, these findings suggest that AGR may not offer an independent contribution beyond what existing risk stratification systems already provide; it should be kept in mind, however, that this evidence is drawn from a small number of studies and does not directly test integration into the EAU, EORTC, or CUETO frameworks. Whether incorporating AGR into such models would add value specifically for predicting pathological stage and grade (the focus of the present study) has not yet been tested, and this remains an open question for future prospective, externally validated research.

This study has several important methodological strengths. First, its prospective design allowed the implementation of a standardized protocol for patient selection and data collection, thereby minimizing retrospective selection bias. The early termination of patient recruitment due to the COVID-19 pandemic does not substantially compromise the methodological strength of the prospective design, as the post hoc power analysis demonstrated that the 80% threshold was exceeded for both comparisons.

The inclusion of only primary tumors eliminated the confounding effect arising from the distinct biological behavior of recurrent tumors and the potential influence of prior intravesical therapies on AGR. Similarly, the systematic exclusion of patients with active infection, autoimmune disease, hepatic pathology, nephrotic syndrome, or immunosuppressive drug use enabled control of the major confounders that could directly affect AGR levels independently of tumor biology. In this respect, the design of our study provided a setting in which the relationship between AGR and tumor biology could be evaluated in as purified a context as possible. Quhal et al. (5) also applied similar exclusion criteria in their multicenter design.

For stage and grade determination, re-TURBT was performed in accordance with EAU guideline recommendations, and the final pathological result was used as the basis for analysis. This approach helps overcome the common problems of insufficient muscle-containing specimens and understaging encountered in initial TURBT specimens, particularly with respect to stage and grade determination, thereby increasing the reliability of pathological assessment (4). Finally, the fact that the Youden index indicated the same cut-off value (1.35) in independent analyses for both clinical endpoints provide clinicians with a single threshold that is easy to remember and apply.

Several important limitations of this study should be considered. First, its single-center design limits the external validity and generalizability of the findings. This limitation becomes more evident when compared with multicenter designs such as the multicenter study by Quhal et al. (n = 1,096) and the large multicenter cohort by Schuettfort et al. (n = 4,335) (5,14). Multicenter prospective studies and external validation cohorts are required to confirm the validity of our findings in different populations. Second, the exclusion criteria applied in this study were comprehensive: as shown in the flow diagram (Figure 1), 84 of 237 eligible primary tumor patients (35.4%) were excluded, most commonly due to missing preoperative laboratory data (n = 64), followed by incomplete resection (n = 10) and active infection or systemic disease (n = 7). While these criteria were necessary to minimize confounding of the AGR measurement, this comprehensive exclusion process may have resulted in a selected cohort that does not fully represent the broader, real-world population of patients undergoing TURBT for primary bladder tumor, which should be considered when interpreting the generalizability of our findings.

Early termination of recruitment due to the COVID-19 pandemic resulted in a smaller-than-intended sample, which may have reduced statistical power for subgroup analyses and limits the generalizability of findings — particularly for the MIBC subgroup (n = 31). Post hoc power analysis confirmed that the 80% threshold was exceeded for both primary comparisons; nevertheless, certain associations may remain undetected in this sample. Furthermore, given the relatively low events-per-variable ratio in the MIBC multivariate model (31 events for 7 covariates), coefficient estimates — including that of AGR — should be interpreted with appropriate caution, as they showed some sensitivity to covariate specification in sensitivity analyses.

The AUC values of AGR in both analyses (MIBC: 0.649, 95% CI: 0.542–0.755; high Grade: 0.656, 95% CI: 0.568–0.744) indicate moderate discriminatory ability. This finding suggests that AGR would be insufficient as a stand-alone decision-making biomarker and should instead be evaluated in combination with existing clinicopathological variables. This result is also consistent with the findings of Schuettfort et al. (14), in which the addition of AGR to existing models did not provide a meaningful improvement in AUC .

The higher proportion of female patients in the MIBC group ($p = 0.048$) indicates a potential demographic imbalance. Although this variable was controlled for in the multivariate model, the interpretation of the association between sex and MIBC requires caution in a predominantly male cohort (n = 136, 88.9%). Furthermore, the absence of follow-up data precludes evaluation of the association between preoperative AGR and long-term clinical outcomes such as recurrence, disease progression, and survival. This naturally limits the scope of interpretation of the present findings.

CONCLUSION

Preoperative AGR was independently associated with MIBC and high-grade disease in this single-center cohort; however, its incremental clinical value and generalizability require external validation. The absence of previous studies addressing this question as a primary endpoint in the current literature provides an original contribution to our findings.

Acknowledgments: The authors have no acknowledgments to declare.

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

Funding: This study received no external funding.

Ethical Approval: This study was approved by the Clinical Research Ethics Committee of University of Health Sciences İzmir Bozyaka Training and Research Hospital (Decision No: 3; Date: March 15, 2017). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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

Author Contributions: Concept and Design: MEA, İB, DB, AA — Data Collection: MEA, İB, DB — Data Analysis and Interpretation: GC, İHB, SÇ, DB, TD — Writing the Manuscript: MEA, İB, GC, AA — Review of Manuscript Content: GC, İHB, EŞ, SÇ, TD — Statistical Analysis: MEA, İHB, EŞ, SÇ, AA, TD — Supervision: MEA, İB, İHB, EŞ, DB, AA

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):239–248. doi: 10.54233/endourolbull-1896965

Diagnostic Value of Dual-Energy CT Attenuation Ratios for Urinary Stone Characterization in Patients Presenting with Acute Abdominal Pain

Akut Karın Başvurularında Üriner Taş Karakterizasyonunda Dual-Enerji BT Atenüasyon Oranlarının Tanısal Değeri

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ABSTRACT

Objective: To evaluate attenuation ratios derived from dual-energy computed tomography (DECT) in patients presenting with acute abdominal pain who were diagnosed with urinary stone disease, and to analyze their distribution among different stone categories in a real-world emergency setting.

Materials and Methods: This prospective single-center study was conducted in the emergency department of a tertiary referral hospital. A total of 210 consecutive adult patients presenting with acute abdominal pain underwent DECT examination. Among these, 56 patients diagnosed with urolithiasis on non-contrast DECT were included in the final analysis. Attenuation values were measured at 80 kVp and 140 kVp, and attenuation ratios were calculated. Stone size, localization, and number were recorded. Differences among stone types were analyzed using One-Way ANOVA or the Kruskal-Wallis test, depending on the normality of data distribution. Post-hoc comparisons were performed using Bonferroni or Games-Howell tests based on the homogeneity of variances.

Results: The mean attenuation ratio across all stones was 1.32 ± 0.20. Uric acid stones demonstrated the lowest mean attenuation ratio (0.96 ± 0.09), whereas hydroxyapatite (1.54 ± 0.07) and calcium oxalate stones (1.40 ± 0.05) showed significantly higher values ($p < 0.001$). Statistically significant differences were observed among stone categories in terms of low-energy attenuation, high-energy attenuation, and attenuation ratios ($p < 0.001$). No significant differences were found regarding age or stone size. Distinct clustering patterns were observed, particularly between uric acid and calcium-containing stones.

Conclusion: DECT-derived attenuation ratios demonstrated significant differentiation among urinary stone types in patients presenting with acute abdominal pain. These findings support the clinical utility of DECT for non-invasive stone characterization in the emergency setting.

Keywords: tomography, x-ray computed, urinary calculi, urolithiasis, absorptiometry, photon, emergency service, hospital

Cite As: *Yesilyurt M, Kantarci A. Diagnostic Value of Dual-Energy CT Attenuation Ratios for Urinary Stone Characterization in Patients Presenting with Acute Abdominal Pain. Endourol Bull. 2026;18(3):239–248.* https://doi.org/10.54233/endourolbull-1896965

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Received : February 25, 2026 ***Accepted*** : June 6, 2026

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ÖZET

Amaç: Bu çalışmada, akut karın ağrısı ile başvuran ve üriner taş hastalığı tanısı alan hastalarda dual enerji bilgisayarlı tomografi (DEBT) ile elde edilen atenüasyon oranlarının değerlendirilmesi ve farklı taş tipleri arasındaki dağılımının gerçek yaşam acil servis pratiğinde analiz edilmesi amaçlandı.

Gereç ve Yöntemler: Bu prospektif, tek merkezli çalışmada üçüncü basamak bir hastanenin acil servisinde akut karın ağrısı nedeniyle dual-enerji bilgisayarlı tomografi (DEBT) uygulanan 210 ardışık erişkin hasta değerlendirildi. Non-kontrast DEBT'de ürolitiazis saptanan 56 hasta analize dahil edildi. Taşların 80 kVp ve 140 kVp düzeylerindeki atenüasyon değerleri ölçülerek atenüasyon oranları hesaplandı. Taş boyutu, lokalizasyonu ve sayısı kaydedildi. Sürekli değişkenlerin normal dağılıma uygunluğu Shapiro-Wilk ve Kolmogorov-Smirnov testleri ile incelendi. Taş tipleri arasındaki farkların analizinde, parametrik varsayımların karşılandığı durumlarda Tek Yönlü Varyans Analizi (ANOVA), karşılanmadığı durumlarda ise Kruskal-Wallis testi kullanıldı. Gruplar arası ikili karşılaştırmalarda (post-hoc), varyansların homojenliğine göre Bonferroni veya Games-Howell testleri tercih edildi.

Bulgular: Tüm taşlarda ortalama atenüasyon oranı 1,32 ± 0,20 olarak bulundu. Ürik asit taşları en düşük ortalama atenüasyon oranını gösterirken (0,96 ± 0,09), hidroksiapatit (1,54 ± 0,07) ve kalsiyum oksalat taşlarında anlamlı derecede daha yüksek oranlar saptandı ($p < 0,001$). Taş tipleri arasında düşük enerji, yüksek enerji atenüasyon değerleri ve atenüasyon oranları açısından istatistiksel olarak anlamlı farklılık vardı ($p < 0,001$). Yaş ve taş boyutu açısından anlamlı fark izlenmedi. Özellikle ürik asit ve kalsiyum içeren taşlar arasında belirgin kümelenme gözlendi.

Sonuçlar: DEBT ile elde edilen atenüasyon oranları, akut karın ağrısı ile başvuran hastalarda üriner taş tiplerinin ayırımında anlamlı farklılık göstermektedir. Bu bulgular, acil servis pratiğinde non-invaziv taş karakterizasyonunda DEBT'nin klinik değerini desteklemektedir.

Anahtar Kelimeler: tomografi, X-ışınlı bilgisayarlı, üriner kalküller, ürolitiyazis, absorpsiyometri, foton, acil servis, hastane

INTRODUCTION

Urinary stone disease is a common condition with increasing global prevalence and a substantial burden on healthcare systems. Lifetime prevalence has been reported between 6–15% in many populations and continues to rise worldwide (1). Acute flank pain caused by urinary calculi represents one of the most frequent causes of emergency department admissions, requiring rapid and accurate diagnostic imaging for timely management (2).

Non-contrast helical computed tomography (CT) is currently considered the imaging modality of choice for detecting urinary calculi due to its high sensitivity and specificity (2). In addition to accurate detection, CT provides valuable information regarding stone size and localization. However, conventional single-energy CT has limited capability in determining stone composition. Although Hounsfield unit (HU) measurements may offer indirect information, significant overlap exists among different stone chemistries, reducing the reliability of single-energy attenuation values for definitive compositional assessment (3).

Dual-energy CT (DECT) has emerged as a valuable imaging modality that utilizes attenuation differences at two distinct energy spectra to improve material differentiation. Early clinical and experimental studies demonstrated that DECT enables reliable discrimination between uric acid and non-uric acid stones (4,5). Subsequent investigations confirmed that energy-dependent attenuation characteristics allow improved stone characterization compared to conventional CT (6,7). Quantitative approaches based on attenuation ratios derived from paired low- and high-energy datasets have been proposed as practical and reproducible tools for urinary stone classification (7,8). Advanced post-processing techniques further enhance compositional analysis and diagnostic confidence (8,9).

From a clinical standpoint, non-invasive identification of stone composition is particularly relevant in acute abdominal

presentations. Uric acid stones may respond to medical dissolution therapy, whereas calcium-containing stones more frequently require interventional procedures (8,10). Several studies have emphasized the potential role of DECT in guiding management decisions and optimizing therapeutic planning in urolithiasis (4,10).

Despite growing evidence supporting the role of DECT in urinary stone characterization, many published investigations have been conducted in controlled or experimental settings, including in vitro or ex vivo analyses (4,5). Data reflecting routine emergency department practice and real-world attenuation ratio distributions remain comparatively limited.

Therefore, in this single-center study, we aimed to assess DECT-derived attenuation ratios in patients presenting with urinary stone disease among acute abdominal presentations and to analyze their distribution across different stone categories in a real-world emergency setting.

MATERIALS AND METHODS

Study Design and Patient Population

This prospective single-center study was approved by the institutional ethics committee (Approval Number: B.30.2.ATA.0.01.00/277, Date: October 4, 2018). Written informed consent was obtained from all participants prior to enrollment, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

The study was carried out in the emergency department of a tertiary referral hospital. A total of 210 consecutive adult patients presenting with acute abdominal pain underwent dual-energy CT (DECT) examination. Among these patients, individuals presenting with acute flank pain and diagnosed with urinary stone disease on non-contrast DECT were considered eligible. The present study represents a predefined subgroup analysis of a broader prospective emergency department cohort undergoing DECT evaluation for acute abdominal presentations. In the present study, the term “acute abdominal pain” refers to the overall emergency department cohort, whereas “acute flank pain” specifically describes the subgroup of patients with suspected urolithiasis included in the final analysis.

Patients aged 18 years or older with at least one urinary stone detected on DECT were included in the study. Patients with incomplete imaging data, insufficient image quality preventing reliable attenuation measurements, prior intervention affecting stone morphology, or significant motion artifacts were excluded. Ultimately, 56 patients met the eligibility criteria and were included in the final analysis.

For each patient, demographic data including age and sex were recorded, along with stone localization, number of stones, and maximum long-axis diameter (mm). When multiple stones were present, attenuation measurements were performed separately for each stone. Attenuation values at 80 kVp and 140 kVp were measured, and attenuation ratios were subsequently calculated.

CT Acquisition Protocol

All examinations were performed using a 256-slice dual-source multidetector CT scanner (Somatom Definition Flash; Siemens Healthineers, Forchheim, Germany). The system is equipped with two X-ray tubes and corresponding detectors positioned at approximately 95° angular offset within the gantry, enabling simultaneous dual-energy acquisition. Dual-energy imaging was performed using tube voltage settings of 80 kVp and 140 kVp. Automatic tube current modulation (CARE Dose 4D; Siemens Healthineers) was applied to optimize radiation exposure. The detector configuration was 32 × 0.6 mm with a gantry rotation time of 500 ms and a pitch of 0.6. The field of view was 50 cm for Tube A and 33 cm for Tube B. Non-contrast acquisition was performed for urinary stone evaluation. Images were reconstructed with a slice thickness of 1 mm and transferred to a dedicated workstation (Syngo Via, version 2.0; Siemens Healthineers) for post-processing and analysis. Circular regions of interest (ROIs) were manually placed on axial images over the largest cross-sectional area of each stone, carefully avoiding adjacent soft tissue and minimizing

partial-volume effects. Attenuation values were recorded separately for 80 kVp and 140 kVp datasets, and attenuation ratios were calculated using matched dual-energy datasets.

Image Analysis

For each urinary stone, circular regions of interest (ROIs) were manually placed on axial images over the largest cross-sectional area of the stone on both low-energy (80 kVp) and high-energy (140 kVp) datasets. ROIc were positioned centrally within the stone to minimize partial-volume effects and to avoid inclusion of adjacent soft tissue. When multiple stones were identified in the same patient, measurements were performed for each stone individually.

The following parameters were recorded for each stone: low-energy attenuation value (HU), high-energy attenuation value (HU), and attenuation ratio calculated as the quotient of low-energy HU divided by high-energy HU. Attenuation ratios were used to evaluate differences among stone categories.

Stone size was measured as the maximum long-axis diameter on axial images. All measurements were performed using the institutional PACS workstation under standardized viewing conditions. Image analysis was performed independently by two radiologists with 8 and 5 years of experience in abdominal radiology, respectively. Both readers were blinded to the clinical and laboratory data during attenuation measurements and stone characterization. Interobserver agreement for attenuation measurements was assessed using the intraclass correlation coefficient (ICC).

Stone classification was based on dual-energy attenuation characteristics consistent with previously reported ranges in the literature (4,5,7). Stones were categorized as calcium oxalate, hydroxyapatite, uric acid, or cystine according to their dual-energy attenuation characteristics and attenuation ratio profiles.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics software (version 20.0; IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation, median, minimum, and maximum values, while categorical variables were expressed as frequencies and percentages.

Normality of continuous variables was assessed using the Shapiro–Wilk test for sample sizes <50 and the Kolmogorov–Smirnov test for sample sizes ≥50. For comparisons between two independent groups, the Independent Samples t-test was used when normal distribution was satisfied, and the Mann-Whitney U test was applied otherwise. For comparisons among more than two independent groups, one-way analysis of variance (ANOVA) was performed when parametric assumptions were met, and the Kruskal–Wallis test was used when they were not. Following ANOVA, post hoc analyses were conducted using the Bonferroni correction when variances were homogeneous and the Games-Howell test when homogeneity assumptions were violated.

Effect sizes for ANOVA analyses were evaluated using eta squared (η^2). According to conventional criteria, η^2 values of 0.01, 0.06, and 0.14 were interpreted as small, medium, and large effect sizes, respectively. A 2-sided p-value < 0.05 was considered statistically significant.

Interobserver agreement for attenuation measurements was evaluated using the intraclass correlation coefficient (ICC). ICC values greater than 0.90 were considered indicative of excellent agreement.

RESULTS

A total of 56 patients with urolithiasis were included in the analysis. Excellent interobserver agreement was achieved between the two readers for attenuation measurements, with an intraclass correlation coefficient (ICC) of 0.92.

Among these patients, 19 (33.9%) were female and 37 (66.1%) were male. The mean age was 51.3 ± 13.16 years. Demographic characteristics, stone localization, stone type distribution, and number of stones are summarized in Table 1. Stone localization was most commonly observed in the ureter (44.6%) and calyceal system (35.7%), followed by the bladder (16.1%) and renal pelvis (3.6%).

Regarding stone size distribution, 16 patients (28.6%) had stones measuring ≤5 mm, 32 patients (57.1%) had stones between 6–15 mm, 6 patients (10.7%) had stones between 16–20 mm, and 2 patients (3.6%) had stones ≥20 mm (Table 2). The mean stone long-axis diameter was 8.53 ± 4.92 mm.

Overall descriptive statistics for age, stone size, attenuation values, and attenuation ratios are presented in Table 3. Across the entire cohort, the mean attenuation value at low energy (80 kVp) was 1,182.14 ± 351.02 HU, and at high energy (140 kVp) was 887.55 ± 177.81 HU. The mean attenuation ratio (80 kVp / 140 kVp) was 1.32 ± 0.20.

Based on dual-energy CT analysis, stones were categorized as calcium oxalate in 30 patients (53.6%), hydroxyapatite in 8 patients (14.3%), uric acid in 10 patients (17.9%), and cystine in 8 patients (14.3%) (Table 1).

Comparative analysis of stone types is summarized in Table 4. When evaluated according to stone composition, calcium oxalate stones demonstrated a mean attenuation ratio of 1.40 ± 0.05, hydroxyapatite stones 1.54 ± 0.07, uric acid stones 0.96 ± 0.09, and cystine stones 1.26 ± 0.15. Statistically significant differences were observed among stone types in terms of low-energy attenuation values, high-energy attenuation values, and attenuation ratios ($p < 0.001$ for all comparisons).

Table 1. Demographic and stone-related characteristics of patients with urolithiasis (n = 56)

Variable	Category	n	%
Sex	Female	19	33.9
	Male	37	66.1
Localization	Calyx	20	35.7
	Renal pelvis	2	3.6
	Ureter	25	44.6
	Bladder	9	16.1
Stone Type	Calcium oxalate	30	53.6
	Hydroxyapatite	8	14.3
	Uric acid	10	17.9
	Cystine	8	14.3
Number of Stones	Single	40	71.4
	Multiple	16	28.6

Table 2. Distribution of stone size according to maximum long-axis diameter (n = 56)

Stone size (mm)	n	%
≤ 5	16	28.6
6–15	32	57.1
16–20	6	10.7
≥ 20	2	3.6

Post hoc comparisons demonstrated significant differences in attenuation ratios among several stone categories, particularly between uric acid stones and calcium-containing stones, as detailed in Table 4. No statistically significant differences were found among stone types with respect to patient age or stone size.

The distribution of attenuation ratios according to stone type is illustrated in Figure 1, demonstrating clear clustering patterns, particularly between uric acid stones and calcium-containing stones.

A representative dual-energy CT case demonstrating attenuation measurements and material characterization is shown in Figure 2.

DISCUSSION

In the present study, we evaluated dual-energy CT (DECT)–derived attenuation ratios in patients presenting with acute abdominal pain who were diagnosed with urinary stone disease. Our findings demonstrated statistically significant differences in both attenuation values and attenuation ratios among stone categories. Most notably, uric acid stones demonstrated distinctly lower attenuation ratios compared with calcium-containing stones, supporting the clinical utility of DECT-based compositional analysis in the emergency setting.

Table 3. Descriptive statistics of demographic and dual-energy CT parameters (n = 56)

Variable	Mean	SD	Median	Minimum	Maximum
Age (years)	51.30	13.16	49.00	28.00	79.00
Stone size (mm)	8.53	4.92	7.45	2.30	25.00
Low-energy attenuation (80 kVp, HU)	1182.14	351.02	1227.00	466.00	1976.00
High-energy attenuation (140 kVp, HU)	887.55	177.81	894.50	535.00	1240.00
Attenuation ratio (80/140 kVp)	1.32	0.20	1.39	0.81	1.65

Table 4. Comparison of dual-energy CT parameters according to stone type

Variable	Calcium Oxalate (n = 30)	Hydroxyapatite (n = 8)	Uric Acid (n = 10)	Cystine (n = 8)	Test statistic	p	Effect Size (η^2)
Age (years), mean ± SD	51.37 ± 11.98	52.88 ± 10.01	57.00 ± 17.66	42.38 ± 11.19	5.143	0.162	-
Stone size (mm), mean ± SD	8.48 ± 5.59	8.05 ± 3.48	8.69 ± 3.94	9.03 ± 5.33	0.517	0.915	-
Low-energy attenuation (80 kVp, HU), mean ± SD	1334.67 ± 194.67 ^{c}	1413.38 ± 367.20 ^{c}	661.70 ± 145.85 ^{a,b,d}	1029.50 ± 273.02 ^{c}	43.163	<0.001	0.72
High-energy attenuation (140 kVp, HU), mean ± SD	959.87 ± 135.28 ^{c}	922.38 ± 211.26 ^{c}	719.90 ± 120.77 ^{a,b}	791.13 ± 186.09 ^{a}	7.436	<0.001	0.36
Attenuation ratio (80/140 kVp), mean ± SD	1.40 ± 0.05 ^{b,c}	1.54 ± 0.07 ^{a,c,d}	0.96± 0.09 ^{a,b,d}	1.26 ± 0.15 ^{b,c}	8.560	<0.001	0.81

Note: Data are presented as mean ± SD. Groups with different superscript letters differ significantly from each other based on Bonferroni or Games-Howell post-hoc analyses ($p < 0.05$). Effect size was calculated using eta squared (η^2).

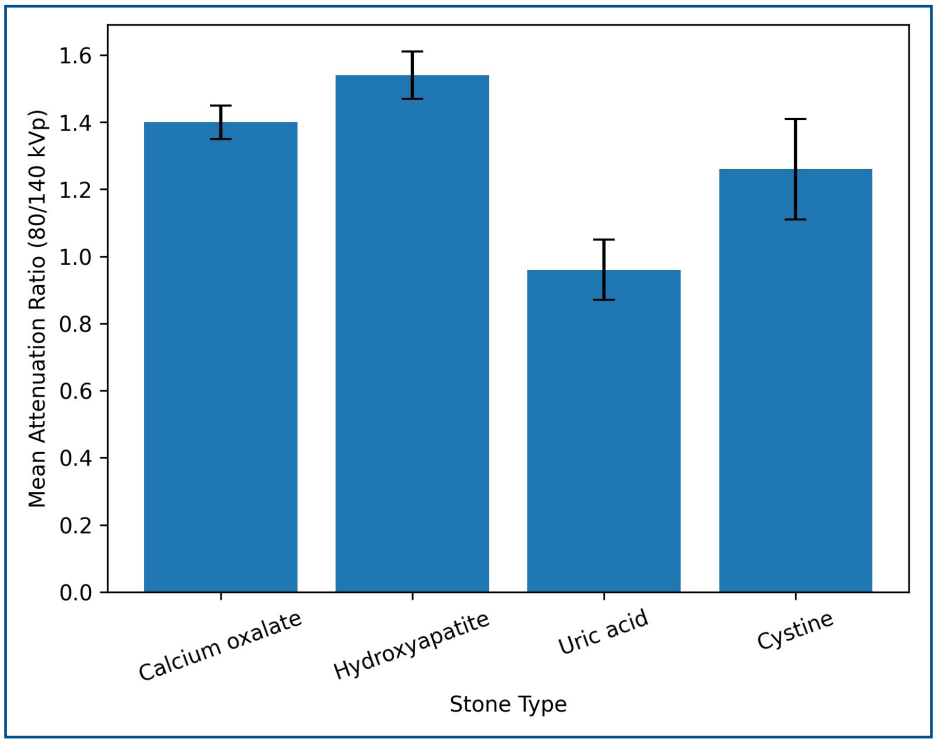


Figure 1. Distribution of mean attenuation ratios according to urinary stone type. Uric acid stones demonstrate significantly lower attenuation ratios compared with calcium-containing stones.

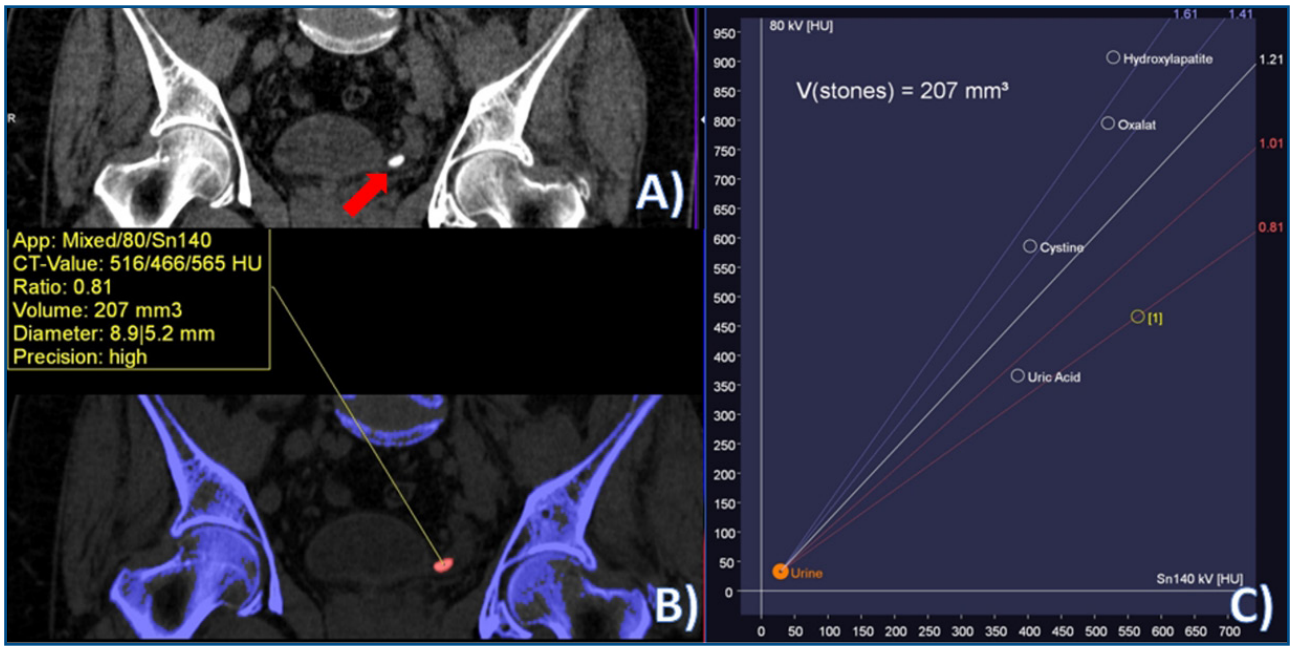


Figure 2. Representative dual-energy CT images of a urinary stone demonstrating attenuation measurements and material characterization. (A) Axial non-contrast image showing a distal ureteral stone (arrow). (B) Dual-energy material decomposition image with region-of-interest (ROI) placement. Attenuation values measured at 80 kVp and 140 kVp are displayed, and the calculated attenuation ratio is provided. (C) Dual-energy attenuation distribution plot illustrating the energy-dependent separation of the stone, supporting material classification based on attenuation characteristics. The calculated attenuation ratio is consistent with uric acid composition.

Non-contrast CT has long been established as the imaging modality of choice for the evaluation of suspected urolithiasis due to its high sensitivity and specificity (2,11). However, conventional single-energy CT provides limited information regarding stone composition, as attenuation values measured in Hounsfield units often overlap among different stone types (3). Previous investigations have demonstrated that attenuation-based differentiation using single-energy CT is unreliable for definitive compositional analysis, particularly among calcium-containing subtypes (3). Our findings further support the utility of energy-dependent techniques to improve material discrimination.

Dual-energy CT enables material characterization by exploiting differences in X-ray attenuation at two distinct energy spectra. Early in vitro and clinical studies by Graser et al. (4) and Stolzmann et al. (5) demonstrated that DECT can reliably differentiate uric acid stones from non-uric acid stones. Similarly, Primak et al. (7) showed that attenuation ratios derived from paired dual-energy datasets provide reproducible discrimination between uric acid and non-uric acid stones. In agreement with these reports, our study demonstrated a clear separation of uric acid stones, which exhibited the lowest mean attenuation ratio (0.96 ± 0.09), while hydroxyapatite and calcium oxalate stones demonstrated significantly higher ratios.

Our results also revealed statistically significant differences among calcium oxalate, hydroxyapatite, cystine, and uric acid stones in terms of attenuation ratios. Hydroxyapatite stones demonstrated the highest attenuation ratios, whereas cystine stones showed intermediate values with partial overlap. Similar observations have been reported in previous clinical studies, which noted that while DECT performs excellently in binary differentiation (uric acid vs. non-uric acid), overlap may occur among certain non-uric acid subtypes (8,9,12). Therefore, although attenuation ratios provide valuable classification information, absolute cut-off thresholds may vary depending on scanner platform, acquisition parameters, and post-processing algorithms.

From a clinical perspective, accurate non-invasive identification of stone composition may have potential therapeutic implications. Uric acid stones may be treated with urinary alkalinization and medical dissolution therapy, potentially avoiding invasive procedures (10). Therefore, early identification of uric acid stones using DECT-derived attenuation ratios may help support more individualized treatment planning, particularly in emergency department settings where rapid therapeutic decision-making is required. In contrast, calcium-containing stones frequently require interventional management such as ureteroscopy or extracorporeal shock wave lithotripsy. Previous studies have emphasized the possible role of DECT in supporting treatment planning and management strategies (8,10). However, the present study did not include direct analyses of treatment decisions, patient management changes, or clinical outcomes. Therefore, the clinical impact of DECT-derived attenuation ratios should be interpreted cautiously.

Another relevant aspect is radiation exposure. Low-dose CT protocols have been widely adopted in the evaluation of renal colic (13), and advances in multidetector CT technology have enabled optimized acquisition protocols while maintaining diagnostic accuracy (11,14). Modern dual-source DECT systems allow simultaneous acquisition without substantially increasing radiation dose compared with conventional single-energy CT (15). Therefore, incorporation of dual-energy protocols into routine emergency imaging may be feasible without compromising patient safety.

Despite these promising findings, several limitations should be acknowledged. First, stone composition was not confirmed by reference standard methods such as chemical analysis or infrared spectroscopy in any of the cases. Instead, stone classification was based on dual-energy attenuation characteristics consistent with previously reported literature ranges (4,5,7). Although this approach reflects real-world clinical practice, the absence of reference standard compositional confirmation limits definitive validation. Second, the study was conducted at a single center, and certain stone subgroups, particularly hydroxyapatite and cystine stones—had relatively small sample sizes. These limited subgroup sizes may have reduced the statistical power of subgroup comparisons and may restrict the generalizability of the findings. Third, attenuation ratio thresholds may be scanner-specific, and results may not be

directly transferable across different DECT platforms. In addition, formal diagnostic performance analyses including ROC-derived cutoff values, sensitivity, and specificity were not performed due to the relatively small subgroup sizes and the absence of chemical reference standard analysis.

Nevertheless, the present study reflects routine emergency department practice and provides real-world attenuation ratio distribution data among different urinary stone types. The statistically significant separation observed between uric acid and calcium-containing stones reinforces the potential role of DECT as a clinically meaningful adjunct tool in the evaluation of acute urolithiasis.

CONCLUSION

In conclusion, dual-energy CT–derived attenuation ratios demonstrated significant differences among urinary stone categories in patients presenting with acute abdominal pain. Clear clustering patterns were observed, particularly between uric acid and calcium-containing stones. These findings support the integration of DECT-based attenuation analysis into emergency imaging protocols for non-invasive urinary stone characterization.

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

Funding: This study received no external funding.

Ethics Approval: This study was approved by the Ethics Committee of Atatürk University (Approval No: B.30.2.ATA.0.01.00/277, Date: October 4, 2018). The study was conducted in accordance with the principles of the Declaration of Helsinki.

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

Acknowledgment: The authors declare that there are no acknowledgments.

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):249–260. doi: 10.54233/endourolbull-1976766

Occupational Radiation Safety and Stone Analysis Practices Among Urologists in Türkiye: A National Cross-Sectional Survey

Türkiye'deki Ürologlar Arasında Mesleki Radyasyon Güvenliği ve Taş Analizi Uygulamaları: Ulusal Bir Kesitsel Araştırma

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ABSTRACT

Objective: To evaluate real-world occupational radiation-safety and post-procedural stone-analysis practices among urologists in Türkiye, and associated factors.

Materials and Methods: A cross-sectional, web-based survey was e-mailed to 2,305 urologists in Türkiye. The Google Forms questionnaire covered demographic, institutional, radiation-safety, and stone-analysis/metabolic-evaluation practices. Categorical comparisons used the Chi-square or Fisher's exact test, and independent factors were assessed with multivariable logistic regression.

Results: Of 346 respondents, 301 were analysed after excluding incomplete responses (61.5% specialists, 23.6% residents, 14.9% academics). A personal dosimeter was unavailable to 68.1%, regular dosimeter feedback was absent in 62.8%, a statutory radiation leave was not granted to 99.0%, and a periodic medical examination was not performed in 81.4%. Lead aprons (95.3%) and thyroid shields (81.7%) were common, whereas protective eyewear (20.6%) and gloves (9.3%) were rare. Routine stone analysis was performed by 47.5%; an in-house analysis facility was available to only 25.9% (0% of state-hospital respondents), while 78.7% referred specimens to an external institute. Metaphylaxis was applied by 56.1%. Routine analysis was independently associated with academic title (OR 2.85) and an in-house facility (OR 3.07), and inversely with >10 years' experience (OR 0.25); metaphylaxis was associated with university (OR 3.99) and training-and-research (OR 2.40) hospital practice.

Conclusion: Occupational radiation protection and guideline-recommended stone analysis are incompletely implemented and vary widely among urologists in Türkiye. The fact that a statutory radiation leave was granted to only 1.0% of respondents, together with the institution-dependent availability of stone analysis, indicates that systemic and regulatory measures, not individual awareness alone, are needed.

Keywords: metaphylaxis, occupational exposure, radiation protection, stone analysis, surveys and questionnaires, urolithiasis

Cite As: *Demirkiran ED, Madendere S, Deger MD, Yildiz HA. Occupational Radiation Safety and Stone Analysis Practices Among Urologists in Türkiye: A National Cross-Sectional Survey. Endourol Bull. 2026;18(3):249–260.* https://doi.org/10.54233/endourolbull-1976766

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Received : June 22, 2026 ***Accepted*** : August 10, 2026

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ÖZET

Amaç: Türkiye'deki ürologların mesleki radyasyon güvenliği ve işlem sonrası taş analizi konusundaki gerçek hayattaki uygulamalarını ve bu uygulamalarla ilişkili faktörleri değerlendirmek.

Gereç ve Yöntemler: Türkiye'deki 2,305 üroloğa e-posta yoluyla kesitsel, web tabanlı bir anket gönderilmiştir. Google Formlar aracılığıyla hazırlanan anket, demografik ve kurumsal özellikleri, radyasyon güvenliği uygulamalarını ve taş analizi/metabolik değerlendirme uygulamalarını kapsamaktadır. Kategorik karşılaştırmalarda ki-kare testi veya Fisher testi kullanılmıştır; bağımsız faktörler ise çok değişkenli lojistik regresyon ile değerlendirilmiştir.

Bulgular: Eksik yanıtlar hariç tutulduktan sonra 346 katılımcıdan 301'i analiz edildi (%61.5'i uzman, %23.6'sı asistan, %14.9'u akademisyen). Katılımcıların %68.1'i kişisel dozimetreye sahip değildi, %62.8'i dozimetre sonuçları hakkında düzenli geri bildirim almıyordu, %99.0'ına yasal radyasyon izni verilmemişti ve %81.4'ü periyodik tıbbi muayeneye tabi tutulmamıştı. Kurşun önlükler (%95.3) ve tiroid kalkanları (%81.7) yaygınken, koruyucu gözlükler (%20.6) ve eldivenler (%9.3) nadirdi. Rutin taş analizi %47.5 oranında gerçekleştirilmiştir; kurum içi analiz imkânı yalnızca %25.9'unda mevcuttu (devlet hastanesi katılımcılarının %0'ında), %78.7'si ise numuneleri harici bir kuruma sevk etmiştir. Metafilaksi %56.1 oranında uygulanmıştır. Rutin analiz, akademik unvan (OR 2.85) ve kurum içi analiz imkânı (OR 3.07) ile pozitif, 10 yıldan fazla deneyim (OR 0.25) ile ise negatif ilişkiliydi; metafilaksi ise üniversite (OR 3.99) ve eğitim-araştırma (OR 2.40) hastanelerinde çalışmakla ilişkiliydi.

Sonuçlar: Mesleki radyasyondan korunma ve kılavuzlarda önerilen taş analizi, Türkiye'deki ürologlar arasında tam olarak uygulanmamakta ve büyük farklılıklar göstermektedir. Yasal radyasyon izninin katılımcıların yalnızca %1'ine verilmiş olması ve taş analizinin kurumlara bağlı olarak değişkenlik göstermesi, yalnızca bireysel farkındalığın değil, sistematik ve düzenleyici önlemlerin de gerekli olduğunu göstermektedir.

Anahtar Kelimeler: anketler ve soru formları, mesleki maruziyet, metafilaksi, radyasyondan korunma, taş analizi, ürolitiyazis

INTRODUCTION

Urinary stone disease is among the most common urological conditions worldwide, with reported lifetime prevalence ranging from approximately 5–9% in Europe and 7–13% in North America, and an estimated prevalence of around 11–15% in Türkiye (1,2). Its incidence has risen over recent decades, and the recurrence rate approaches 50% within 10-years of an initial episode, making long-term prevention an integral part of management (2,3).

Contemporary management of urinary stones has shifted overwhelmingly towards minimally invasive endourological techniques such as ureteroscopy and percutaneous nephrolithotomy, the majority of which rely on intraoperative fluoroscopy; fluoroscopic guidance also remains the standard imaging modality for extracorporeal shock-wave lithotripsy (SWL) in many centres, despite growing interest in ultrasound-guided alternatives (4). As these procedures have multiplied, so has the occupational ionising-radiation burden borne by urologists and operating-room staff, with documented associations between cumulative exposure and cataract formation and malignancy (5,6). The principle of keeping exposure "As Low As Reasonably Achievable" (ALARA), the dose limits defined by the International Commission on Radiological Protection (ICRP), and the routine use of personal dosimetry and shielding are therefore cornerstones of safe endourological practice (7,8). Yet surveys across several countries have repeatedly shown incomplete adoption of these measures (6,9,10).

The second pillar of stone care that depends heavily on real-world practice is secondary prevention. Current European Association of Urology (EAU) guidelines recommend that an attempt be made to analyse the stone in every patient—ideally by infrared spectroscopy or X-ray diffraction—together with a basic metabolic work-up for all stone formers and an extended evaluation for those at high risk of recurrence (11,12). Stone composition guides targeted metaphylaxis, and reliable analysis is therefore the entry point to recurrence prevention (12,13). Nonetheless, comprehensive metabolic evaluation is reported to be performed in only a minority of stone formers internationally (14).

Real-world data on how urologists in Türkiye approach these two domains -occupational radiation safety and post-procedural stone analysis- are scarce, and the supporting infrastructure (dosimetry services, statutory radiation leave, in-house stone-analysis laboratories) varies between institution types. Both domains are increasingly regarded as quality indicators of comprehensive stone-disease management: unsafe radiation practice exposes the treating team to avoidable long-term risk, while inadequate stone analysis undermines evidence-based secondary prevention; the present survey therefore examined them jointly as complementary markers of endourological care quality. The present national survey was designed to describe these practices, quantify the variation between practitioner and institutional groups, and identify factors independently associated with guideline-concordant behaviour.

MATERIALS AND METHODS

Study Design and Participants

This was a cross-sectional, questionnaire-based study conducted among urologists (residents, specialists, and academic faculty) practising in Türkiye in 2025. An invitation to participate was sent by e-mail to 2,305 urologists. The questionnaire was created in Google Forms and was self-administered; participation was voluntary and anonymous, and informed consent was obtained on the first page of the form before any item was displayed. A total of 346 responses were received (15.0% of those invited); after excluding 45 incomplete or inappropriate responses, 301 responses were included in the analysis (13.1% of those invited). Responses were classified as incomplete if key sections addressing radiation-safety or stone-analysis practices were left unanswered, and as inappropriate if submitted by respondents outside the target population (e.g., trainees or physicians outside urology) or as apparent duplicate entries from the same respondent. Reporting of the web-based survey followed the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) where applicable (15).

Questionnaire

The questionnaire was developed by the study group and pilot-tested among 15 urologists to assess clarity, comprehensibility, item interpretation, and completion time. Minor wording and formatting revisions were made before national distribution. As only minor revisions were required after pilot testing, responses from the 15 pilot participants were retained and included in the final analytic sample (n = 301). The instrument comprised three domains. The first captured demographic and institutional characteristics (academic title, institution type, age group, and years in practice, including residency). The second addressed occupational radiation safety: procedures performed without a safety guidewire or without fluoroscopy, availability and type of a personally allocated dosimeter, regularity of dosimeter measurement and feedback, availability of personal protective equipment, granting of an annual statutory radiation leave, periodic occupational medical examination, and difficulty in accessing a shared fluoroscopy unit. The third domain addressed stone analysis and secondary prevention: routine post-procedural stone analysis, availability of an in-house analysis facility, referral of specimens to an external mineral-research institute for analysis, intraoperative stone-sampling behaviour in semirigid ureteroscopy (URS), flexible URS and mini-percutaneous nephrolithotomy (mini-PNL), application of metaphylaxis, provision of dietary and lifestyle advice, the patient groups selected for metabolic evaluation, and access to specific metabolic tests. Multiple-response options were permitted where indicated. The full survey instrument (English translation) is provided as a Supplementary File (Appendix 1) to facilitate replication and future comparative survey design.

Stone Analysis Referral Pathway

In Türkiye, where dedicated in-hospital crystallographic analysis is frequently unavailable, urologists may refer retrieved stone specimens for compositional analysis to an external public geological institute (the General Directorate of Mineral Research and Exploration). Referral to this institute was recorded as a distinct practice variable.

Ethics

This study was approved by the Ethics Committee for Non-Interventional Clinical Research at Zonguldak Bülent

Ecevit University at its meeting dated May 13, 2020 (No. 2020/10), regarding the research titled "An Investigation of Differences in Clinical Approaches Among Urologists in Turkey: Prostate Biopsy, Urinary Tract Stone Disease, and Interdisciplinary Collaborations," was unanimously approved as compliant with the ethics committee's principles.

Approval for the study was obtained from the local ethics committee, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent was obtained from all participants.

Statistical Analysis

Categorical variables were summarised as frequencies and percentages. For analysis, academic title was grouped as resident, specialist, and academic (assistant professor, associate professor, and professor); institution type as university, training-and-research, state, private, and city hospital; and experience as ≤10 versus >10 years. Selected multi-response items were dichotomised (e.g., any personal dosimeter versus none; any in-house analysis facility versus none). Between-group differences were tested with the Pearson Chi-square test or the Fisher's exact test as appropriate. Factors independently associated with routine stone analysis, personal-dosimeter availability, and metaphylaxis were examined with multivariable logistic regression, with results expressed as odds ratios (OR) and 95% confidence intervals (CI). $p < 0.05$ was considered statistically significant. All analyses were performed using Jamovi (Version 2.7.31; The Jamovi project, Sydney, Australia).

RESULTS

Participant Characteristics

Of 2,305 invited urologists, 346 responded (15.0%); after excluding 45 incomplete or inappropriate responses, 301 (13.1%) were included in the analysis. Most were specialists (185; 61.5%), followed by residents (71; 23.6%) and academic faculty (45; 14.9%). State hospitals accounted for 107 respondents (35.5%), university hospitals 74 (24.6%), training-and-research hospitals 59 (19.6%), private institutions 51 (16.9%), and city hospitals 10 (3.3%). Most respondents were aged 20–44 years (78.1%). Full characteristics are shown in Table 1.

Table 1. Demographic and institutional characteristics of respondents (n=301).

Characteristic	Category	n (%)
Academic title	Specialist	185 (61.5)
	Resident	71 (23.6)
	Academic (Asst./Assoc./Prof.)	45 (14.9)
Institution	State hospital	107 (35.5)
	University hospital	74 (24.6)
	Training & research hospital	59 (19.6)
	Private institution	51 (16.9)
	City hospital	10 (3.3)
Age, years	20–34	139 (46.2)
	35–44	96 (31.9)
	45–54	42 (14.0)
	55–64	21 (7.0)
	≥65	3 (1.0)
Experience, years	0–5	58 (19.3)
	5–10	110 (36.5)
	10–15	48 (15.9)
	15–20	32 (10.6)
	>20	53 (17.6)

Radiation-Safety Practices

A personally allocated dosimeter was unavailable to 205 respondents (68.1%); where present, it was most often a collar/chest badge (29.2%). Regular dosimeter measurement with result feedback was not performed for 189 respondents (62.8%), and a further 41 (13.6%) were unaware whether it occurred. An annual statutory radiation ("shua") leave was not granted to 298 respondents (99.0%), and periodic occupational medical examination was not performed for 245 (81.4%). Lead aprons (95.3%) and thyroid shields (81.7%) were widely available, but protective eyewear (20.6%), radiation shields (19.3%), and protective gloves (9.3%) were used by a minority, and 13 respondents (4.3%) reported no protective equipment. A safety guidewire was used in all procedures by 80.7%, whereas fluoroscopy was used in all listed procedures by only 40.5%; semirigid URS was the procedure most often performed without fluoroscopy. Difficulty accessing a shared fluoroscopy unit was reported by 82 respondents (27.2%) (Table 2).

Stone Analysis and Metabolic Practices

Routine post-procedural stone analysis was performed by 143 respondents (47.5%). An in-house analysis facility was available to only 25.9% (biochemical 21.3%; X-ray diffraction 4.7%), and notably to none of the state-hospital respondents. Referral of specimens to the external geological institute was reported by 237 respondents (78.7%). Intraoperative stone-sampling behaviour varied by procedure: the whole stone was retrieved when feasible by 44.5% in semirigid URS, 8.6% in flexible URS, and 60.1% in mini-PNL, whereas no sample was taken by 16.9%, 44.5%, and 9.3%, respectively. Flexible URS represented the procedure with the greatest loss of compositional information, with 44.5% reporting that no sample was taken. Metaphylaxis was applied by 169 respondents (56.1%), dietary and lifestyle advice was given by 291 (96.7%), and metabolic evaluation was performed by 89.7% (directed at high-risk recurrent stone formers in 86.4%). Access to spot urine (95.3%), serum electrolytes (97.3%), urine culture (96.0%), hormonal tests (92.4%), and 24-hour urine (81.4%) was widespread, whereas genetic analysis was available to 36.5%

Table 2. Occupational radiation-safety practices.

Item	Response	n (%)
Personal dosimeter	None	205 (68.1)
	Collar/chest badge	88 (29.2)
	Both badge + ring	6 (2.0)
	Ring/wrist only	2 (0.7)
Dosimeter measurement & feedback	None	189 (62.8)
	Every 6 months	54 (17.9)
	Unaware	41 (13.6)
	Yearly	17 (5.6)
Annual statutory radiation leave	Not granted	298 (99.0)
	Granted	3 (1.0)
Periodic medical examination	Not performed	245 (81.4)
	Performed	56 (18.6)
Protective equipment*	Lead apron	287 (95.3)
	Thyroid shield	246 (81.7)
	Protective eyewear	62 (20.6)
	Radiation shield	58 (19.3)
	Protective gloves	28 (9.3)
	None	13 (4.3)
Fluoroscopy used in all listed procedures	Yes	122 (40.5)
Safety guidewire used in all procedures	Yes	243 (80.7)
Difficulty accessing shared fluoroscopy	Yes	82 (27.2)

*Multiple responses permitted; percentages exceed 100%.

(Table 3). Despite high reported rates of dietary/lifestyle counselling and metabolic evaluation, routine stone analysis and in-house analytical capacity remained substantially lower, indicating a discontinuity in the stone-prevention care pathway (Figure 1).

Table 3. Stone-analysis and metabolic-evaluation practices.

Item	Response	n (%)
Routine post-procedural stone analysis	Yes	143 (47.5)
	No	158 (52.5)
In-house analysis facility	None	217 (72.1)
	Biochemical	64 (21.3)
	X-ray diffraction	14 (4.7)
	Unaware	6 (2.0)
Referral to external geological institute	Yes	237 (78.7)
	No	64 (21.3)
Sampling – retrieves whole stone	Semirigid URS	134 (44.5)
	Flexible URS	26 (8.6)
	Mini-PNL	181 (60.1)
Sampling – takes no sample	Semirigid URS	51 (16.9)
	Flexible URS	134 (44.5)
	Mini-PNL	28 (9.3)
Applies metaphylaxis	Yes	169 (56.1)
Gives diet/lifestyle advice	Yes	291 (96.7)
Performs metabolic evaluation	Yes	270 (89.7)
Metabolic evaluation directed at	High-risk recurrent formers	260 (86.4)
	First-time formers	10 (3.3)
	Not applied	31 (10.3)

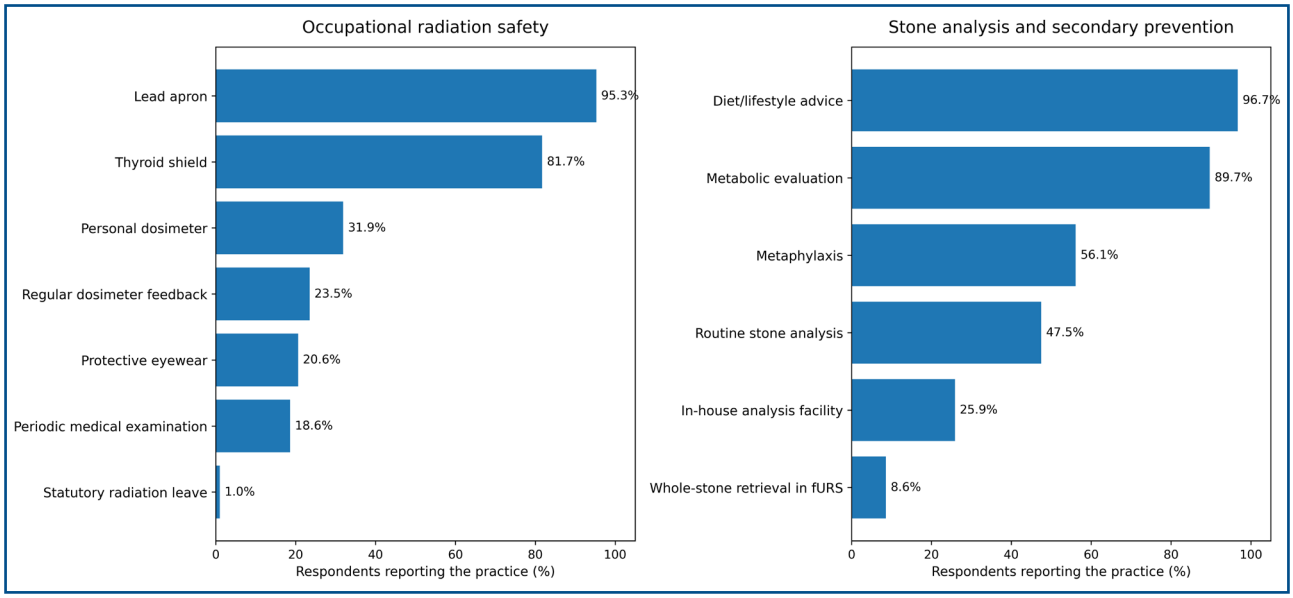


Figure 1. Two parallel care gaps in stone surgery

The left panel shows occupational radiation-safety practices, while the right panel shows stone analysis and secondary-prevention practices.

Factors Associated with Practice

Personal-dosimeter availability differed by academic title (academics 48.9% vs specialists 25.4%; $p = 0.005$). Routine stone analysis differed by institution type ($p = 0.005$), title ($p = 0.009$), and experience ($p = 0.020$), and in-house analysis availability differed strongly by institution type ($p < 0.001$) and title ($p < 0.001$). Referral to the external institute was more frequent among less experienced respondents (≤10 years, 87.5% vs >10 years, 67.7%; $p < 0.001$). Metaphylaxis differed by institution type (university 68.9%, training-and-research 62.7%, state 45.8%; $p = 0.020$) (Table 4). In multivariable analysis, routine stone analysis was independently associated with academic title (OR 2.85, 95% CI 1.16–6.99), availability of an in-house analysis facility (OR 3.07, 95% CI 1.59–5.93), and, inversely, with >10 years of experience (OR 0.25, 95% CI 0.13–0.50) (Table 5). Personal-dosimeter availability was independently associated with academic title (OR 3.04, 95% CI 1.24–7.42), and metaphylaxis with university (OR 3.99, 95% CI 1.45–10.93) and training-and-research (OR 2.40, 95% CI 1.14–5.05) hospital practice.

DISCUSSION

This national survey of 301 urologists in Türkiye reveals two parallel findings. First, occupational radiation protection is incomplete and, in its regulatory dimension, almost entirely absent: more than 2-thirds of respondents had no personal dosimeter, only about one quarter received regular dose feedback, and a statutory radiation leave and periodic medical examination were essentially unavailable to the vast majority. Second, guideline-recommended post-procedural stone analysis was performed by fewer than half of respondents and was tightly constrained by institutional infrastructure rather than by individual preference alone.

Table 4. Selected subgroup comparisons (proportion answering "yes").

Outcome	Subgroup (rates)	p
Personal dosimeter	Academic 48.9% / Resident 38.0% / Specialist 25.4%	0.005
Dosimeter monitoring	Academic 42.2% / Resident 25.4% / Specialist 18.4%	0.003
Routine stone analysis	By institution (City 10.0% – Training&Res. 57.6%)	0.005
Routine stone analysis	Academic 66.7% / Resident 50.7% / Specialist 41.6%	0.009
Routine stone analysis	≤10 yr 53.6% / >10 yr 39.8%	0.020
In-house analysis facility	State 0% / others 39–45%	<0.001
In-house analysis facility	Academic 55.6% / Resident 26.8% / Specialist 18.4%	<0.001
Referral to external institute	≤10 yr 87.5% / >10 yr 67.7%	<0.001
Metaphylaxis	University 68.9% / Training&Res. 62.7% / State 45.8%	0.020

Pearson chi-square or Fisher exact test.

Table 5. Multivariable logistic regression for selected practices.

Outcome / predictor	OR (95% CI)	p
Routine stone analysis (ref: *State / Specialist / ≤10 yr / no facility)*		
Academic title	2.85 (1.16–6.99)	0.022
In-house analysis facility	3.07 (1.59–5.93)	<0.001
>10 years of experience	0.25 (0.13–0.50)	<0.001
Personal dosimeter (ref: State / Specialist / ≤10 yr)		
Academic title	3.04 (1.24–7.42)	0.015
Metaphylaxis (ref: State / Specialist / ≤10 yr)		
University hospital	3.99 (1.45–10.93)	0.007
Training & research hospital	2.40 (1.14–5.05)	0.021

Only statistically significant predictors are shown; each model also included institution type, title and experience as covariates. OR, odds ratio; CI, confidence interval.

The pattern of protective-equipment use mirrors international surveys, in which lead aprons and thyroid shields are nearly universal, while eyewear, shielding, and gloves lag far behind (6,9,10). Similar gaps have been reported in surveys from Türkiye, the United States, Egypt, and Saudi Arabia, where awareness of radiation hazards did not consistently translate into dosimeter use, protective eyewear adoption, or formal radiation-safety training (16–19). However, the figures for personal dosimetry and statutory monitoring observed here are substantially lower than those reported among European and other cohorts, where personal dosimeter use, although still suboptimal, is more established (6,9). Notably, the proportion of respondents without a personal dosimeter (68.1%) is almost unchanged from the 73.9% of Turkish urologists who reported not using a dosimeter nearly a decade earlier in a similarly designed national e-mail survey, indicating that this gap has persisted despite the intervening expansion of endourological practice (20). Given the documented relationship between cumulative ocular exposure and cataract formation and the relatively high eye-lens doses recorded during endourology, the rarity of protective eyewear and eye dosimetry is of particular concern (5,6). This is clinically relevant because the eye lens has become a specific focus of occupational radiation protection after the reduction of recommended occupational lens-dose limits, and experimental as well as clinical studies suggest that eyewear design, operator position, and C-arm geometry substantially influence lens exposure (21,22). The near-complete absence of statutory radiation leave and periodic examination is best interpreted not as a failure of individual awareness but as a gap in institutional and regulatory implementation, since these provisions are administered at the level of the employing institution. Consistent with this, the only practitioner-level factor independently associated with dosimeter availability was academic title, plausibly reflecting better-resourced academic centres rather than differing attitudes. Although radiation-safety education is necessary, the magnitude of dosimetry and occupational-health gaps observed in the present study suggests that education alone is unlikely to be sufficient without institution-level monitoring, mandatory feedback systems, and enforceable occupational-safety policies (8,9,23).

On the stone-analysis side, the EAU guidelines recommend that stone composition be determined in every patient, preferably by infrared spectroscopy or X-ray diffraction, as the basis for targeted prevention (11–13). The observation that routine analysis was performed by under half of respondents is in keeping with the recognised international gap between guideline recommendations and practice (14). The most striking structural finding was that an in-house analysis facility was available to only about a quarter of respondents and to no state-hospital respondent, which explains the heavy reliance (78.7%) on referral to an external geological institute as a pragmatic substitute. However, such external referral pathways can only replace in-house analysis if the analytical method, reporting format, turnaround time, and quality-control standards are clearly defined. Multicentre European data have shown that the accuracy of urinary stone analysis varies across laboratories and analytical methods, supporting the need for standardized, quality-assured pathways (24). The independent association of routine analysis with an in-house facility (OR 3.07) confirms that access, more than intent, drives this behaviour. This mismatch was further illustrated by the stone-prevention cascade. Although dietary/lifestyle counselling and metabolic evaluation were frequently reported, routine stone analysis and in-house analytical capacity were much less common. This suggests that secondary prevention is often initiated without robust compositional confirmation, particularly in centres without local stone-analysis infrastructure. The inverse association with experience -more senior urologists performing analysis less often and referring less frequently to the external institute- may reflect entrenched habits formed before analysis pathways became widely promoted and represents a potential target for continuing education.promoted and

Procedure-specific sampling patterns also deserve attention. In the present survey, no stone sample was obtained in nearly half of flexible URS cases, whereas this was uncommon during mini-PNL. This may partly reflect the increasing use of dusting strategies in flexible ureteroscopy, where an intact fragment is not routinely retrieved. However, dusting alone is unlikely to fully explain this pattern: true dusting to fragments of only a few millimetres is often incomplete, particularly for lower-pole stones with narrow infundibula, where residual fragments may not pass spontaneously and could in principle still be retrieved for analysis; procedural time and cost considerations may therefore also contribute

to the decision not to sample. The finding that no sample was taken in 9.3% of mini-PNL cases is more difficult to reconcile with the technique itself, since an intact or fragmented stone is typically extracted through the nephrostomy tract; this pattern may instead reflect variability in respondents' endourological experience or engagement with stone-analysis practice, and it underscores that self-reported survey data cannot fully capture the reasons underlying non-sampling behaviour. Biochemical analysis of dust or small retrieved fragments has been proposed as a pragmatic route to preserve compositional diagnosis when intact stones are unavailable (25). Nevertheless, visual endoscopic recognition is not sufficiently reliable to replace formal stone analysis (26).

Encouragingly, dietary and lifestyle advice was almost universal, and metabolic evaluation was reported by nearly 90% of respondents, appropriately concentrated on high-risk recurrent stone formers, with broad access to the relevant biochemical tests. This high self-reported rate contrasts with claims-based and patient-level studies showing low uptake of 24-hour urine testing and follow-up metabolic monitoring, suggesting that survey-based physician reports may capture intent or selected high-risk practice rather than universal implementation (27,28).

The higher likelihood of metaphylaxis in university and training-and-research settings suggests that academic environments more readily translate guideline recommendations into routine practice. Taken together, the findings argue that improving secondary prevention in Türkiye depends less on changing attitudes than on widening access to reliable stone analysis—whether by equipping more centres or by formalising and quality-assuring external referral pathways.

Limitations

This study has several limitations. Its cross-sectional, self-reported design is subject to recall and social-desirability bias. Although the number of invited urologists was defined (2,305), the response rate was modest (13.1%), which raises the possibility of non-response bias and limits generalisability. This response rate is consistent with the generally low and often declining rates reported for non-incentivized, single-mailing e-mail surveys of physicians, in which web-based invitations without reminders or incentives typically yield lower participation than mailed or mixed-mode approaches (29). Because respondents with a specific interest in endourology, radiation safety, or stone prevention may have been more likely to participate, the observed adherence rates may overestimate national practice. This selection effect is particularly relevant to personal-dosimeter availability (31.9%), which may overestimate true coverage among the broader population of Turkish urologists, including those in general urological practice with less focus on endourology and radiation safety. The instrument recorded sampling behaviour for semirigid URS, flexible URS, and mini-PNL but not for standard PNL or bladder-stone surgery, and the analytical validity and turnaround time of external referral were not assessed. Data on institutional stone-surgery case volume were not collected, precluding comparison of practice patterns between high-volume and low-volume centres; this represents an additional limitation. Finally, associations are observational and cannot establish causation.

CONCLUSION

Occupational radiation protection and guideline-recommended stone analysis are incompletely implemented among urologists in Türkiye. The very low rates of dosimetry feedback, occupational surveillance, and in-house stone-analysis access suggest that improvement requires institutional and regulatory interventions, in addition to individual education.

Acknowledgments: The manuscript's language and structure were enhanced using artificial intelligence (Claude Opus 4.8; Anthropic). The author has thoroughly examined and verified the content, taking full responsibility for the scientific accuracy and integrity of the completed document.

Funding: This research received no external funding.

Informed Consent: Electronic informed consent was obtained on the first page of the form before any item was displayed.

Conflict of Interest: The authors declare no competing interests.

Ethics Approval: This study was approved by the Ethics Committee for Non-Interventional Clinical Research at Zonguldak Bülent Ecevit University at its meeting dated May 13, 2020 (No. 2020/10), regarding the research titled "An Investigation of Differences in Clinical Approaches Among Urologists in Turkey: Prostate Biopsy, Urinary Tract Stone Disease, and Interdisciplinary Collaborations," was unanimously approved as compliant with the ethics committee's principles.

Author contributions

Conceptualization: EDD, SM, MDD, HAY
Methodology: EDD, SM, MDD, HAY
Formal Analysis: EDD
Investigation: EDD, SM, MDD, HAY
Resources: EDD
Data Curation: EDD, SM, MDD, HAY
Writing – Original Draft: EDD
Writing – Review & Editing: EDD, SM, MDD, HAY
Visualization: EDD

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Original Article
Özgün Araştırma

Endourol Bull. 2026;18(3):261–275. doi: 10.54233/endourolbull-2003419

Assessing Awareness and Knowledge Regarding the Popularity of Robotic Surgery in Prostate Cancer Treatment Preferences, Survey Research

Prostat Kanseri Tedavisinin Tercihinde Robotik Cerrahinin Popülaritesi Hakkında Farkındalık ve Bilgi Düzeyinin Ölçülmesi, Anket Çalışması

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ABSTRACT

Objective: The goal is to enhance patient education and consent procedures by assessing the awareness of robotic surgery among prostate cancer patients and their families, the determinants influencing their treatment choices, and their technological misunderstandings.

Materials and Methods: This cross-sectional survey research, carried out from February to May 2026, encompassed 50 patients with prostate cancer and 50 families of those patients. Data were gathered via surveys and analyzed employing multivariable logistic regression.

Results: The majority of participants (76% of patients, 78% of patients' families) favored robotic surgery. Across all socio-demographic categories, irrespective of age and educational background, a prevalent "autonomous robot fallacy" (the misconception that the robot independently conducts the surgery) has been recognized. An affinity for technology is associated with 5.6-fold higher odds of preferring robotic surgery and 4.9-fold higher odds of expecting extraordinary outcomes. The odds of encountering technical safety anxiety (device malfunction, wrong procedure, etc.) are 6.8 times (OR: 6,794) greater for individuals who source their initial information from media or the internet than for those who consult a physician. Individuals possessing a bachelor's degree or higher are 5.2 times more likely to perceive robotic surgery as a symbol of institutional status.

Conclusion: Patients' choices regarding surgery are influenced more by their fascination with technology, the media's portrayal of "autonomy," and the perceived prestige of institutions than by actual medical requirements. It is essential for physicians to openly address patients' unrealistic aspirations for perfection and baseless safety apprehensions stemming from media influence during collaborative decision-making.

Keywords: awareness, robotic surgery, autonomous robot fallacy, technological perception

Cite As: *Sandikci F, Bescocuklu A. Assessing Awareness and Knowledge Regarding the Popularity of Robotic Surgery in Prostate Cancer Treatment Preferences, Survey Research. Endourol Bull. 2026;18(3):261–275.* https://doi.org/10.54233/endourolbull-2003419

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Received : July 25, 2026 ***Accepted*** : September 29, 2026

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ÖZET

Amaç: Prostat kanseri hastaları ve hasta yakınlarının robotik cerrahiye yönelik farkındalıklarını, tedavi tercihlerini etkileyen faktörleri ve teknolojik yanılgılarını belirleyerek hasta bilgilendirme ve onam süreçlerini iyileştirmektir.

Gereç ve Yöntemler: Şubat-Mayıs 2026 tarihleri arasında yürütülen bu kesitsel anket çalışmasına, 50 prostat kanseri hastası ve 50 hasta yakını dahil edilmiştir. Veriler anketler aracılığıyla toplanmış ve çok değişkenli lojistik regresyon analizi ile değerlendirilmiştir.

Bulgular: Katılımcıların çoğu (hastalar %76, hasta yakınları %78) robotik cerrahiyi tercih etmiştir. Tüm sosyo-demografik gruplarda yaş ve eğitimden bağımsız, yaygın bir "otonom robot yanılgısı" (robotun ameliyatı kendi başına yaptığı inancı) saptanmıştır. Teknolojiye ilgili olmakla, robotik cerrahi tercihi 5.6 kat, mucizevi sonuç beklentisi ise 4.9 kat daha yüksek olarak belirlendi. İlk bilgiyi medyadan/internetten edinenlerin teknik güvenlik endişesi (cihaz arızası, yanlış prosedür vb.) yaşama riski, bilgiyi hekimden alanlara göre 6.8 kat (OR: 6,794) daha yüksektir. Lisans ve üzeri mezunlarda robotik cerrahiyi kurumsal prestij göstergesi olarak görme eğilimi 5.2 kat fazladır.

Sonuçlar: Hastaların cerrahi tercihi; tıbbi gerekliliklerden ziyade teknoloji merakı, medyanın "otonomi" imajı ve kurumsal prestij algısıyla şekillenmektedir. Hekimlerin, ortak karar verme süreçlerinde hastaların gerçek dışı kusursuzluk beklentilerini ve medyadan kaynaklı yersiz güvenlik endişelerini şeffaf bir şekilde yönetmesi gereklidir.

Anahtar Kelimeler: farkındalık, robotik cerrahi, otonom yanılgı, teknolojik algı

GİRİŞ

Prostat kanseri (PKa), dünya genelinde en sık görülen malignitelerden biridir. 2022'de dünya çapında 1.4 milyon yeni vaka ve buna bağlı yaklaşık 400,000 mortaliteye sahiptir. Erkeklerde en sık görülen ikinci kanser türüdür. Yaşla beraber sıklığı artar (1). Radikal prostatektomi, küratif tedavi seçeneği olarak dünya genelinde sıklıkla uygulanır. Cerrahi olarak; açık, laparoskopik ve robotik tekniklerle uygulanabilmektedir (2). Son yıllarda, teknolojik gelişmelerdeki ivmelenme ile açık cerrahi teknikten Robot Yardımlı Radikal Prostatektomi (RYRP) tekniğine doğru hızlıca bir geçiş dikkat çekicidir (3). RYRP; daha az kan kaybı, daha kısa hastanede yatış süresi ve daha hızlı iyileşme gibi avantajlarıyla dünyada popüler bir teknik olarak önemi giderek artmaktadır (4).

Hastaların bu ileri teknoloji hakkındaki farkındalıklarında ciddi teknik bilgi eksikliklerinin olduğu ve mevcut farkındalıklarının genellikle medya kaynaklı bilgilerden oluştuğu düşünülmektedir. Açık cerrahi ile robotik cerrahi arasındaki farkın ne olduğu ve robotik cerrahi tekniğin nasıl gerçekleştirildiği hakkındaki bilgilerin hastalar ve yakınları açısından eksikliği ciddi orandadır. Özellikle hastaların büyük bir kısmı, ameliyatın cerrahtan bağımsız olarak tamamen robotun otonom kontrolünde olduğu gibi yanlış bir algıya sahiptirler (5). Hastaların kendilerine uygulanacak tedavi seçenekleriyle ilgili doğru bilgilere sahip olması, hekimleriyle beraber tedavileri için ortak karar verme sürecine dahil olmaları çok önemlidir. Bu durum, hastaların operasyon sonrası tedavi pişmanlıklarını azaltan önemli bir faktördür.

Çalışmamız, hastaların robotik prostat cerrahisi açısından farkındalık düzeylerini, bu yöntemi tercih etme nedenlerini ve robotik cerrahi sistemin işleyişine dair yanılgıların belirlenmesini amaçlamaktadır. Ayrıca, yanlış bilinenlerin farkındalığı ile hasta bilgilendirme ve onam süreçlerinin daha etkili yapılmasının sağlanması da önemli bir amacımızdır.

GEREÇ VE YÖNTEMLER

Çalışma, tanımlayıcı ve kesitsel tip nicel bir çalışma olarak etik onay Ankara Etlik Şehir Hastanesi Bilimsel Araştırmalar Etik Kurulu'ndan alınmıştır (Onay numarası: AEŞH-BADEK2-2026-239, Tarih: 24.03.2026). İki farklı grubun karşılaştırılması planlandı. Birinci grup (Hasta grubu), prostat kanseri tanılı, 50–75 yaş arası, okuma-yazma bilen 50 erkek hasta olarak oluşturuldu. İkinci grup (genel popülasyon), genel popülasyonun farkındalığını ölçmek için 50 hasta yakını olarak oluşturuldu. Örneklem büyüklüğü G*power analizi (α: 0.05, Güç: 0.80, Etki Büyüklüğü: 0.6) ile belirlendi. Bilimsel geçerliliği artırmak için her bir grup için 50 hasta ile değerlendirme planlandı.

Hasta grubu için 50–75 yaş arası, klinik olarak lokalize (T1-T2) veya lokal ileri evre (T3a) prostat kanseri teşhisi almış ve cerrahi planlanan hastalar çalışmaya dahil edildi. Genel popülasyon grubu (hasta yakınları) için 18 yaş ve üzeri bireyler dahil edildi. Her iki grupta çalışma için katılımcılardan aydınlatılmış onam formu alındı. Sağlık profesyonelleri, verileri saptırma riski nedeniyle çalışma dışı bırakıldılar. Uzak metastazı olan veya cerrahiye uygun olmayan hastalar ve bilişsel engeli veya iletişim sorunları olan hastalar da çalışma dışında bırakıldı.

Veriler, Şubat 2026 ile Mayıs 2026 tarihleri arasında anket yöntemiyle toplandı. Katılımcıların; demografik ve sosyo-ekonomik durumları, robotik cerrahiyle alakalı teknik bilgi ve yanılgılarına dair veriler ve operasyona karar verme süreci hakkındaki verilerin toplanması planlandı. Ayrıca cerrahi tekniğin tercihine neden olan avantajlar ve dezavantajlar değerlendirildi. Anket soruları, demografik ve sosyo-ekonomik soruları içeren alt başlıkla birlikte; "bilgi kaynakları, farkındalık ve teknoloji algısı", "karar verme süreci ve tercih nedenleri", "robotik cerrahiye yönelik beklentiler ve klinik sonuç algısı" alt başlıklarındaki sorulardan oluşturuldu.

İstatistiksel Analiz

Elde edilen verilerden sürekli değişkenler için ortalama ± standart sapma (SD) ve medyan (minimum-maksimum) değerleri, kategorik değişkenler için frekans ve yüzde (n, %) değerleri belirtildi. Verilerin normal dağılıma uygunluğu Shapiro-Wilk testi ile değerlendirildi. Gruplar arası farklar için Ki-Kare, Fisher's Exact veya Mann-Whitney U testleri kullanıldı. Çalışmanın birincil sonlanım noktası olan hasta ve hasta yakını gruplarının karşılaştırılmasına (Ki-Kare testi) yönelik örneklem büyüklüğü gerekçelendirmesi G*Power (v3.1.9.7) programı ile yapılmıştır. İki bağımsız oran arasındaki fark testine göre (çift yönlü, büyük etki büyüklüğü d = 0.60, α = 0.05 ve %80, güç [1-β = 0.80]) gerekli minimum örneklem büyüklüğü 96 (her grup için 48) olarak hesaplanmış ve toplam N=100 katılımcı ile çalışma tamamlanmıştır.

Robotik cerrahi tercihini, otonom robot yanılgısına sahip olmayı, ortak karar verme sürecini, kurumsal prestij algısını, teknik güvenlik endişelerini ve klinik üstünlük beklentisini etkileyen bağımsız faktörleri belirlemek için çok değişkenli lojistik regresyon analizleri uygulandı. Modellerdeki bağımlı değişkenlerin kategori büyüklükleri ve Olay Başına Değişken (EPV) oranları raporlandı. Hücre seyrekliği (cell sparsity) nedeniyle yarı-ayrışma (quasi-separation) problemi sergileyen ve olağanüstü geniş güven aralıkları üreten lojistik regresyon modeli (Tablo 11), daha stabil nokta tahminleri elde etmek amacıyla Firth'in Penalize Edilmiş Lojistik Regresyonu (Firth's Penalized Likelihood Regression) yöntemi ile analiz edilerek stabilize edildi. Anketin yapı geçerliliği Keşfedici Faktör Analizi (EFA) ile değerlendirildi; Kaiser-Meyer-Olkin (KMO) ve Bartlett Küresellik Testleri uygulandı. Anketin iç tutarlılığı Cronbach's Alpha katsayısı ile değerlendirildi. Tüm istatistiksel analizlerde anlamlılık düzeyi çift yönlü olarak $p < 0.05$ kabul edildi.

BULGULAR

Çalışmamızın hasta grubunda yaş ortalaması 65.06 ± 5.99 (Ortalama ± SD) idi. Hasta yakınlarından oluşan genel popülasyon grubunun yaş ortalaması daha düşük olarak tespit edildi (53.58 ± 13.62) (Ortalama ± SD). Hasta grubunda en yüksek eğitim düzeyi lise (15, %30) olarak tespit edildi. Ekonomik durum açısından hastaların 26 (%52)'sı 21–40 bin gelir aralığındaydı. Kırk altı (%96) hasta evli olduğunu belirtti. Otuz dokuz (%78) hastanın sağlık sigortası Sosyal Güvenlik Kurumu (SGK) idi. Otuz yedi (%74) hasta şehir merkezinde ikamet etmekteydi. Hastaların 23 (%46)'ü emekliydi (Tablo 1). Anket soruları ve cevaplarına ait veriler, sayı (%) olarak tablolarda belirtildi (Tablo 2,3,4).

Hasta ve hasta yakınları arasında sosyo-ekonomik ve demografik özellikler karşılaştırıldı. Yaş ve meslek grupları arasında istatistiksel olarak anlamlı fark saptandı (sırasıyla $p < 0.001$, p:0.005). Teknolojik gelişmelere ilgi duyma, hasta yakınları grubunda yüksek olarak saptandı. Gruplar arası fark istatistiksel olarak anlamlı saptandı (p:0.011). Diğer parametreler arası karşılaştırmada istatistiksel fark görülmedi (Tablo 5).

Tablo 1. Demografik ve Sosyo-Ekonomik Özellikler

Değişken (Parametre)	Hasta Grubu (n=50)	Hasta Yakını (n=50)	Toplam (n=100)
Yaş (Ortalama ± SD)	65.06 ± 5.99	53.58 ± 13.62	59.32 ± 11.95
Eğitim Durumu			
- İlkokul	12 (%24)	10 (%20)	22 (%22)
- Ortaokul	13 (%26)	4 (%8)	17 (%17)
- Lise	15 (%30)	12 (%24)	27 (%27)
- Lisans	8 (%16)	20 (%40)	28 (%28)
- Yüksek Lisans	2 (%4)	4 (%8)	6 (%6)
Aylık Ortalama Gelir			
- 10.000 - 20.000 TL	1 (%2)	4 (%8)	5 (%5)
- 21.000 - 40.000 TL	26 (%52)	18 (%36)	44 (%44)
- 41.000 - 60.000 TL	18 (%36)	18 (%36)	36 (%36)
- 61.000 - 100.000 TL	4 (%8)	8 (%16)	12 (%12)
- 100.000 TL Üzeri	1 (%2)	2 (%4)	3 (%3)
Medeni Durum			
- Evli	48 (%96)	43 (%86)	91 (%91)
- Bekar	2 (%4)	7 (%14)	9 (%9)
Sağlık Sigortası Türü			
- SGK	39 (%78)	33 (%66)	72 (%72)
- Özel Sağlık Sigortası	11 (%22)	17 (%34)	28 (%28)
Yaşadığı Bölgenin Niteliği			
- Şehir Merkezi	37 (%74)	44 (%88)	81 (%81)
- Kırsal Bölge	13 (%26)	6 (%12)	19 (%19)
Meslek			
- Emekli	23 (%46)	15 (%30)	38 (%38)
- Esnaf	18 (%36)	10 (%20)	28 (%28)
- Öğretmen	2 (%4)	7 (%14)	9 (%9)
- Ev Hanımı	0 (%0)	7 (%14)	7 (%7)
- Mühendis	0 (%0)	6 (%12)	6 (%6)
- Çiftçi	3 (%6)	1 (%2)	4 (%4)
- Asker	2 (%4)	1 (%2)	3 (%3)
- İşçi	1 (%2)	2 (%4)	3 (%3)
- Bankacı	1 (%2)	0 (%0)	1 (%1)
- Diğer Meslekler	0 (%0)	1 (%2)	1 (%1)

Tablo 2. "Bilgi Kaynakları, Farkındalık ve Teknoloji Algısı" hakkındaki anket soruları ve cevapları

Değişken (Parametre)	Hasta Grubu (n=50)	Hasta Yakını (n=50)	Toplam (n=100)
Teknolojik Gelişmelere İlgi Duyma			
- Var	32 (%64)	43 (%86)	75 (%75)
- Yok	18 (%36)	7 (%14)	25 (%25)
Ameliyat Yöntemleriyle İlgili İlk Bilgi Kaynağı			
- Hekimimden	29 (%58)	21 (%42)	50 (%50)
- İnternet/Sosyal Medya	10 (%20)	14 (%28)	24 (%24)
- Tanıdık Tavsiyesi	7 (%14)	10 (%20)	17 (%17)
- Televizyon	4 (%8)	5 (%10)	9 (%9)
Daha Önce Robotik Cerrahiyi Duyma Durumu			
- Evet	30 (%60)	34 (%68)	64 (%64)
- Hayır	20 (%40)	16 (%32)	36 (%36)
Tercih Edilen Ameliyat Yöntemi			
- Robotik Cerrahi	38 (%76)	39 (%78)	77 (%77)
- Fikrim Yok	10 (%20)	10 (%20)	20 (%20)
- Laparoskopik Cerrahi	1 (%2)	1 (%2)	2 (%2)
- Açık Cerrahi	1 (%2)	0 (%0)	1 (%1)
Robotik Cerrahide Ameliyatı Kimin Yaptığı Algısı (Otonom Robot Yanılgısı)			
- Cerrah robotu kullanır *(Doğru Bilgi)*	26 (%52)	31 (%62)	57 (%57)
- Robot kendi başına yapar *(Yanılgı)*	8 (%16)	10 (%20)	18 (%18)
- Robot ameliyatı yapar, cerrah gözetler *(Yanılgı)*	9 (%18)	8 (%16)	17 (%17)
- Robot önceden programlanmıştır *(Yanılgı)*	6 (%12)	1 (%2)	7 (%7)
- Fikrim Yok / Cevapsız	1 (%2)	0 (%0)	1 (%1)

Tablo 3. "Karar Verme Süreci ve Tercih Nedenleri" hakkındaki anket soruları ve cevapları

Değişken (Parametre)	Hasta Grubu (n=50)	Hasta Yakını (n=50)	Toplam (n=100)
Ameliyat Yöntemine Karar Verirken En Belirleyici Faktör			
- İyileşme süreci beklentisi	21 (%42)	25 (%50)	46 (%46)
- Hekimimin tavsiyesi	12 (%24)	11 (%22)	23 (%23)
- Ameliyatın maliyeti	10 (%20)	9 (%18)	19 (%19)
- Kendi araştırmalarım	7 (%14)	5 (%10)	12 (%12)
Hekim Her İki Seçenek (Açık/Robotik) Hakkında Detaylı Bilgi Verdi mi?			
- Evet	43 (%86)	43 (%86)	86 (%86)
- Hayır	7 (%14)	7 (%14)	14 (%14)
Ameliyat Yöntemine Karar Verme Süreci Nasıl İşledi?			
- Doktorumla birlikte karar verdik (Ortak Karar)	32 (%64)	32 (%64)	64 (%64)
- Doktorum karar verdi	16 (%32)	16 (%32)	32 (%32)
- Sadece ben karar verdim	2 (%4)	2 (%4)	4 (%4)

Robotik Cerrahiyi Seçmedeki En Önemli Motivasyon / Neden			
- Daha kısa sürede günlük hayata dönmek	17 (%34)	18 (%36)	35 (%35)
- Daha küçük yara izi	14 (%28)	9 (%18)	23 (%23)
- Cinsel fonksiyonların/idrar kontrolünün daha iyi olacağı	9 (%18)	14 (%28)	23 (%23)
- Daha az kan kaybı ve daha az ağrı beklentisi	10 (%20)	9 (%18)	19 (%19)
Açık Cerrahiyi Seçmenin Önündeki Bariyerler / Nedenler			
- Doktorumun bu yöntemde daha deneyimli olması	20 (%40)	22 (%44)	42 (%42)
- Cerrahın dokulara doğrudan dokunmasının daha güvenli olması	11 (%22)	15 (%30)	26 (%26)
- Robotik teknolojiye güvensizlik / teknik hata korkusu	14 (%28)	11 (%22)	25 (%25)
- Daha düşük maliyet / kolay ulaşılabilirlik	5 (%10)	2 (%4)	7 (%7)
Robotik Cerrahi İle İlgili En Büyük Endişe (Korku Profili)			
- Endişem yok	16 (%32)	18 (%36)	34 (%34)
- Yanlış prosedür uygulanması	17 (%34)	15 (%30)	32 (%32)
- Yüksek maliyet	7 (%14)	8 (%16)	15 (%15)
- Robotun arızalanması	8 (%16)	7 (%14)	15 (%15)
- Hekimin kontrolü kaybetmesi	2 (%4)	2 (%4)	4 (%4)

Tablo 4. "Robotik Cerrahiye Yönelik Beklentiler ve Klinik Sonuç Algısı" hakkındaki anket soruları ve cevapları

Değişken (Parametre)	Hasta Grubu (n=50)	Hasta Yakını (n=50)	Toplam (n=100)
Hangi Yöntemin Onkolojik (Kanser Kontrolü) ve Fonksiyonel Sonuçları Daha İyidir?			
- Robotik Cerrahi	36 (%72)	36 (%72)	72 (%72)
- Açık Cerrahi	7 (%14)	6 (%12)	13 (%13)
- Hiçbiri	4 (%8)	5 (%10)	9 (%9)
- Laparoskopik Cerrahi	1 (%2)	2 (%4)	3 (%3)
- Hepsi / Fikrim Yok	2 (%4)	1 (%2)	3 (%3)
Hangi Yöntemde Hastaneden Daha Hızlı Taburcu Olursunuz?			
- Robotik Cerrahi	47 (%94)	47 (%94)	94 (%94)
- Açık Cerrahi	2 (%4)	1 (%2)	3 (%3)
- Laparoskopik Cerrahi	1 (%2)	0 (%0)	1 (%1)
- Hiçbiri	0 (%0)	2 (%4)	2 (%2)
Hangi Yöntemde Cinsel Fonksiyonlar Daha İyi Korunur?			
- Robotik Cerrahi	41 (%82)	41 (%82)	82 (%82)
- Hiçbiri	4 (%8)	6 (%12)	10 (%10)
- Açık Cerrahi	4 (%8)	2 (%4)	6 (%6)
- Laparoskopik Cerrahi	1 (%2)	1 (%2)	2 (%2)
Hangi Yöntemde Daha Az Komplikasyon Olur?			
- Robotik Cerrahi	45 (%90)	45 (%90)	90 (%90)
- Hiçbiri	0 (%0)	4 (%8)	4 (%4)

- Açık Cerrahi	3 (%6)	1 (%2)	4 (%4)
- Laparoskopik Cerrahi	1 (%2)	0 (%0)	1 (%1)
- Hepsi	1 (%2)	0 (%0)	1 (%1)
Hangi Yöntemin Daha Pahalı Olduğu Algısı			
- Robotik Cerrahi	45 (%90)	40 (%80)	85 (%85)
- Hiçbiri	1 (%2)	6 (%12)	7 (%7)
- Açık Cerrahi	2 (%4)	2 (%4)	4 (%4)
- Laparoskopik Cerrahi	2 (%4)	1 (%2)	3 (%3)
- Hepsi	0 (%0)	1 (%2)	1 (%1)

Tablo 5. Her iki gruba ait parametrelerin ve anket sorularına ait cevapların karşılaştırılması

Demografik ve Sosyo-Ekonomik Özellikler	**p-değeri**
Yaş	**< 0,001**
Meslek Grupları	**0,005**
Yaşadığı Bölgenin Niteliği (Şehir/Kırsal)	0,074
Medeni Durum	0,081
Sağlık Sigortası Türü	0,181
Aylık Ortalama Gelir Dağılımı	0,278
Eğitim Durumu	0,295

Bilgi Düzeyi, Farkındalık ve Teknoloji Algısı

Teknolojik Gelişmelere İlgi Duyma	**0,011**
Robotik Cerrahide Ameliyatı Kimin Yaptığı Algısı (Otonom Robot Yanılgısı)	0,259
Robotik Cerrahiyi Daha Önce Duyma Durumu	0,405
Ameliyat Yöntemleriyle İlgili Bilgi Edinilen İlk Kaynak	0,460

Tedavi Karar Verme Süreci ve Tercih Nedenleri

Açık Cerrahiyi Seçmenin Önündeki Bariyerler / Nedenler	0,502
Robotik Cerrahiyi Seçmedeki En Önemli Motivasyon / Neden	0,521
Prostat Kanseri Ameliyatında Tercih Edilen Yöntem	0,798
Ameliyat Yöntemine Karar Verirken En Belirleyici Faktör	0,855
Karar Verme Sürecinin Kiminle İşlediği (Hekim/Ortak/Sadece Hasta)	1,000
Hekimin Her İki Seçenek (Açık/Robotik) Hakkında Detaylı Bilgi Vermesi	1,000

Robotik Cerrahiye Yönelik Beklentiler, Endişeler ve Klinik Algı

Hangi Yöntemde Daha Az Komplikasyon Olacağı Beklentisi	0,136
Hangi Yöntemin Daha Pahalı Olduğu Algısı	0,267
Hastanede Robot Bulunmasının O Hastaneyi Daha Kaliteli Yapıp Yapmadığı	0,328
Hangi Yöntemle Hastaneden Daha Hızlı Taburcu Olunacağı İnancı	0,343
Hangi Yöntemde Cinsel Fonksiyonların Daha İyi Korunacağı İnancı	0,785
Hangi Yöntemin Onkolojik ve Fonksiyonel Sonuçlarının Daha İyi Olduğu	0,911
Robotik Cerrahiyle İlgili En Büyük Endişe (Korku Profili)	0,984

Robotik prostat cerrahisini tercih etme kararını etkileyen bağımsız faktörleri belirlemek için çok değişkenli Lojistik Regresyon analizi uygulandı. Teknolojik gelişmelere ilgi duyan katılımcıların, ilgi duymayanlara kıyasla robotik prostat cerrahisini tercih etme olasılıklarının (odds) 5.6 kat daha yüksek olduğu saptandı (OR: 5,613; %95 GA: 1,739 - 18,117; p = 0.004). Yöntem tercihinde, yaş değişkeni (p = 0.075) ve kararda hekim yönlendirmesinin etkisi (p = 0.082) ise istatistiksel anlamlılık sınırında saptandı.

Otonom robot yanılgısına (ameliyatın cerrah kontrolünde değil, robotun kendi başına uyguladığına dair yanlış inanca) sahip olmayı öngören faktörler; hastanın yaşı, eğitim düzeyinin düşüklüğü, bilgi kaynağının medyadaki spekülatif bilgiler olması veya hasta ya da hasta yakını grubu olma durumu gibi değerlendirilen sosyo-demografik bağımsız faktörlerin hiçbirinin söz konusu teknik yanılgıya düşme riskini tek başına etkilemediği saptanmıştır (tüm değişkenler için p > 0.05). İstatistiksel olarak herhangi bir faktörün belirleyici olmadığı bu negatif bulgu, çarpıcı bir durumu işaret etmektedir. Otonom robot algısı; düşük eğitim ya da ileri yaş ile bağlantılı olmayıp, üniversite mezunları, gençler ve hatta bilgilendirmeyi doğrudan hekimden alan hasta ya da hasta yakınlarının da sahip olduğu ciddi bir yanılgıdır.

Ortak karar verme süreci; hastanın yaşından, grup özelliğinden ve eğitim seviyesinden bağımsızdır. Ortak karar verme süreci, hastanın bireysel özelliklerinden ziyade, tamamen hekim iletişimine ve bilgilendirme şeffaflığına bağlıdır.

Tablo 6: Lojistik Regresyon Bağımlı Değişken Dağılım Tablosu (EPV Değerlendirmesi İçin)

Model No (İlgili Tablo)	Bağımlı Değişken (Dependent Variable)	Olay Sayısı (Event, 1)	Olay-Dışı Sayısı (Non-Event, 0)	Toplam Gözlem (N)
Model 1 (Tablo 7)	Robotik Cerrahi Tercihi (1=Evet, 0=Diğerleri)	77	23	100
Model 2 (Tablo 8)	Otonom Robot Yanılgısı (1=Evet, 0=Diğerleri)	18	82	100
Model 3 (Tablo 9)	Ortak Karar Verme Süreci (1=Birlikte, 0=Diğerleri)	61	39	100
Model 4 (Tablo 10)	Kurumsal Kalite/Prestij Algısı (1=Evet, 0=Diğerleri)	77	23	100
Model 5 (Tablo 11)	Teknik Güvenlik Endişeleri (1=Evet, 0=Diğerleri)	51	49	100
Model 6 (Tablo 12)	Klinik Üstünlük Beklenti Algısı (1=Evet, 0=Diğerleri)	72	28	100

Tablo 7: Robotik Cerrahi Tercihini Etkileyen Bağımsız Faktörler (Lojistik Regresyon Analizi)

Bağımsız Değişkenler**	p-değeri	OR	%95 (CI)
Yaş	0.075	1.060	0.994 - 1.129
Grup	0.728	1.250	0.355 - 4.397
Eğitim Düzeyi	0.532	1.645	0.346 - 7.827
Teknolojik Gelişmelere İlgi	**0.004**	**5.613**	1.739 - 18.117
Kararda Hekimin Etkisi	0.082	0.368	0.119 - 1.137

Not: Hosmer-Lemeshow Uyum İyiliği Testi p > 0.05, Nagelkerke R^2 değerleri ilgili modeller için raporlanmıştır.

*Bağımlı Değişken: Robotik cerrahiyi tercih etme = 1, Diğerleri = 0

**Bağımsız Değişkenler: Grup, Hasta Yakını=1, Ref.: Hasta=0; Eğitim Düzeyi, Lisans ve Üzeri=1, Ref.: Lise/Altı=0; Teknolojik Gelişmelere İlgi, Var=1, Ref.: Yok=0; Kararda Hekimin Etkisi, Hekim Tavsiyesi=1, Diğerleri=0

Tablo 8: "Otonom Robot Yanılgısına" Sahip Olmayı Öngören Bağımsız Faktörler (Lojistik Regresyon Analizi)

Bağımsız Değişkenler**	p-değeri	OR	%95 (CI)
Yaş	0.178	1.045	0.980 - 1.114
Grup	0.245	1.960	0.631 - 6.089
Eğitim Düzeyi	0.925	0.935	0.229 - 3.811
İlk Bilgi Kaynağı	0.638	1.328	0.407 - 4.338

Not: Hosmer-Lemeshow Uyum İyiliği Testi p > 0.05, Nagelkerke R^2 değerleri ilgili modeller için raporlanmıştır.

*Bağımlı Değişken: Ameliyatı robot kendi başına yapar diyenler = 1, Diğerleri = 0

**Bağımsız Değişkenler: Grup, Hasta Yakını=1, Ref.: Hasta=0; Eğitim Düzeyi, Lisans ve Üzeri=1, Ref.: Lise/Altı=0; İlk Bilgi Kaynağı, İnternet/Medya=1, Ref.: Diğer/Hekim=0

Tablo 9: Ortak Karar Verme (Shared Decision-Making) Sürecini Etkileyen Bağımsız Faktörler (Lojistik Regresyon Analizi)

Bağımsız Değişkenler	p-değeri	OR	%95 (CI)
Yaş	0.179	0.962	0.909 - 1.018
Grup	0.990	1.006	0.355 - 2.851
Eğitim Düzeyi	0.937	0.960	0.343 - 2.684

Not: Hosmer-Lemeshow Uyum İyiliği Testi p > 0.05, Nagelkerke R^2 değerleri ilgili modeller için raporlanmıştır.

*Bağımlı Değişken: Doktorumla birlikte ortak karar verdik = 1, Diğerleri = 0

**Bağımsız Değişkenler: Grup, Hasta Yakını=1, Ref.: Hasta=0; Eğitim Düzeyi, Lisans ve Üzeri=1, Ref.: Lise/Altı=0

Tablo 10: Kurumsal İmaj ve Prestij (Pazarlama) Algısı Modelini Etkileyen Bağımsız Faktörler (Lojistik Regresyon Analizi)

Bağımsız Değişkenler	p-değeri	OR	%95 (CI)
Eğitim Düzeyi	**0.006**	**5.250**	1.615 - 17.067
İlk Bilgi Kaynağı	0.697	1.194	0.490 - 2.912
Grup	0.470	0.725	0.303 - 1.736

Not: Hosmer-Lemeshow Uyum İyiliği Testi p > 0.05, Nagelkerke R^2 değerleri ilgili modeller için raporlanmıştır.

*Bağımlı Değişken: Hastanede robotik sistem bulunması o hastanenin daha kaliteli olduğunu gösterir = 1, Diğerleri = 0

**Bağımsız Değişkenler: Eğitim Düzeyi, Lisans ve Üzeri=1, Ref.: Lise/Altı=0, İlk Bilgi Kaynağı, İnternet/Medya=1, Ref.: Diğer/Hekim=0, Grup, Hasta Yakını=1, Ref.: Hasta=0;

Medyanın oluşturduğu pazarlama stratejilerinin hastane seçimine etkisini bu model ile test ettik. Eğitim düzeyi yüksek (lisans ve üzeri) olan katılımcılarda, hastanede robotik sistem bulunmasını bir kurumsal kalite ve prestij göstergesi olarak algılama olasılığının, lise ve altı eğitim düzeyindekilere kıyasla 5.2 kat daha yüksek olduğu belirlenmiştir (OR: 5,250; %95 GA: 1,615 - 17,067; p = 0.006). Farklı olarak, yüksek eğitim düzeyine sahip bireylerde, ileri teknolojinin getirdiği yüksek maliyet, kaliteli ve mükemmel olma algısıyla eşleştirilen pazarlama stratejileriyle daha güçlü bir ilişki sergilediği söylenebilir.

Tablo 11: Teknolojiye Güvensizlik ve Güvenlik Endişeleri Modelini Etkileyen Bağımsız Faktörler (Lojistik Regresyon Analizi)

Bağımsız Değişkenler	Kat sayı (β)	p-değeri	OR	%95 (CI)
İlk Bilgi Kaynağı (İnternet/Medya=1, Ref: Hekim/Diğer=0)	1.916	0.008	6.794	1.632 - 28.309
Yaş	-0.014	0.041	0.986	0.942 - 0.999
Eğitim Düzeyi (Lisans/Üzeri=1, Ref: Lise/Altı=0)	-0.775	0.152	0.461	0.161 - 1.312

Not: Hosmer-Lemeshow Uyum İyiliği Testi p > 0.05, Nagelkerke R^2 değerleri ilgili modeller için raporlanmıştır.
*Bağımlı Değişken: En büyük endişesi cihazın arızalanması, yanlış prosedür, kontrol kaybı = 1, Endişem yok/Maliyet = 0
**Bağımsız Değişkenler: Eğitim Düzeyi, Lisans ve Üzeri=1, Ref.: Lise/Altı=0, İlk Bilgi Kaynağı, İnternet/Medya=1, Ref.: Diğer/Hekim=0

Hastaların, ileri teknolojiye karşı sahip oldukları belirli güvenlik endişeleri (cihaz arızası, mekanik hata, yanlış prosedür) incelendiğinde; cerrahi yöntem hakkındaki ilk bilgisini medya/internet kaynaklarından alan katılımcıların, teknik güvenlik endişesi (cihaz arızası, yanlış prosedür vb.) taşıma olasılıklarının (odds), bilgiyi hekimden alanlara kıyasla 6.8 kat daha yüksek olduğu saptanmıştır (OR: 6,794; %95 GA: 1,632 - 28,309; p = 0.008). Katılımcıların yaşı arttıkça teknolojik güvenlik endişesi taşıma olasılıklarının hafif düzeyde azaldığı görülmüştür (OR: 0.986; %95 GA: 0.942 - 0.999; p = 0.041). Bu sonuçlardan, ileri yaştaki hastaların "cerraha" (paternalistik güven) daha çok odaklandıkları, internetten araştırma yapan genç hastaların ise teknik detaylardan kaynaklı spekülatif kaygılara daha açık oldukları çıkarımı yapılabilir.

Tablo 12: Klinik Üstünlük ve "Mucizevi" Beklenti Algısı Modelini Etkileyen Bağımsız Faktörler (Lojistik Regresyon Analizi)

Bağımsız Değişkenler**	p-değeri	OR	%95 (CI)
Teknolojik Gelişmelere İlgi	**0.004**	**4.923**	1.682 - 14.411
Grup	0.268	0.512	0.157 - 1.673
Yaş	0.512	0.982	0.930 - 1.037

Not: Hosmer-Lemeshow Uyum İyiliği Testi p > 0.05, Nagelkerke R^2 değerleri ilgili modeller için raporlanmıştır.
*Bağımlı Değişken: Onkolojik ve fonksiyonel sonuçlar açısından en iyisi robotiktir = 1, Diğerleri = 0
**Bağımsız Değişkenler: Grup, Hasta Yakını=1, Ref.: Hasta=0; Teknolojik Gelişmelere İlgi, Var=1, Ref.: Yok=0

Tablo 13: Anket Yapı Geçerliliği ve Keşfedici Faktör Analizi (EFA) Bulguları

Faktörler ve Anket Maddeleri (Factors & Items)	F1	F2	F3	F4	F5
Faktör 1: Klinik Üstünlük ve Hızlı İyileşme Beklentisi (Açıklanan Varyans: %21.17)					
- Taburcu süresi farkındalığı (Item 41)	**0.652**	0.326	0.045	0.074	-0.127
- Cinsel fonksiyonların korunması algısı (Item 45)	**0.547**	-0.383	0.052	0.169	0.405
- Komplikasyon oranları algısı (Item 47)	**0.693**	-0.033	-0.132	-0.336	0.082
- Yöntem maliyet farkındalığı (Item 43)	**0.543**	0.366	0.028	-0.166	-0.196
Faktör 2: Cerrahi Teknik Bilgi ve Otonom Robot Algısı (Açıklanan Varyans: %12.90)					
- Ameliyatı kimin yaptığı inancı (Item 24)	0.138	**0.639**	-0.045	0.551	0.309
- Onkolojik ve fonksiyonel sonuç algısı (Item 40)	0.326	**-0.549**	0.549	0.153	0.199
Faktör 3: Hekim Aydınlatması ve Bilgilendirme Kalitesi (Açıklanan Varyans: %12.30)					
- Hekimin her iki yöntem hakkında detaylı bilgi vermesi (Item 28)	0.385	0.245	**0.614**	-0.069	-0.103
Faktör 4: Kurumsal Prestij ve Hastane Kalite Algısı (Açıklanan Varyans: %10.82)					
- Hastanede robot olması kaliteli olduğunu gösterir (Item 38)	-0.192	-0.078	0.394	**0.543**	-0.518
Faktör 5: Kişisel Teknoloji İlgi Düzeyi ve Aşinalığı (Açıklanan Varyans: %10.17)					
- Teknolojik gelişmelere ilgi duyma durumu (Item 20)	-0.448	0.292	0.329	-0.032	**0.612**
- Robotik cerrahiyi daha önce duyma durumu (Item 18)	0.327	-0.205	-0.514	0.529	**0.054**
Cronbach's Alpha (α) Spearman-Brown (r)***	0.55	0.26	N/A**	N/A**	0.24

Kaiser-Meyer-Olkin (KMO) Değeri: 0.518, Bartlett Küresellik Testi: $\chi 2 = 484.76$, $p < 0.001$, Genel Cronbach's Alpha Katsayısı: 0.298.
*Not: Faktör yükleri Keşfedici Faktör Analizi (EFA) ve Varimax rotasyonu sonrasında hesaplanmıştır. İlgili faktörün ana yükleri kalın

olarak gösterilmiştir. Anketin geneline ait Cronbach's Alpha katsayısı ölçeğin çok boyutlu (multidimensional) yapısı gereği $\alpha = 0.298$'dir. Psikometri literatürü uyarınca, tek maddeli faktörlerde (F3 ve F4) iç tutarlılık katsayısı hesaplanamamakta; 2 maddeli alt boyutlarda (F2 ve F5) ise Spearman-Brown katsayıları raporlanmaktadır.

** Tek maddeli (single-item) boyutta α matematiksel olarak tanımlı değildir.

*** 2 maddeli yapılarda Cronbach's α yerine Spearman-Brown önerilir.

Hastaların tedavi yöntemlerinin kanser kontrolü (onkolojik) ve cinsel/idrar fonksiyonları koruma yeteneklerine dair algıları modellendiğinde; teknolojik gelişmelere ilgi duyma faktörünün istatistiksel olarak yüksek düzeyde anlamlı bir bağımsız belirleyici olduğu tespit edildi (p = 0.004). Teknolojik gelişmelere ilgi duyma durumu, klinik üstünlük algısı üzerinde anlamlı bir ilişki sergilemiştir. Teknolojiye ilgi duyan katılımcıların, ilgi duymayanlara kıyasla robotik cerrahinin daha üstün klinik sonuçlar vereceğine inanma olasılıklarının 4.9 kat daha yüksek olduğu saptanmıştır (OR: 4,923; %95 GA: 1,682 - 14,411; p = 0.004). Yöntemin mucizevi iyileşme beklentisi, kanıta dayalı tibbi okuryazarlıktan ziyade teknoloji ilgisiyle ilişkili olduğu görülmüştür.

TARTIŞMA

Çalışmamız, prostat kanseri için uyguladığımız robotik cerrahi yönteminin hastalar ve genel popülasyonda farkındalık düzeylerini, tedavi tercihlerini yönlendiren durumların tespiti, ileri teknoloji hakkında sahip oldukları yanılgıları prospektif bir anket yöntemiyle inceleyen bir çalışmadır. Robotik cerrahinin tercih edilmesinin, geleneksel tıbbi karar verme süreçlerinden ziyade, hastaların teknolojiye olan merakları, teknolojiye yönelik algıları ve medyanın oluşturduğu robotik cerrahi imajı tarafından şekillendiği sonucu ortaya çıktı.

Teknoloji Algısı ve Otonom Robot Yanılgısı

Dikkat çeken bir bulgu, hastaların robotik cerrahinin işleyişi hakkında sahip oldukları bilgi eksikliğidir. Çalışmaya katılanlar (hasta ve hasta yakınları), yüksek oranda robotun ameliyatı kendi başına yaptığına veya önceden programlandığına inanmaktadır. Robotun otonomluğu hakkındaki yanlış bilgiyi katılımcıların yaşı, eğitim düzeyi ve bilgi kaynakları parametreleriyle tek başına ön göremeyeceğimiz sonucuna ulaştık. Ayrıca bu yanılgıyı öngörmek üzere kurulan modelin AUC (Eğri Altında Kalan Alan) değeri 0.550 olarak saptandı. Bu zayıf ayırt edicilik gücü, robotların ameliyatı otonom bir şekilde kendi başına yaptığına dair medyanın yarattığı algının öylesine güçlü olduğunu ve hiçbir sosyo-ekonomik profilin bu yanılgıdan muaf olmadığını; yanılgının toplumun her kesimine homojen bir şekilde yerleştiğini matematiksel olarak işaret etmektedir. Yaş, eğitim veya gelir düzeyi gibi faktörlerin otonomi yanılgısını değiştirememesine sebep olan sosyolojik ve psikolojik nedenler, Torrent-Sellens ve ark. tarafından, Avrupa Komisyonu bünyesinde 28 ülkede 27,000'den fazla katılımcıyla yapılan "Eurobarometer" araştırmasıyla da saptandı. Bireylerin otonom teknolojilere güven duymasını sağlayan tek güçlü belirleyici faktörün "önceki pratik kullanım deneyimi" olduğu bu çalışma ile belirlendi (6). Robotik sistemlerle doğrudan fiziksel bir deneyimi olmayan bireylerde, salt medyadan veya ikincil kaynaklardan edinilen teorik bilgiler güveni artırmak yerine şüpheyi, güvensizliği ve algısal belirsizliği derinleştirmektedir. Bizim kohortumuzdaki hastaların da neredeyse tamamının ileri robotik sistemlerle gerçek bir fiziksel temas geçmişinin olmaması (sıfır deneyim); sosyo-demografik ayrıcalıkların neden işe yaramadığını ve toplumun medyanın yarattığı "bilim kurgusal otonomi" imajına neden bu kadar kolay teslim olduğunu açıklamaktadır.

Literatürde Chan ve ark. tarafından, yapılan benzer bir çalışmada da katılımcıların %43.6'sının robotik cerrahinin otonom bir robot ile yapıldığı yanılgısına sahip olduğu ve hastaların %67.5' inin robot kollarının cerrah tarafından manuel olarak hareket ettirildiğini bilmediği raporlandı. Bu durum, hekimlerin ameliyat öncesi onam süreçlerinde "cihazın cerrah tarafından yönlendirildiği" gerçeğini çok daha net bir şekilde vurgulamaları gerektiğini düşündürmektedir (5). Çıkan sonuçlarımız, otonomi yanılgısının sadece lokal değil, küresel ölçekte de sorun olduğunu gösteren güncel literatürle güçlü şekilde örtüşmektedir. Brar ve ark. tarafından yapılan çalışmada, önemli bir orandaki hastanın robota otonom bir işlev atfetmesinden kaynaklı olarak "insan kontrolünden çıkma" algısı, cihazın arızalanması, yanlış cerrahi işlem yapılması ya da "dışarıdan hacklenmesi" gibi abartılı güvenlik endişelerinin de oluşması sonucunu saptadılar (7).

Benzer şekilde, Shen ve ark. toplumun, cerrah tarafından kontrol edilen bir "cerrahi uzantı" kavramına, tam otonom sistem kavramından daha ılımlı baktığına, ancak günlük hayatta çok sık kullanılan "robot" kelimesinin oluşturduğu otonomi algısı nedenli bu sistemlerin kabulünün zorlaştığını vurguladılar (8).

Cerrahi Yöntem Tercihini Yönlendiren Faktörler, Hekim Etkisi ve Beklentiler

Robotik cerrahinin tercih edilme durumunu incelendiğimiz çalışmamızda, çok değişkenli modelde bireyin "teknolojik gelişmelere ilgi duyması" robotik cerrahiyi tercih etme olasılığını (odds) 5.6 kat daha yüksek kılan (OR: 5,613) en güçlü bağımsız faktör olarak bulunmuştur. Hekim tavsiyesi ise istatistiksel olarak anlamlılık sınırında kaldı. Bu durum, paternalistik modelden (yöntemi tamamen hekimin seçtiği) uzaklaşıldığını ve kararın tıbbi yönlendirmeden ziyade hastanın ya da hasta yakınının kişisel teknoloji merakı ve medyanın oluşturduğu etki olduğunu göstermektedir. Chan ve ark. çalışmasında, hastaların robotik cerrahiyi tercih etmesindeki en güçlü ve bağımsız faktör, robotik cerrahinin "daha iyi sonuçlar vereceği yönündeki algı" olduğu saptandı ve karar sürecinde hasta beklentisinin gücü doğrulandı (5). Çalışmamızda, teknolojiye ilgi duyan hastalar, robotik cerrahinin kanser kontrolü ve fonksiyonel sonuçlar açısından açık cerrahiden kesinlikle daha üstün "mucizevi" sonuçlar vereceğine yaklaşık 4.9 kat daha fazla inanmaktaydılar. Bununla birlikte, güncel literatür verilerinde klinik gerçeklik daha vurguludur. Lee ve ark. 4,883 hastalık popülasyon çalışmasında, Jeong ve ark. prospektif verileri içeren çalışmasında, RARP (robot yardımlı radikal prostatektomi)'ın kan kaybını azaltma, hastane yatış süresini kısaltma ve komplikasyon oranlarını belirgin şekilde düşürme (RARP %8.9 vs. RRP %26.4), cinsel fonksiyon iyileşmesinde (RARP %11.4 vs. RRP %5.2) gibi net perioperatif avantajları olduğu kanıtlanmaktadır (1,2). Medyanın pompaladığı "teknolojik kusursuzluk" algısı nedeniyle, operasyon sonrası oluşabilecek olası komplikasyon veya üriner inkontinans nedeniyle ciddi bir karar pişmanlığı oluşma potansiyeli yüksektir. Wolff ve ark.'nın gerçekleştirdiği çok merkezli IMPROVE çalışması, medyatik beklentilerin aşırılığına rağmen RARP sonrasında kritik karar pişmanlığı yaşayan hasta oranının (%28.1), açık cerrahiye (%46.2) kıyasla anlamlı ölçüde daha düşük olduğu gösterildi. Karar pişmanlığını azaltan asıl faktörün hastayla hekimin yöntemi birlikte seçtiği "ortak karar verme" süreci olduğu vurgulandı (3). Teknoloji ve medya kaynaklı kusursuzluk algısı, hasta ve hekimin ortak karar verme süreciyle gerçekçi bir zemine oturtulmalıdır.

Çalışmamızda hasta grubu (yaş ortalaması 65.06 ± 5.99) ile hasta yakınları grubu (yaş ortalaması 53.58 ± 13.62) arasında yaş ($p < 0.001$) ve meslek dağılımı ($p = 0.005$) açısından istatistiksel olarak anlamlı fark saptanmıştır. İki grup arasındaki bu yaş farkı, teknolojik gelişmelere ilgi duyma oranının hasta yakınlarında (%86) hasta grubuna (%64) kıyasla belirgin şekilde yüksek olmasını ($p = 0.011$) etkileyen olası bir karıştırıcı (confounding) faktör olarak değerlendirilmelidir. Genç yaş grubunu oluşturan hasta yakınlarının dijital medya ve internet kullanım sıklığının fazla olması, teknolojik yeniliklere erişimlerini ve ilgi düzeylerini artırırken; ileri yaştaki hastaların ise teknolojiden ziyade geleneksel hekim-hasta ilişkisine ve paternalistik güvene odaklandıkları görülmektedir. Çok değişkenli lojistik regresyon modellerimizde yaş değişkeninin kontrol (karıştırıcı) faktör olarak modele dahil edilmesiyle, bağımsız değişkenlerin (örneğin ilk bilgi kaynağı ve eğitim düzeyi) net etkileri izole edilmiştir.

Güvenlik Endişeleri, Medya Etkisi ve Kurumsal Prestij

Hastaların bilgi edinme kaynaklarının, hasta psikolojisi üzerine etkilerini incelediğimiz çalışmamızda, robotun arızalanması veya yanlış prosedür uygulanması gibi teknik güvenlik endişeleri yaşama riskinin doğrudan hekimden bilgi alanlara kıyasla internet ya da medyadan bilgi alan bireylerde 6.8 kat daha yüksek olduğu (OR: 6,794) saptanmıştır. Bu ciddi artış, medyanın sansasyonel bilgi sunumunun hastayı hekimin güven verici ve gerçekçi klinik süzgecinden mahrum bırakmasından kaynaklanmaktadır. Nitekim Almanya'da yapılan güncel bir çalışmada, Hirtsiefer ve ark. (9), toplumun %39'unun robotik cerrahide temel olarak makinenin arıza yapmasından korktuğu; özellikle ileri yaştaki hastaların donanımsal/mekanik hatadan, genç hastaların ise cerrahın teknik yetersizliğinden endişe duyduğu saptanmıştır. Benzer şekilde, Szabó ve ark.'nın (10), psikolojik güven modeli üzerine yaptığı çalışmada da, hastaların robotik cerrahiye katılım isteğini (willingness) azaltan en güçlü negatif faktörün "cihazın hata yapma korkusu" olduğu matematiksel olarak kanıtlanmıştır. Medyanın pompaladığı "kusursuz makine" pazarlaması ile "elektronik bir cihazın

arıza yapabileceği" ihtimali arasındaki bu zıtlık, empatik bir hekimin rehberliği olmadığında hastanın zihninde derin bir teknolojik anksiyeteye dönüşmektedir. Hatta bu durum o kadar ciddi bir boyuta ulaşmıştır ki; Amerikan Gıda ve İlaç Dairesi (FDA), robotik cerrahinin uzun dönem sağkalım faydalarının geleneksel cerrahiye kıyasla henüz tam olarak kanıtlanmadığına (Boyina ve ark. 2020) dikkat çekerek sağlık hizmeti sunucularının medyatik pazarlama yerine hastalarla potansiyel riskleri ve alternatifleri şeffaf bir şekilde tartışması gerektiği konusunda resmi güvenlik uyarıları yayımlamak zorunda kalmıştır (11).

Bu deneyimsizlik ve bilgi karmaşası ile robotik cerrahi sağlık kuruluşları tarafından da pazarlama, hizmet artışı ve prestij aracına dönüştürülmüştür. Çalışmamızda, yüksek eğitimli (lisans ve üzeri) hastaların robotik sistemi doğrudan bir "hastane kalite ve prestij" göstergesi olarak algılama eğilimlerinin 5.2 kat daha yüksek çıkması, tıbbi teknoloji pazarlamasının algı yönetimindeki gücünü ispatlamaktadır. Bu algının kurumsal ve ekonomik sonuçları, Güney Kore'de Ro ve Do tarafından ulusal sağlık verileri (NHIS) kullanılarak yapılan çok güncel bir çalışmayla da somutlaştırılmıştır. Söz konusu çalışmada, robotik cerrahi sistemini hastaneye entegre eden kurumların prostat kanseri cerrahisi hacimlerinde ve yatan hasta sayılarında anında muazzam bir artış (çeyreklik bazda belirgin sıçrama) yaşadıklarını düşündürmekte; bu artışın doğrudan "reklam ve pazarlama etkisi" (advertising effect) ile çevre bölgelerdeki hastaların kuruma çekilmesiyle (merkezileşme) ilişkili olduğu belirtilmiştir (12). Robotik teknolojinin kurumsal pazarlamadaki bu agresif çekim gücü, reklamların oldukça zayıf olduğu kadın pelvik cerrahisindeki verilerle kıyaslandığında, öncesinde robotik reklam görmeyen hastaların sadece %6.4'ünün robotiği tercih etmesiyle de keskin bir zıtlık oluşturmaktadır (13). Tüm bu güncel literatür verisiyle kendi verimizi değerlendirdiğimizde, yüksek robotik cerrahi tercihi ve eğitimli gruptaki güçlü prestij algısı, nesnel klinik ihtiyaçlara değil, büyük oranda medyanın yarattığı abartılı popülarite ve teknolojinin prestij aracı olarak kullanılmasıyla alakalıdır.

Kısıtlıklar

Çalışmamızın önemli metodolojik kısıtlılıklarından biri, birincil amaç doğrultusunda (iki grubun non-parametrik karşılaştırılması için) belirlenen N=100 örneklem büyüklüğünün, kurulan bazı çok değişkenli lojistik regresyon modellerinde değişken başına düşen olay sayısının (EPV) düşük kalmasına yol açmasıdır. Bu durum, bazı modellerde güven aralıklarının genişlemesine ve aşırı uyum (overfitting) riskine zemin hazırlayabilir. Özellikle Tablo 11' de bilgi kaynağının teknik güvenlik endişesi üzerindeki etkisini inceleyen regresyon modelinde veri seyrekliğinden (quasi-separation) kaynaklı aşırı geniş güven aralığı sorunu yaşanmıştır. Bu kısıtlılığı aşmak ve tahmini standardize etmek adına Firth'in penalize edilmiş regresyon analizi uygulanmış olsa da, elde edilen bulguların gelecekte daha yüksek örneklem büyüklüğüne sahip çok merkezli çalışmalarla doğrulanması gerekmektedir.

SONUÇ

Dijital çağda prostat kanseri hastalarının cerrahi yöntem tercihi, hekimin tıbbi yönlendirmesinden ziyade hastanın teknoloji merakı, medyanın yarattığı algı ve kurumsal prestij beklentisi tarafından şekillenmektedir. Ancak bu popülarite, hastaların cihazın otonomisine ve klinik sonuçlarına dair ciddi yanılgılara düşmesine de zemin hazırlamaktadır. Robotik cerrahinin minimal invaziv avantajları literatürde sabittir; ancak cerrahların temel görevi, bu yöntemi sunarken hastanın gerçek dışı "kusursuzluk" beklentilerini yönetmek, medyadan kaynaklanan yersiz güvenlik endişelerini gidermek ve onam süreçlerinde teknolojinin sınırlarını şeffaf bir ortak karar alma mekanizmasıyla hastaya aktarmak olmalıdır.

Veri Kullanılabilirlik Bildirimi: Uygulanamaz. Bu makale veri üretimi veya analizi bildirmemektedir.

Beyan Bildirimi: Bildirilecek herhangi bir husus bulunmamaktadır.

Çıkar Çatışması: Tüm yazarlar herhangi bir çıkar çatışmaları olmadığını beyan ederler.

Hasta Onam Beyanı: Çalışmaya dahil edilen tüm hastalardan bilgilendirilmiş onam formu alınmıştır.

Finansman: Yoktur

Etik Onay: Bu çalışma için etik onay Ankara Etlik Şehir Hastanesi Bilimsel Araştırmalar Etik Kurulu'ndan alınmıştır (Onay numarası: AEŞH-BADEK2-2026-239, Tarih: 24.03.2026).

Yazar Katkıları:

F. Sandıkçı: Proje geliştirme, veri toplama, makale yazımı ve veri analizi

A. Beşçocuklu: Veri toplama, veri analizi ve makale düzenlemesi

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Review Article
Derleme

Endourol Bull. 2026;18(3):276–284. doi: 10.54233/endourolbull-1851389

Immunology of Urinary Tract Infections: Historical and Scientific Development From Uroscopy to the Present Day

Üriner Sistem Enfeksiyonlarının İmmünolojisi: Üroskopiden Günümüze Tarihsel ve Bilimsel Gelişim

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ABSTRACT

For thousands of years, uroscopy has served as one of the fundamental diagnostic methods in medicine and has played an important role in the understanding of urinary system diseases. The earliest written records of urinary tract infections (UTIs) date back to the Ebers Papyrus, reflecting early historical descriptions of the disease (1). In this review, the evolution of knowledge regarding UTIs from early observational approaches to modern immunological understanding is evaluated, with particular emphasis on the role of innate and adaptive immune response mechanisms in disease pathogenesis. Key immunological pathways, including Toll-like receptors (TLRs), Th1/Th2 balance, and tissue-resident memory T (TRM) cells, are discussed in relation to infection control and recurrence, while differences in immune responses between animal models and human systems are highlighted. In conclusion, a deeper understanding of immunological mechanisms in UTI pathogenesis represents an important research area that may contribute to the development of targeted and immunomodulatory therapeutic strategies.

Keywords: history of medicine, immunology, immune response, infection, urinary system

ÖZET

Binlerce yıl boyunca tıbbın temel tanı yöntemlerinden biri olan üroskopi, üriner sistem hastalıklarının anlaşılmasında önemli bir rol oynamıştır. İdrar yolu enfeksiyonlarına (İYE) ilişkin ilk yazılı kayıtlar, Ebers Papirüsü'ne kadar uzanmakta olup hastalığın tarihsel süreç içerisindeki tanımlamalarını içermektedir (1). Bu derlemede, İYE'ye yönelik bilginin tarihsel gözlemsel yaklaşımlardan modern immünolojik anlayışa uzanan gelişimi değerlendirilmiş; özellikle doğal ve edinsel immün yanıt mekanizmalarının hastalık patogenezindeki rolü ele alınmıştır. Toll-benzeri reseptörler (TLR), Th1/Th2 dengesi ve doku yerleşik hafıza T (TRM) hücreleri gibi temel immünolojik mekanizmaların enfeksiyon kontrolü ve rekürrens üzerindeki etkileri tartışılmış, ayrıca hayvan modelleri ile insan verileri arasındaki immünolojik yanıt farklılıkları vurgulanmıştır. Sonuç olarak, İYE patogenezine ilişkin immünolojik mekanizmaların daha iyi anlaşılması, hedefe yönelik ve immünomodülatör tedavi stratejilerinin geliştirilmesine katkı sağlayabilecek önemli bir araştırma alanı oluşturmaktadır.

Anahtar Kelimeler: enfeksiyon, immünoloji, immün yanıt, tıp tarihi, üriner sistem

Cite As: *Ilgar E. Immunology of Urinary Tract Infections: Historical and Scientific Development from Uroscopy to the Present Day. Endourol Bull. 2026;18(3):276–284.* https://doi.org/10.54233/endourolbull-1851389

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Received : December 29, 2025 ***Accepted*** : August 21, 2026

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GİRİŞ

Günümüzde doktorlar idrarı belirli hastalıkları teşhis etmek için kullansa da antik çağlardan Viktorya dönemine kadar idrar, birincil tanı aracı olarak değerlendirilmiştir. Laboratuvar tıbbı, üroskopi olarak adlandırılan ve günümüzde idrar tahlili olarak bilinen insan idrarının analiziyle başlamıştır (2). Hekimler idrarı "ilahi bir sıvı" ya da vücuda açılan bir pencere olarak tanımlamışlardır. Üroskopi sanatının temelleri Babil ve Mısırlı hekimlere kadar uzanmaktadır. "Uroscopia" kelimesinden türeyen üroskopi, "idrarın bilimsel muayenesi" anlamına gelir. Kelime, Yunanca "idrar" anlamındaki "*ouron*" ve "bakmak, incelemek" anlamındaki *skopeo* sözcüklerinden türetilmiştir (3). Arapça'da şişe anlamına gelen idrar örneğinin toplanması ve incelenmesi için kullanılan kaba "Quaroorah" adı verilmiştir. Üroskopi üzerine şiir yazan, Gilles de Corbeil (1,165–1,213), Matula›yı tanıtmıştır. Matula, şeffaf ve ince camdan yapılmış mesane şeklinde bir idrar kabıydı.

Yalnızca sağ elde tutulması gereken bu kap, günümüzde beyaz önlük ve stetoskopun taşıdığı sembolik anlam gibi, hekimler için bir prestij göstergesi olarak kabul edilmiştir (Şekil 1). Döneme ait birçok çizim ve illüstrasyonda, hekimlerin matulayı göz hizasında tutarak hastanın içsel rahatsızlıklarını anlamaya çalıştıkları görülmektedir (Şekil 2).

İslam tıbbı döneminde de üroskopi önemli bir tanı yöntemi olmaya devam etmiştir. İbn-i Sina (MS 980–1,037), El-Kanûn Fi't-Tıb adlı eserinde üroskopi için idrar örneğinin nasıl toplanması gerektiğini ve örneğin karakterini değiştirebilecek faktörleri ayrıntılı şekilde açıklamıştır. Sabah alınan idrar örneğinin analiz için en iyi örnek olduğunu belirtmiştir (4).

Bir diğer Fars hekimi İsmail Cürcani (MS 1,040–1,136) ise 24 saatlik idrar örneğinin mesane şeklindeki bir kapta saklanması gerektiğini, örneğin renginde değişiklik olmaması için güneş ışığı ve ısıdan korunmasının önemini vurgulamıştır (5).

Johannes de Ketham tarafından 1,491 yılında yayınlanan "Fasciculus Medicinae" adlı eserde, kendi kendine tanıya yardımcı olan bir idrar renk çemberinden söz edilmektedir. . Bu büyük ve dairesel çemberin etrafında, farklı renklerde idrar içeren 21 adet Matula yer almaktaydı (6).



Şekil 1. Tarihsel üroskopi pratiği. Hekim, matula adı verilen idrar kabını ışığa tutarak idrarın renk, koku ve berraklığına göre hastalık tanısı koymaya çalışırken, hasta yatağında gözlemlenmektedir (Wellcome Library Collection 44725i)



Şekil 2. Üroskopi geleneği kapsamında hekim, idrar dolu cam şişeyi inceleyerek hastalık tanısı koymaya çalışmakta; laboratuvar öncesi tıp anlayışı yansıtılmaktadır. (Wellcome Library Collection 47456i)

Çemberin etrafı 21 farklı renkte idrar dolu Matula ile çevriliydi. Test edilen idrar örneğinin rengi ve kıvamı, tanı koyabilmek amacıyla bu örneklerle karşılaştırılıyordu (Şekil 3).

Çemberin dört köşesinde ise dört beden mizacını temsil eden küçük daireler bulunmaktaydı. Bu yaklaşım, hastalıkların humoral teori çerçevesinde değerlendirilmesine dayanıyordu (7). İdrar renginin vücuttaki mizaca ilişkin bilgi verdiği düşünülmüş; kolerik, melankolik, kanlı ve balgamlı olmak üzere dört temel mizacın idrar incelemesiyle değerlendirilebileceği kabul edilmiştir. Zamanla bu yöntem o kadar yaygınlaşmıştır ki, bazı hekimler klinik muayene yapmaksızın yalnızca idrar incelemesiyle tanı koymaya başlamıştır. Böylece idrar, "hastanın dilsiz habercisi" olarak tanımlanmıştır (8).

Üriner sistem fizyolojisinin anlaşılmasındaki önemli dönüm noktalarından biri, böbreklerin idrar oluşumundaki temel rolünü ilk kez ortaya koyan Galen'e dayanmaktadır.

İbn Sina ise, o dönemde idrar tahliliyle ilgili bilinen Yunan ve Uzak Doğu uygulamalarını ve bilgilerini korumuştur. Daha sonraki süreçte İbn-i Sina, Yunan ve Uzak Doğu tıbbına ait idrar analizi bilgisini sistematik biçimde koruyup geliştirmiş ve "İdrar, hastalığın bilgisi için sadık bir rehberdir" ifadesiyle idrar analizinin tanısal önemini vurgulamıştır. William Roberts 1,881 yılında, taze idrarda çubuk şeklindeki bakterileri tanımlamış ve bakterilerin idrarda gözlenmesine ilişkin ilk çalışmayı yayımlamıştır (9). Bu gelişmeler, bakterilerin üriner sistem enfeksiyonlarının temel etkeni olduğunun anlaşılmasına zemin hazırlamıştır.

Zamanla immünoloji alanındaki ilerlemeler, üriner sistem enfeksiyonlarının yalnızca mikrobiyal etkenlerle açıklanamayacağını; konak immün yanıtının da enfeksiyonun gelişimi, kontrolü ve rekürrensinde belirleyici rol oynadığını ortaya koymuştur. Özellikle Toll-benzeri reseptörler (TLR), Th1/Th2 dengesi ve doku yerleşik hafıza T (TRM) hücreleri gibi immünolojik mekanizmaların enfeksiyonun klinik seyri üzerindeki etkileri güncel çalışmalarla gösterilmektedir. Böylece tarihsel gözlemsel yaklaşımlardan modern moleküler immünolojiye uzanan süreçte, idrar yolu enfeksiyonlarına ilişkin anlayış önemli ölçüde derinleşmiştir.



Şekil 3. Üroskopi geleneğinde idrarın renklerine göre sınıflandırıldığı ve her rengin farklı bir hastalık durumunu temsil ettiği dairesel tıbbi şema. (Wellcome collection)

Bu derlemede, üroskopiden modern immünolojiye uzanan tarihsel süreç içerisinde idrar yolu enfeksiyonlarına ilişkin bilgi birikiminin gelişimi değerlendirilmekte; doğal ve edinsel immün yanıt mekanizmalarının hastalık patogenezindeki rolü güncel literatür eşliğinde tartışılmaktadır.

Üriner Sistem Enfeksiyonlarında Doğal İmmün Yanıt

Üriner sistem enfeksiyonları (İYE), dünya genelinde en yaygın görülen bakteriyel enfeksiyonlardan biridir. İdrar yolu, gastrointestinal sistemi kolonize eden farklı mikroorganizmalara sürekli olarak maruz kalmaktadır. İdrar yolu enfeksiyonları, komplike ve komplike olmayan olmak üzere iki ana kategoride sınıflandırılabilir. Komplike olmayan idrar yolu enfeksiyonları, genellikle *Escherichia coli* tarafından meydana gelirken, komplike idrar yolu enfeksiyonları, özellikle uzun süreli kateterizasyon gibi faktörlerle ilişkilendirilenler, polimikrobiyal olabilmektedir. Bu tür enfeksiyonlar genellikle *Proteus mirabilis*, *Providencia stuartii*, *Morganella morganii*, *Klebsiella pneumoniae*, *E. coli* ve *Pseudomonas aeruginosa* gibi patojenler tarafından oluşabilmektedir (10).

İdrar yolu epitel hücreleri, patojenlere karşı ilk savunma hattını oluşturarak, enfeksiyonun önlenmesinde önemli bir rol oynamaktadır. Bu epitel hücreleri, patojenlerin tanınmasında ve ortadan kaldırılmasında etkili bir savunma mekanizması sağlayan PRR'lerin (Patern Tanıma Reseptörleri) büyük bir ailesi olan TLR tarafından modüle edilir. TLR›ler, idrar yolunu kaplayan epitel hücrelerinde yaygın olarak ifade edilir ve idrar yolu enfeksiyonları sırasında mikrobiyal bileşenlerin tanınmasında kritik bir rol oynamaktadır (11).

TLR aracılı yanıt yalnızca enfeksiyonun erken kontrolünü sağlamakla kalmamakta, aynı zamanda klinik seyri de belirleyen çift yönlü bir immün mekanizma olarak değerlendirilmektedir. Aşırı TLR aktivasyonu inflamatuvar doku hasarını artırarak semptom şiddetini yükseltebilirken, yetersiz yanıt bakteriyel klirensin gecikmesine ve rekürren enfeksiyonlara zemin hazırlayabilmektedir. Bu durum, doğal immün yanıtın koruyucu ve patolojik etkiler arasında hassas bir dengeye sahip olduğunu göstermektedir.

İYE ile ilgili en kapsamlı şekilde incelenen PRR'lerden biri TLR4'tür. TLR4, hem insanlarda hem de farelerde mesane yüzey epitel hücrelerinde ve böbrek epitel hücrelerinde ifade edilmektedir (12). TLR4'ün fonksiyonu, İYE'nin etkili bir şekilde çözülmesi için kritik öneme sahiptir. TLR4, Gram-negatif bakterilerin lipopolisakkarit (LPS) molekülleri tarafından aktive edilir ve adaptör proteinler aracılığıyla NF-κB transkripsiyonel yanıtlarının başlatılmasına yol

açar. Bu süreç, mesane epitel hücrelerinden IL-6 ve IL-8 gibi inflamatuvar mediatörlerin salınımını tetikler. Fare mesanesinde TLR4 sinyallemesinin eksikliği ($TLR4^{-/-}$), konak inflamatuvar yanıtını ve nötrofil alımını azaltarak persistan enfeksiyon gelişimine neden olmaktadır. Bununla birlikte, murin modellerde gösterilen bu güçlü inflamatuvar yanıtın insan çalışmalarında daha heterojen klinik karşılıklar göstermesi, önemli bir translasyonel sınırlılık olarak değerlendirilmektedir.

TLR4 aktivasyonu ayrıca hücre içi vezikül oluşumunun engellenmesi ve bakterilerin ekzositoz yoluyla atılması gibi mekanizmalarla bakteriyel invazyonu sınırlar. TLR5 (bakteriyel flagellini tanır) ve TLR2 (peptidoglikan tarafından aktive edilir) ise mesane epitel hücrelerinde proinflamatuvar sinyallemeyi başlatarak CXCL1, IL-6 ve TNF-α gibi mediatörlerin üretimini artırır (13). Ancak farklı TLR alt tiplerinin enfeksiyonun farklı evrelerinde değişken etkiler göstermesi, immün yanıtın tek yönlü değil dinamik ve bağlama bağımlı olduğunu göstermektedir.

Antimikrobiyal peptitler, doğal bağışıklık yanıtının önemli bir bileşenini oluşturmaktadır. Bu peptitler, bakteriyel zarlarına bağlanarak onları parçalamada etkin rol oynayan, kısa ve pozitif yüklü moleküllerdir. Örneğin, β-defensin 1 ve katelisidin LL-37, idrar yolu enfeksiyonlarına (İYE) yanıt olarak önemli işlevler üstlenen antimikrobiyal peptitler arasında yer almaktadır (14,15)

RNase A süper ailesine ait antimikrobiyal peptitler (AMP'ler), insan idrar yolundaki yüksek konsantrasyonları ve güçlü bakterisidal özellikleri nedeniyle büyük ilgi görmüştür. İnsan idrar yolu enfeksiyonlarında (İYE) en iyi karakterize edilen AMP olan RNase7, idrar yolu boyunca başlangıçta ifade edilir ve sağlıklı idrarda mikromolar konsantrasyonlarda tespit edildikten sonra İYE sırasında daha da artmaktadır. RNase7 içeren insan idrarı veya fizyolojik konsantrasyonlardaki rekombinant RNase7 ile yapılan in vitro inkübasyonlar, *Escherichia coli* ve *Enterococcus sp*. gibi altı yaygın üropatojenik türün öldürülmesine neden olmuştur (16).

LCN2 ise, *UPEC* üzerinde antibakteriyel etkilere sahipken, LL-37 ise hem *UPEC* hem de *Candida* üzerinde antibakteriyel etki göstermektedir (17).

Üropatojenik bakteriler, özellikle *UPEC* (Üropatojenik Escherichia coli), fimbria adı verilen yapışma organellerini ifade eder. FimH gibi yapışma molekülleri, *UPEC*'in mesane epitel hücrelerine (BEC'ler) tutunmasına ve invazyonuna yardımcı olmak amacıyla fimbria uçlarında ifade edilmektedir. Konak, mesanedeki hem hücre dışı hem de hücre içi bakterileri temizlemek için güçlü bir doğal bağışıklık yanıtı başlatsa da, yüksek insidans ve tekrarlama oranları, mesanedeki edinsel bağışıklık sisteminin patojen bakterilerle etkin bir şekilde başa çıkamadığını göstermektedir (18).

UPEC ile enfekte olmuş farelerin mesanelerinin enfeksiyon sırasında ve doğal iyileşme sonrasında mikroskobik incelemesinden elde edilen bulgular, hücre içi *UPEC*'in küçük bir kısmının mesane epitel hücreleri (BEC'ler) içinde varlığını sürdürmeye devam ettiğini ve uzun süreli, hareketsiz hücre içi rezervuarlar oluşturabildiğini ortaya koymuştur. Bu durum, mesane edinsel bağışıklık yanıtlarında ve kalıcı bakterilerin tanınması ile ortadan kaldırılmasında önemli eksiklikler bulunduğunu göstermektedir. Bu gözlem, üropatojenler tarafından ifade edilen *FimH*'nin, kemokin salgılanması yoluyla fare BEC'lerini çok sayıda T hücresi toplamaya teşvik edebileceğini gösteren diğer çalışmalarla da desteklenmektedir (19).

Üriner Sistem Enfeksiyonlarında Edinsel İmmün yanıt

Bakteriyel enfeksiyon hastalıklarının prevalansı, özellikle yaşlanan popülasyonla birlikte artış göstermektedir. Son çalışmalar, bu hastalıkların ilerleyişinde edinsel immün yanıtın temel bileşeni olan T hücre alt gruplarının kritik rol oynadığını ortaya koymuştur. Bakteriyel mesane enfeksiyonları sırasında CD8+ T hücreleri, γδ T hücreleri, Th2 hücreleri ve daha az oranda Th1 hücreleri enfekte dokuya yönlendirilmekte ve lokal immün yanıtın şekillenmesinde rol oynamaktadır. Bununla birlikte, son dönem çalışmalar enfeksiyon sonrası aktive olan bazı T hücre alt tiplerinin

mesaneye göç ettiğini, ancak bakteriyel klirens kapasitesinin sınırlı olduğunu göstermektedir. Bu durum, edinsel immün yanıtın her zaman koruyucu olmadığını, bazı durumlarda enfeksiyonun kronikleşmesine katkıda bulunabileceğini düşündürmektedir (20,21).

IFN-γ sinyalizasyonu ve IL-4 sinyalizasyon raporlayıcı fare modelleri kullanılarak yapılan akış sitometrisi temelli çalışmalarda, enfekte mesaneye yönlendirilen CD4+ T hücrelerinin belirgin şekilde Th1 (IFN-γ üreten) yanıt yerine Th2 (IL-4 üreten) yanıt yönünde polarize olduğu gösterilmiştir. Bu Th2 ağırlıklı yanıtın, bakteriyel eliminasyondan çok doku onarım süreçleriyle ilişkili olduğu ve özellikle tekrarlayan idrar yolu enfeksiyonu modellerinde daha da belirgin hale geldiği bildirilmiştir. Bu bulgular, Th2 baskın immün yanıtın yalnızca iyileşme sürecinin bir parçası olmadığını, aynı zamanda rekürren enfeksiyonlara yatkın bireylerde patolojik bir immün profil oluşturabileceğini düşündürmektedir (22,23).

IL-17 sinyal yolu ve γδ T hücrelerinin, İYE'nin akut fazında inflamatuvar yanıtın düzenlenmesinde önemli rol oynadığı bilinmektedir. Ancak IL-17A eksikliğinin farklı fare modellerinde farklı klinik sonuçlara yol açması, bu yolun bağlama bağımlı etkilerini göstermektedir. Örneğin IL-17A$^{-/-}$ C57BL/6 farelerinde ikincil *Escherichia coli* enfeksiyonuna karşı koruyucu yanıtın büyük ölçüde değişmediği bildirilirken, aynı genetik eksikliğe sahip BALB/c (BALB/c fare suşu) farelerinde böbreklerde artmış bakteri yükü ve kronik piyelonefrit gelişimine yatkınlık gözlenmiştir. Bu durum, IL-17 aracılı yanıtın yalnızca akut enfeksiyon kontrolünde değil, aynı zamanda üst üriner sistem tutulumunun önlenmesinde de kritik rol oynadığını ve genetik/immünolojik zeminle güçlü şekilde etkileştiğini göstermektedir (24).

Genel olarak bu veriler, edinsel immün yanıtın İYE'de tek yönlü bir koruyucu mekanizma olmadığını; aksine Th1/Th2 dengesi, IL-17 ekseni ve T hücre alt tiplerinin dağılımının klinik sonuçları doğrudan etkilediğini göstermektedir. Özellikle bazı immün yanıtların bakteriyel temizliği artırmak yerine doku onarımı veya persistan inflamasyon yönünde kayabilmesi, rekürren ve kronik İYE patogenezini açıklamada önemli bir immünolojik temel oluşturmaktadır.

Başka bir açıdan, *Escherichia coli* ile oluşturulan tekrarlayan üriner sistem enfeksiyonu (ÜSE) modellerinde, dokuya yerleşmiş hafıza (TRM) T hücrelerinin birincil enfeksiyon sonrası mesane mukozasında biriktiği ve yaklaşık 28 gün sonra gelişen yeniden enfeksiyonlara karşı patojen kontrolünü belirgin şekilde iyileştirdiği gösterilmiştir. Bununla birlikte, dolaşımdaki CD4+ ve CD8+ T hücrelerinin antikor aracılı eliminasyonunun azaltılmasının koruyucu etki sağlamadığı bildirilmiştir. Bu bulgu, sistemik dolaşımdan ziyade lokal dokuya yerleşmiş TRM hücrelerinin rekürren İYE kontrolünde belirleyici olduğunu ve mukozal immünitenin klinik açıdan daha kritik bir rol oynayabileceğini düşündürmektedir. Bununla birlikte TRM hücrelerinin etkili genişlemesi için enfeksiyon sonrası en az 24 saat süreyle yeterli antijen varlığının gerekli olması, bu yanıtın zamanlamaya duyarlı olduğunu ve erken antibiyotik tedavisi ile etkileşebileceğini göstermektedir. Bu durum, TRM temelli immünomodülatör yaklaşımların rekürren İYE önlenmesinde potansiyel bir tedavi stratejisi olabileceğini düşündürmektedir (25).

İnsan çalışmalarında ise idrar yolu enfeksiyonlarına karşı humoral immün yanıtın daha heterojen ve klinik bağlama bağımlı olduğu görülmektedir. *Escherichia coli* O ve K antijenlerine karşı gelişen antikorlar, akut piyelonefritli çocukların hem serumunda hem de idrarında saptanabilmektedir. Özellikle spesifik IgA yanıtının, düşük IgG düzeylerini takiben mukozal yüzeyde baskın hale geldiği bildirilmektedir. Antibiyotik tedavisi almayan İYE'li çocuklarda idrarda *E. coli*'ye karşı IgA varlığına karşın serumda saptanmaması, yanıtın lokal mukozal immünite ile sınırlı olduğunu göstermektedir.

Benzer şekilde yapılan bir çalışmada, 30 sağlıklı kadın, semptomatik ve asemptomatik İYE'li kadın grupları karşılaştırıldığında; *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae* ve *Proteus mirabilis* gibi patojenlere karşı hem serum hem de idrarda IgM, IgG ve IgA düzeylerinde artış saptanmıştır. Ancak bu antikor yanıtının yalnızca enfeksiyonun varlığını yansıttığı, koruyucu immünite ile her zaman doğrudan ilişkili olmadığı değerlendirilmektedir.

Bu durum, humoral yanıtın İYE'de çoğu zaman bir "koruyucu mekanizma" olmaktan ziyade "maruziyet ve enfeksiyon aktivitesinin biyolojik göstergesi" olarak yorumlanması gerektiğini düşündürmektedir (26).

Genel olarak bu veriler, ÜSE'de koruyucu immünitenin büyük ölçüde lokal dokuya yerleşmiş hücresel yanıt (özellikle TRM hücreleri) üzerinden şekillendiğini, buna karşılık humoral yanıtın ise enfeksiyonun klinik aktivitesiyle daha çok ilişkili olduğunu göstermektedir. Bu ayrım, rekürren enfeksiyonların anlaşılmasında mukozal immünitenin sistemik immün yanıta göre daha belirleyici olabileceğini ortaya koymaktadır.

SONUÇ

İdrar yolu enfeksiyonlarının anlaşılmasına yönelik tarihsel süreç, üroskopiden başlayarak günümüzde moleküler immünolojiye uzanan bir dönüşümü yansıtmaktadır. Bu süreç, konak-patojen etkileşiminin yalnızca mikrobiyolojik değil, aynı zamanda immünolojik mekanizmalar üzerinden şekillendiğini ortaya koymuştur. Güncel veriler, özellikle TLR aracılı doğal immün yanıt, adaptif immün dengeler ve dokuya yerleşik hafıza T hücrelerinin (TRM) enfeksiyonun klinik seyri ve rekürrensinde belirleyici olduğunu göstermektedir.

Bu nedenle gelecekteki yaklaşımların yalnızca antimikrobiyal tedavilere değil, aynı zamanda konak immün yanıtını modüle eden stratejilere odaklanması; özellikle mukozal immünitenin güçlendirilmesi ve inflamatuvar yanıtın dengelenmesi hedeflenmelidir. Böylece idrar yolu enfeksiyonlarının daha etkili ve rekürrensi azaltılmış şekilde yönetilmesi mümkün olabilecektir.

Finansman: Bu araştırma, kamu, ticari veya kâr amacı gütmeyen sektörlerdeki finansman kuruluşlarından herhangi bir özel hibe almamıştır.

Çıkar Çatışması: Bu makalenin yayımlanmasıyla ilgili herhangi bir çıkar çatışması bulunmadığını beyan ederim.

Bilgilendirilmiş Onam: Bu çalışma insan katılımcıları içermemektedir; bu nedenle bilgilendirilmiş onam alınması gerekmemiştir.

Etik Onay: Bu çalışma için etik onay gerekmemiştir.

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Author Guidelines

Yazarlara Bilgi

Dergi, yazarların yayın haklarını kısıtlama olmaksızın saklamasını sağlar.

Yazarların kimlik bilgileri ve e-posta adresleri hiçbir şekilde başka amaçlar için kullanılmamaktadır.

Gönderilen yazıların daha önce yayınlanmamış olması veya başka bir dergide değerlendirme aşamasında olmaması gerekmektedir.

Gönderilen yazılar herhangi bir kongrede takdim edilmiş ise bu durum gönderilen makalede dipnot olarak bildirilmelidir.

Derginin Yayın Kurulu, tüm itirazları Yayın Etik Komitesi (COPE) kuralları çerçevesinde ele alır. Bu gibi durumlarda, yazarlar temyiz ve şikayetleri ile ilgili olarak yayın kuruluyla doğrudan iletişime geçmelidir. Gerektiğinde, dahili olarak çözülemeyen sorunları çözmek için bir ombudsman atanabilir. Editör, tüm temyiz ve şikayetler için karar verme sürecindeki nihai otoritedir.

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Bir yazının yayın için kabul edilmesinde en önemli kriterler özgünlük, yüksek bilimsel kalite ve alıntı potansiyelinin varlığıdır. Dergide yayınlanmak üzere gönderilen yazılar, daha önce başka bir yerde yayınlanmamış ve yayınlanmak üzere gönderilmemiş olmalıdır. Bir kongrede tebliğ edilmiş ve özeti yayınlanmış çalışmalar organizasyonun adı, yeri ve tarihi belirtilmek şartı ile kabul edilebilir.

Deneysel, klinik, ilaç çalışmalarının ve bazı vaka raporlarının araştırma protokollerinin Etik Kurul tarafından uluslararası sözleşmelere uygun olarak onaylanması (Dünya Tıp Birliği Helsinki Deklarasyonu "İnsan Denekleri ile İlgili Tıbbi Araştırmalar İçin Etik İlkeler") gereklidir.

Etik kurul izni gerektiren tüm araştırmalar için etik kurul onayı alınmalı, bu onay makalede belirtilmeli ve belgelenmelidir.

Etik kurul izni gerektiren çalışmalarda izne ilişkin bilgiler (kurulun adı, tarih ve sayısı) yöntem bölümünde ve makalenin ilk/son sayfalarından birinde yer alabilir; Olgu sunumlarında aydınlatılmış onam/rıza formunun imzalanması ile ilgili bilgilere makalede yer verilmelidir.

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Koşullar:

Orijinal yazarlara atıf sağlanmalıdır. Uyarlamalar aynı şartlar altında lisanslanmalıdır.

Eser ticari amaçlarla kullanılamaz.

Yazar Sorumlulukları

Telif Hakkı Sözleşmesi: Yazarlar, yazılarını göndermeden önce " Yazar Başvuru ve Telif Hakları Formu"nda belirtilen şartları incelemeli ve kabul etmelidir. Bu sözleşmenin imzalı bir kopyası gönderimle birlikte yüklenmelidir.

Çalışmanın Özgünlüğü: Yazarlar, gönderilen yazının kendi özgün yaratımları olduğunu ve intihal içermediğini teyit eder. Kullanılan herhangi bir üçüncü taraf materyali, Creative Commons Atıf-Ticari Olmayan-Benzer Paylaşım 4.0 Uluslararası (CC BY-NC-SA 4.0) lisansına uygun şekilde uygun şekilde atıfta bulunulmalıdır.

Yazar Sorumluluğu: Her yazar çalışmaya bireysel olarak katkıda bulunmuştur ve içeriğinden tamamen sorumludur. Yazarlar ayrıca atıf standartlarına ve lisanslama şartlarına uyumu teyit eder.

Gönderinin Onayı: Tüm yazarlar, gönderimden önce yazının son halini incelemeli ve onaylamalıdır.

Önceki Yayın: Yazarlar, yazının başka bir yerde yayınlanmadığını ve aynı anda başka bir dergide yayınlanmak üzere değerlendirilmediğini teyit eder.

Fikri Mülkiyet Uyumluluğu: Yazarlar, çalışmalarında yer alan herhangi bir metin, şekil veya belgenin üçüncü taraf telif haklarını ihlal etmemesini sağlamaktan sorumludur.

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Üçüncü Taraf Kullanımı: Yazarlar, uygun atıf verildiği ve uygun atıf ayrıntıları eklendiği sürece üçüncü tarafların yayınlanan makaleyi serbestçe kullanmasına izin verir. Lisans, çalışmanın bütünlüğünü veya sahipliğini kısıtlamaz.

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Preparation of Manuscript
Yazının Gönderimi

Makaleler yalnızca online olarak https://dergipark.org.tr/pub/endouroloji adresinden gönderilebilir. Başka bir yolla gönderilen yazılar değerlendirilmeye alınmayacaktır.
Dergiye gönderilen yazılar, öncelikle yazının dergi kurallarına uygun olarak hazırlanmasını ve sunulmasını sağlayacakları teknik değerlendirme sürecinden geçer. Derginin kurallarına uymayan yazılar, teknik düzeltme talepleri ile gönderen yazara iade edilir. Editör, ana metni değiştirmeden düzeltme yapabilir. Editör, yukarıda belirtilen şartlara uymayan makaleleri reddetme hakkını saklı tutar.
Yazarların aşağıdaki belgeleri göndermeleri gerekir:

- Yazar Katkı ve Telif Hakları Formu
- Bilgilendirilmiş Onam Formu
- ICMJE Çıkar Çatışması Formu
- Başlık Sayfası (Makale Başlığı, kısa başlık, yazarın adı, unvanı ve kurumu, sorumlu yazarın iletişim bilgileri, araştırmayı destekleyen kuruluş varsa kuruluşun adı)
- Ana belge (Tüm makalelerde, ana metinden önce de Özet bölümü yer almalıdır)
- Şekiller (JPEG formatı)
- Tablolar (en fazla 6 tablo)

Ana Belgenin Yayına Hazırlığı

Yazılar bilgisayar ile çift aralıklı olarak 12 punto büyüklüğünde ve Times New Roman karakteri ile yazılmalıdır. Her sayfanın bütün kenarlarında en az 2.5 cm boşluk bırakılmalıdır. Ana metin, yazarların adları ve kurulları hakkında hiçbir bilgi içermemelidir.
Yayın çeşitleri;

Araştırma Türü	Özet	Kelime Sayısı	Referans Sayısı	Tablo ve Figürler
Özgün Araştırma	250	4000	30	10
Derleme	250	5000	100	10
Olgu Sunumu	300	2000	20	10

Özgün makaleler yapılandırılmış bir Özet (abstract) (Giriş, Gereç ve yöntemler, Bulgular, Sonuçlar, Referanslar, Tartışma, gerekli ise Onam, Figürler; resim, grafik çizim, video, Tablolar) içermelidir.
Olgu sunumları için yapılandırılmış Özet gerekmez. Özet bölümü 300 sözcük ile sınırlandırılmalıdır. Özet de kaynaklar, tablolar ve atıflar kullanılamaz. Özün bittiği satırın altında sayısı 3-5 arasında olmak üzere anahtar kelimeler verilmelidir.
Türkiye dışındaki ülkelerden yazı gönderen yazarlar için Başlık, Özet, Anahtar Kelimeler ve yazıyla ilgili diğer bazı temel bölümlerin Türkçe olarak gönderilmesi zorunlu değildir. Bu bölümlerin çevirileri, yazarlar tarafından gönderilen özgün İngilizce metinler dikkate alınarak dergi editörlüğü tarafından yapılacaktır.
Makalede kullanılan tüm kısaltmalar, ilk kullanımda tanımlanmalıdır. Kısaltma, tanımı ardından parantez içinde verilmelidir.
Ana metinde bir ilaç, ürün, donanım veya yazılım programından bahsedildiğinde, ürünün adı, ürünün üreticisi, üretim şehri ve üreten şirketin ülkesi de dahil olmak üzere ürün bilgileri (ABD'de ise devlet dahil) parantez içinde verilmelidir.
Anahtar kelime seçimi için lütfen Index Medicus'un (MeSH) tıbbi konu başlıklarına bakınız: https://meshb.nlm.nih.gov/MeSHonDemand .
Tüm kaynaklara, tablolara ve şekillere ana metinde atıfta bulunulmalı ve kaynaklar, ana metinde geçen sıraya göre numaralandırılmalıdır. Kullanılan semboller, sembollerin standart kullanımlarına uygun olmalıdır.

1. Orijinal Araştırma Makaleleri

Amaç

Orijinal Araştırma Makaleleri, eleştirel okuyucular için güvenilirliği garanti altına almak için yeterli dokümantasyonla klinik veya temel araştırma sonuçlarını sunmalıdır. Bu makaleler alana yeni bakış açıları katmalı ve sağlam veriler ve sağlam metodoloji ile desteklenmelidir.

Gönderme Yönergeleri
Kelime Sınırı: Maksimum 4.000 kelime (kaynaklar, tablolar ve şekil başlıkları hariç).
Yapı: El yazmaları aşağıdaki şekilde yapılandırılmalıdır:
Başlık (hem Türkçe hem de İngilizce)
Özet (hem Türkçe hem İngilizce)
Anahtar Kelimeler (hem Türkçe hem İngilizce)
Giriş
Materyaller ve Yöntemler
Sonuçlar
Tartışma
Sonuçlar
Şekil ve Tablo Başlıkları (varsa)
Referanslar

İnceleme Süreci
Gönderilen tüm araştırma makaleleri, bilimsel değerlerini, özgünlüklerini ve derginin kapsamıyla alakalarını değerlendirmek için çift kör hakem incelemesinden geçecektir. İstatistiksel analizler ve metodoloji açıkça sunulmalı ve yeniden üretilebilir olmalıdır.

2. Olgu Sunumları
Amaç
Vaka Raporları, tanı zorlukları, tedavi yaklaşımları veya yeni gözlemler hakkında değerli içgörüler sağlayan benzersiz veya nadir klinik vakaları tanımlamalıdır. Bu raporlar iyi belgelenmeli ve tıbbi bilginin ilerlemesine katkıda bulunmalıdır.

Gönderme Yönergeleri
Kelime Sınırı: Maksimum 2.000 kelime (referanslar, tablolar ve şekil başlıkları hariç).
Yapı: El yazmaları aşağıdaki gibi yapılandırılmalıdır:
Başlık (hem Türkçe hem de İngilizce)
Özet (hem Türkçe hem de İngilizce)
Anahtar Kelimeler (hem Türkçe hem de İngilizce)
Giriş
Vaka Sunumu
Tartışma ve Sonuç
Şekil ve Tablo Başlıkları (varsa)
Referanslar

İnceleme Süreci
Vaka Raporları, önemli bir öğrenme fırsatı sunduklarından, uygun şekilde referanslandırıldıklarından ve klinik uygulamaya veya tıbbi araştırmaya katkıda bulunduklarından emin olmak için editöryal ve çift kör hakem değerlendirmesine tabidir.

3. Derleme Makaleleri
Amaç
Derleme Makaleleri, belirli bir konunun kapsamlı ve yapılandırılmış bir analizini sunar, mevcut literatürü özetler ve eleştirel olarak değerlendirir. Bu makaleler iyi organize edilmeli ve araştırma bulgularının güncel bir sentezini içermelidir.

Gönderme Yönergeleri
Kelime Sınırı: Maksimum 5.000 kelime (kaynaklar, tablolar ve şekil başlıkları hariç).
Yapı: El yazmaları aşağıdaki gibi yapılandırılmalıdır:
Başlık (hem Türkçe hem de İngilizce)
Özet (hem Türkçe hem İngilizce)
Anahtar Kelimeler (hem Türkçe hem İngilizce)
Ana Metin

Sonuç
Şekil ve Tablo Başlıkları (varsa)
Referanslar

Sistematik İncelemeler
Sistematik inceleme gönderen yazarlar, şeffaflığı ve metodolojik titizliği sağlamak için PRISMA yönergelerine uymalıdır. PRISMA kontrol listesine şu adresten ulaşılabilir: PRISMA Kontrol Listesi

İnceleme Süreci
İnceleme Makaleleri, analiz derinliği, alaka düzeyi ve bilimsel topluluğa katkısı açısından editör kurulu ve editöryal ve çift kör hakem değerlendirmesi tarafından değerlendirilecektir.

4. Editöre Mektuplar
Amaç
Editöre Mektuplar, okuyucuların daha önce yayınlanmış makalelere yanıt vererek, kısa bilimsel gözlemler sunarak veya derginin okuyucularının ilgisini çeken konulara değinerek akademik tartışmalara katılmalarını sağlar.

Gönderim Yönergeleri
Yapı: El yazmaları aşağıdaki şekilde yapılandırılmalıdır:
Başlık (hem Türkçe hem de İngilizce)
Anahtar Sözcükler (hem Türkçe hem İngilizce)
Ana Metin
Şekil ve Tablo Başlıkları (varsa)
Referanslar

İçerik: Mektuplar öz olmalı, söz konusu makalenin belirli yönlerine odaklanmalı ve akademik söyleme anlamlı bir şekilde katkıda bulunmalıdır. Bunlar şunları içerebilir:
Yayınlanmış bir makalenin metodolojileri, yorumları veya sonuçları hakkında eleştirel analiz veya yorum.
Konuyu daha iyi anlamayı sağlayan doğrulayıcı veya çelişkili verilerin sunumu.
Makalenin bulgularını daha geniş çalışma alanı içinde bağlamlandıran tartışmalar.
Uzunluk: Genellikle, mektuplar referanslar dahil 1.000 kelimeyi geçmemelidir.
Başlık: Orijinal makaleye atıfta bulunan bir başlıkla başlayın, örn. “[Yazar Adı(ları)] tarafından [Makale Başlığı] hakkında yorum.”
Yazar Bilgileri: Tüm katkıda bulunan yazarların tam adlarını, akademik bağlantılarını ve iletişim bilgilerini ekleyin.
Referanslar: Orijinal makaleyi ve diğer ilgili literatürü uygun şekilde atıfta bulunun.
Ton: Kişisel yorumlardan ziyade akademik eleştiriye odaklanarak saygılı ve profesyonel bir ton koruyun.

İnceleme Süreci
Gönderilen tüm mektuplar, açıklık, akademik değer ve etik standartlara uyumu sağlamak için editör ekibi tarafından incelenecektir. Mektuplar profesyonel bir üslupla yazılmalı ve anlamlı bir akademik söyleme katkıda bulunmalıdır.

5. Araştırma Notu
Amaç
Bir Araştırma Notu, tam uzunlukta bir makaleyi gerektirmeyen ancak yine de bilim camiası için değerli olan ön bulguların, yeni metodolojilerin veya önemli gözlemlerin kısa raporlarını yaymak için kullanılır.

Gönderme Yönergeleri
Uzunluk: Ana metin, referanslar, şekiller ve tablolar hariç 2.000 kelimeyi geçmemelidir.
İçerik: Araştırma Notları şunları içerebilir:
Potansiyel bir atılım veya yeni bir içgörü öneren ön veriler.
Yenilikçi tekniklerin veya metodolojilerin açıklamaları.
Daha fazla araştırmayı teşvik eden veya ortaya çıkan eğilimleri vurgulayan gözlemler.

Yapı
Notu, aşağıdaki gibi net başlıklarla düzenleyin:
Başlık (hem Türkçe hem de İngilizce)
Özet (hem Türkçe hem İngilizce)
Anahtar Kelimeler (hem Türkçe hem İngilizce)
Giriş: Çalışmanın bağlamını ve önemini kısaca ana hatlarıyla belirtin.
Yöntemler: Kullanılan yaklaşımı ve teknikleri özetleyin.
Sonuçlar: Temel bulguları özlü bir şekilde sunun.
Tartışma: Sonuçları ve potansiyel gelecekteki yönleri tartışın. Referanslar: Çalışmayı destekleyen temel alıntılarla sınırlayın.
Şekiller ve Tablolar: Yalnızca notun netliğini ve etkisini artırıyorsa ekleyin.

İnceleme Süreci
Araştırma Notları, bilimsel geçerliliği, özgünlüğü ve derginin kapsamıyla alakalı olmasını sağlamak için çift kör hakem incelemesinden geçecektir.

6. Kitap İncelemesi
Amaç: Kitap İncelemesi, alandaki son yayınların eleştirel bir değerlendirmesini sunarak okuyuculara kitabın içeriği, önemi ve devam eden akademik tartışmalarla alakalılığı hakkında fikir verir.

Gönderim Yönergeleri
İçerik: İncelemeler şunları içermelidir:
Uzunluk: Genellikle 1.500 ila 2.500 kelime arasındadır.
Kitabın ana temalarını ve argümanlarını özetleyin.
Çalışmanın güçlü ve zayıf yönlerini değerlendirin.
Kitabın alana katkısını ve güncel araştırma veya uygulamayla alakalılığını tartışın.
Kitabı mevcut literatüre yerleştirin ve benzersiz bakış açılarını veya yaklaşımları not edin.
Başlık: İncelemenin başında kitabın tam başlığını, yazar(lar), yayıncı, yayın yılı, sayfa sayısı ve ISBN'yi ekleyin.
Ton: Nesnel ve akademik bir ton koruyun, kanıtlarla desteklenen dengeli eleştiriler sunun.

İnceleme Süreci
Kitap İncelemeleri, editör ekibi tarafından açıklık, analiz derinliği ve derginin okuyucu kitlesiyle alakalılık açısından değerlendirilecektir.

Şekillerin ve Tabloların Yayına Hazırlığı
Şekiller, grafikler ve fotoğraflar, makale yükleme sistemi aracılığıyla ayrı dosyalar (JPEG formatında) halinde sunulmalıdır.
Dosyalar bir Word belgesine veya ana belgeye gömülmemelidir.
Şeklin alt birimleri olduğunda; alt birimler tek bir görüntü oluşturmak için birleştirilmemelidir. Her alt birim, başvuru sistemi aracılığıyla ayrı ayrı sunulmalıdır.
Şekil alt birimlerini belirtmek için görüntüler Arabik rakamlarla (1,2,3...) numaralandırılmalıdır.
Gönderilen her bir şeklin en düşük çözünürlüğü 300 DPI olmalıdır.
Şekillerin başlıkları ana belgenin sonunda listelenmelidir.
Bilgi veya resimler hastaların tanımlanmasına izin vermemelidir. Kullanılan herhangi bir fotoğraf için hastadan ve/veya yasal temsilcisinden yazılı bilgilendirilmiş onam alınmalıdır.

Tablolar ana belgeye gömülmeli veya ayrı dosyalar halinde sunulmalıdır. Tablo sayısı altı adet ile sınırlandırılmalıdır. Tüm tablolar, ana metinde kullanıldığı sırayla art arda numaralandırılmalıdır. Tablo başlıkları ve açıklamaları ana belgenin sonunda listelenmelidir.

Kaynaklar
Kaynaklar yazıda kullanılan kaynaklar cümlenin sonunda parantez içinde belirtilmelidir. Kaynaklar makalenin sonunda yer almalı ve makalede geçiş sırasına göre sıralanmalıdır. Kaynaklar yazarların soyadlarını ve adlarının baş harflerini, makalenin başlığını, derginin adını, basım yılını, sayısını, başlangıç ve bitiş sayfalarını belirtmelidir. Altı ve daha fazla yazarı olan makalelerde ilk

3 yazardan sonrası için ‘et al.’ veya ‘ve ark.’ ifadesi kullanılmalıdır. Kısaltmalar Index Medicus’ a uygun olmalıdır.
Kaynakların sonuna alıntı yapılan makalelerin doi linki eklenmelidir.

Örnekler

Makaleler için:

1. Tasci A, Tugcu V, Ozbay B, Mutlu B, Cicekler O. Stone formation in prostatic urethra after potassium-titanyl-phosphate laser ablation of the prostate for benign prostatic hyperplasia. J Endourol 2009;23:1879-81. https://doi.org/10.1089/end.2008.0596

Kitap için:

1.Günalp İ: Modern Üroloji. Ankara: Yargıçoğlu matbaası, 1975. Kitap bölümleri için: Anderson JL, Muhlestein JB. Extra corporeal ureteric stenting during laparoscopic pyeloplasty. Philadelphia: W.B. Saunders; 2003. p. 288-307

Web sitesi için;

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

Bildiriler için;

Proceedings of the Symposium on Robotics, Mechatronics and Animatronics in the Creative and Entertainment Industries and Arts. SSAISB 2005 Convention. University of Hertfordshire, Hatfield, UK; 2005.

Tez için;

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

Geri Çekme veya Reddetme

Yazıyı Geri Çekme: Gönderilen yazının değerlendirme sürecinde gecikme olması vb. gibi gerekçelerle yazıyı geri çekmek ve başka bir yerde yayınlatmak isteyen yazarlar yazılı bir başvuru ile yazılarını dergiden geri çekebilirler.

Yazı Reddi: Yayınlanması kabul edilmeyen yazılar, gerekçesi ile geri gönderilir.

Kabul Sonrası

Makalenin kabul edilmesi durumunda, kabul mektubu iki hafta içinde sorumlu yazara gönderilir. Makalenin baskıdan önceki son hali yazarın son kontrolüne sunulur. Dergi sahibi ve yayın kurulu, kabul edilen makalenin derginin hangi sayısında basılacağına karar vermeye yetkilidir.

Yazarlar, makalelerini kişisel veya kurumsal web sitelerinde, uygun alıntı ve kütüphane kurallarına bağlı kalarak yayınlayabilirler. Yazar değişikliği (isim, yazar ekleme) talebi, değerlendirme süreci tamamlanmadan önce tüm yazarlar tarafından imzalanmış bir mektupla Yayın Kurulu’na (yayıncı/dergi adresi) iletilmelidir.

Geri çekme ve düzeltmeler hakkında daha fazla bilgi için lütfen Geri Çekme ve Düzeltme Politikası sayfasını inceleyiniz.

PREPARATION OF MANUSCRIPT

Manuscripts can only be submitted through the journal's online manuscript submission and evaluation system, available at https://dergipark.org.tr/ Manuscripts submitted via any other medium will not be evaluated.

Manuscripts submitted to the journal will first go through a technical evaluation process where the editorial office staff will ensure that the manuscript has been prepared and submitted following the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the submitting author with technical correction requests. The editor reserves the right to reject manuscripts that do not comply with the aforementioned requirements. Corrections may be done without changing the main text.

Authors are required to submit the following:

- Copyright Agreement&Acknowledgement of Authorship Form
- Informed Consent Form
- ICMJE Disclosure of Interest Form
- Title Page (including Title of Manuscript, Running title, author (s) 's name, title, and institution, corresponding author's contact information, Name of the organization supporting the research)
- Main document (All articles should have an abstract before the main text).
- Figures (Jpeg format)
- Tables (max 6 tables)

Preparation of the Main Document

The articles should be written double-spaced in 12 pt, Times New Roman character and at least 2.5 cm from all edges of each page. The main text should not contain any information about the authors' names and affiliations.

Publication Types;

Type of Article	Abstract	Text (Word)	References	Table&Figures
Original Article	250	4000	30	10
Review Article	250	5000	100	10
Case Reports	300	2000	20	10

Original articles should have a structured abstract. (Aim, Material and Methods, Results, Conclusion). For case reports, the structured abstract is not used. Limit the abstract to 300 words. References, tables, and citations should not be used in an abstract. Authors must include relevant keywords (3-5) on the line following the end of the abstract. The Turkish title, abstracts, and Turkish keywords are not required for the international authors. The editorial office will provide these.

All acronyms and abbreviations used in the manuscript should be defined first, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in the USA), should be provided in parentheses.

All references, tables, and figures should be referred to within the main text, and they should be numbered consecutively in the order they are referred to within the main text. The symbols used must be nomenclature used standards.

1. Original Research Articles

Purpose

Original Research Articles should present the results of clinical or basic research with sufficient documentation to ensure credibility for critical readers. These articles must contribute novel insights to the field and be supported by robust data and sound methodology.

Submission Guidelines
Word Limit: Maximum 4,000 words (excluding references, tables, and figure captions).
Structure: Manuscripts must be structured as follows:
Title (in both Turkish and English)
Abstract (in both Turkish and English)
Keywords (in both Turkish and English)
Introduction
Materials and Methods
Results
Discussion
Conclusions
Figure and Table Captions (if applicable)
References
Review Process

All submitted research articles will undergo double-blind peer review to assess their scientific merit, originality, and relevance to the journal's scope. Statistical analyses and methodology must be clearly presented and reproducible.

2. Case Reports

Purpose

Case Reports should describe unique or rare clinical cases that provide valuable insights into diagnostic challenges, treatment approaches, or novel observations. These reports should be well-documented and contribute to the advancement of medical knowledge.

Submission Guidelines
Word Limit: Maximum 2,000 words (excluding references, tables, and figure captions).
Structure: Manuscripts must be structured as follows:
Title (in both Turkish and English)
Abstract (in both Turkish and English)
Keywords (in both Turkish and English)
Introduction
Case Presentation
Discussion and Conclusion
Figure and Table Captions (if applicable)
References

Review Process

Case Reports are subject to editorial and double-blind peer review to ensure they present a significant learning opportunity, are properly referenced, and contribute to clinical practice or medical research.

3. Review Articles

Purpose

Review Articles provide a comprehensive and structured analysis of a specific topic, summarizing and critically evaluating existing literature. These articles should be well-organized and include an up-to-date synthesis of research findings.

Submission Guidelines
Word Limit: Maximum 5,000 words (excluding references, tables, and figure captions).
Structure: Manuscripts must be structured as follows:
Title (in both Turkish and English)
Abstract (in both Turkish and English)
Keywords (in both Turkish and English)
Main Text

Conclusion
Figure and Table Captions (if applicable)
References

Systematic Reviews
Authors submitting systematic reviews must adhere to PRISMA guidelines to ensure transparency and methodological rigor. The PRISMA checklist can be accessed at: PRISMA Checklist

Review Process
Review Articles will be evaluated by the editorial board and editorial and double-blind peer review for their depth of analysis, relevance, and contribution to the scientific community.

4. Letters to the Editor

Purpose
Letters to the Editor allow readers to engage in academic discussions by responding to previously published articles, presenting brief scientific observations, or addressing issues of interest to the journal's readership.

Submission Guidelines
Structure: Manuscripts must be structured as follows:
Title (in both Turkish and English)
Keywords (in both Turkish and English)
Main Text
Figure and Table Captions (if applicable)
References

Content: Letters should be concise, focused on specific aspects of the article in question, and contribute meaningfully to the academic discourse. They may include:
Critical analysis or commentary on the methodologies, interpretations, or conclusions of a published article.
Presentation of corroborative or contradictory data that enhances the understanding of the topic.
Discussions that contextualize the article's findings within the broader field of study.

Length: Typically, letters should not exceed 1,000 words, including references.
Title: Begin with a title that references the original article, e.g., "Comment on [Article Title] by [Author Name(s)]."
Author Information: Include full names, academic affiliations, and contact details of all contributing authors.
References: Cite the original article and any other relevant literature appropriately.
Tone: Maintain a respectful and professional tone, focusing on academic critique rather than personal remarks.

Review Process:
All submitted letters will be reviewed by the editorial team to ensure clarity, academic merit, and adherence to ethical standards. Letters must be professional in tone and contribute to meaningful scholarly discourse.

5. Research Note

Purpose: A Research Note serves to disseminate brief reports of preliminary findings, novel methodologies, or significant observations that may not warrant a full-length article but are nonetheless valuable to the scientific community.
Submission Guidelines
Length: The main text should not exceed 2,000 words, excluding references, figures, and tables.
Content: Research Notes may include:
Preliminary data that suggest a potential breakthrough or novel insight.
Descriptions of innovative techniques or methodologies.
Observations that prompt further investigation or highlight emerging trends.

Structure
Organize the note with clear headings, such as:
Title (in both Turkish and English)
Abstract (in both Turkish and English)
Keywords (in both Turkish and English)
Introduction: Briefly outline the context and significance of the work.
Methods: Summarize the approach and techniques employed.
Results: Present key findings succinctly.
Discussion: Discuss the implications and potential future directions.
References: Limit to essential citations that support the work.
Figures and Tables: Include only if they enhance the clarity and impact of the note.

Review Process
Research Notes will undergo double-blind peer review to ensure scientific validity, originality, and relevance to the journal's scope.

6. Book Review

Purpose: A Book Review offers a critical evaluation of recent publications in the field, providing readers with insights into the book's content, significance, and relevance to ongoing scholarly discussions.

Submission Guidelines
Content: Reviews should:
Length: Typically between 1,500 to 2,500 words.
Summarize the book's main themes and arguments.
Assess the strengths and weaknesses of the work.
Discuss the book's contribution to the field and its relevance to current research or practice.
Situate the book within the existing literature, noting any unique perspectives or approaches.
Title: Include the book's full title, author(s), publisher, publication year, page count, and ISBN at the beginning of the review.
Tone: Maintain an objective and scholarly tone, offering balanced critiques supported by evidence.

Review Process
Book Reviews will be evaluated by the editorial team for clarity, depth of analysis, and relevance to the journal's readership

Preparation of the Figures and Tables

The submission system should submit figures, graphics, and photographs as separate files (in JPEG format).

- The files should not be embedded in a Word document or the main document.
- When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system.
- Arabic numbers should number images to indicate figure subunits.
- The minimum resolution of each submitted figure should be 300 DPI.
- Figure legends should be listed at the end of the main document.
- Information or illustrations must not permit the identification of patients, and written informed consent for publication must be sought for any photograph.

Tables should be embedded in the main document or submitted as separate files, but if tables are submitted separately, please note where it is suitable in the main text. Tables are limited to six tables. All tables should be numbered consecutively in the order they are used to within the main text. Tables legends should be listed at the end of the main document.

References

The references used in the article must be written in parenthesis at the end of the sentences. References should be numbered in the order they appear in the text and placed at the end of the article. References must contain surnames and initials of all authors, article title, name of the journal, the year, and the first and last page numbers. Articles with 6 or more authors 'et al.' are mixed with the first three authors. Abbreviations should be according to index Medicus.
Authors must add the DOI (Digital object identifier) at the end of each reference.

For Examples;
Article in journal: 1. Tasci A, Tugcu V, Ozbay B, Mutlu B, Cicekler O. Stone formation in prostatic urethra after potassium-titanyl-phosphate laser ablation of the prostate for benign prostatic hyperplasia. J Endourol 2009;23:1879-81. https://doi.org/10.1089/end.2008.0596
For Books: 1.Günalp İ: Modern Üroloji. Ankara: Yargıçoğlu matbaası, 1975. Chapters in books: Anderson JL, Muhlestein JB. Extra corporeal ureteric stenting during laparoscopic pyeloplasty. Philadelphia: W.B. Saunders; 2003. p. 288-307
For website; Gaudin S. How moon landing changed technology history [Internet]. Computerworld UK. 2009 [cited 15 June 2014]. Available from: http://www.computerworlduk.com/in-depth/it-business/2387/how-moon-landing-changed-technology-history/
For conference proceeding; Proceedings of the Symposium on Robotics, Mechatronics and Animatronics in the Creative and Entertainment Industries and Arts. SSAISB 2005 Convention. University of Hertfordshire, Hatfield, UK; 2005.
For Thesis; Ercan S. Venöz yetmezlikli hastalarda kalf kası egzersizlerinin venöz fonksiyona ve kas gücüne etkisi. Suleyman Demirel University Faculty of Medicine Sports Medicine Department Thesis. Isparta: Suleyman Demirel University. 2016.
Retraction or Reject; Manuscript Retraction: For other reasons, authors may withdraw their manuscript from the journal with a written declaration.

Manuscript Reject

Withdrawal of the Article: Authors are required to submit a written application addressed to the Editor who has declared their withdrawal request and justification. They must wait for the Editor's response before submitting the manuscript to another journal.
Rejection: The manuscripts which are not accepted to be published are rejected with explanations.

AFTER ACCEPTANCE

If the manuscript is accepted, the acceptance letter is sent within two weeks, the last version of the manuscript is sent to the author for the last correspondence. The journal owner and the editorial board are authorized to decide which volume of the accepted article will be printed.
Authors may publish their articles on their personal or corporate websites by linking them to the appropriate cite and library rules.
Should you wish to request a change of author (name, author addition), we kindly ask that you submit this to the Editorial Board (publisher/journal address) with a letter signed by all authors before the evaluation process is completed.

For more information about withdrawals and corrections, please see the Retraction and Correction Policy page.

Peer Review Process
Yayın Değerlendirme Süreci

Çift-Kör Değerlendirme Süreci

1. Makale Başvurusu

İlgili yazar, makalesini Dergipark çevrimiçi sistemi aracılığıyla dergiye gönderir.

2. Editöryal Değerlendirme

Editörlük, ilgili makalenin derginin yazım kurallarına göre düzenlenip düzenlenmediğini kontrol eder. Bilimsel içeriği bu aşamada değerlendirmez.

3. Editör tarafından değerlendirme

Editör, makalenin orijinal olup olmadığını denetler. Değilse, makale ret edilerek süreç tamamlanır.

4. Hakem Daveti

Editör, makalenin bilimsel içeriğinin değerlendirilmesi için konu ile ilgili hakemlere davet gönderir. Genellikle 2 hakeme davet gönderilir. İlgili yazıyı hakemlerden birisi ret diğeri kabul ettiği takdirde, bölüm editörü uygun görürse üçüncü bir hakemin incelemesi için davetiye gönderebilir.

5. Davete Yanıt

Seçilen hakemler, daveti gönderilen yazıyı kendi uzmanlıklarına, çıkar çatışmalarına ve kullanılabilirlik durumlarına karşı gizli olarak değerlendirir. Daha sonra kabul veya reddetmektedirler.

6. İnceleme Süreci

Hakem, makaleyi çeşitli açılardan değerlendirdikten sonra (15 gün içerisinde) eleştiri ve önerilerini içeren hakem değerlendirme formunu editöre gönderir. Major veya minör revizyonlar sonrasında hakem yazıyı tekrar değerlendirmek istemiş ise öneri ve eleştiriler yazarlara iletilerek düzeltilmiş yazıyı tekrar sisteme yüklemeleri istenir. Bu süreç hakemin kabul veya ret cevabı verene kadar devam eder.

7. Derginin Değerlendirme Süreci

Bölüm Editörü, genel bir karar vermeden önce geri gönderilen tüm değerlendirmeleri dikkate alır. Hakem değerlendirme sonuçları çok farklıysa, editör bir karar almadan önce fazladan bir fikir edinmek için ek bir inceleme isteyebilir.

8. Kararın İletilmesi

Bölüm Editörü, yazı hakkındaki son kararına hakem isimleri gizlenerek hakem raporlarını da ekler ve yazara çevrimiçi sistem ve e-mail aracılığı ile gönderir.

9. Sonraki Adımlar

Makale kabul edilirse, dil editörüne gönderilir. Bu aşamalardan sonraki adımlar;

- Son kopya gönderisi
- Mizanpaj
- Düzeltmeler
- Yayınlanacak gönderilerin erken baskı olarak web sayfasına yerleştirilmesi
- Sayı oluşturulması
- İçindekiler sayfası düzenlenmesi
- Web sitesinde sayı olarak yayınlanması ve baskı

**Kurum içi değerlendirme sürecinde; çift kör değerlendirme sürecindeki adımlar izlenmektedir.*

The Double-Blind Peer Review Process

1. Submission of Paper

The corresponding author submits the paper via Dergipark online system to the journal.new

2. Editorial Office Assessment

Editorial Office checks the paper's composition and arrangement against the journal's Author Guidelines to make sure it includes the required sections and stylizations. The quality of the paper is not assessed at this point.

3. Appraisal by the Editor

Editor checks that the paper is appropriate for the journal and is sufficiently original and interesting. If not, the paper may be rejected without being reviewed any further.

4. Invitation to Reviewers

Editor sends invitations to individuals he or she believes would be appropriate reviewers. As responses are received, further invitations are issued, if necessary, until the required number of acceptances is obtained – commonly this is 2.

5. Response to Invitations

Potential reviewers consider the invitation as anonymous against their own expertise, conflicts of interest and availability. They then accept or decline. If possible, when declining, they might also suggest alternative reviewers.

6. Review is Conducted

The reviewer sets time aside to read the paper several times. The first read is used to form an initial impression of the work. If major problems are found at this stage, the reviewer may feel comfortable rejecting the paper without further work. Otherwise they will read the paper several more times, taking notes so as to build a detailed point-by-point review. The review is then submitted to the journal, with a recommendation to accept or reject it – or else with a request for revision (usually flagged as either major or minor) before it is reconsidered.

7. Journal Evaluates the Reviews

The Section Editor considers all the returned reviews before making an overall decision. If the reviews differ widely, the editor may invite an additional reviewer so as to get an extra opinion before making a decision.

8. The Decision is Communicated

The Section Editor sends a decision email to the author including any relevant reviewer comments as anonymous.

9. Next Steps

If accepted, the paper is sent to language Editor. If the article is rejected or sent back for either major or minor revision, the Section Editor should include constructive comments from the reviewers to help the author improve the article. At this point, reviewers should also be sent an email or letter letting them know the outcome of their review. If the paper was sent back for revision, the reviewers should expect to receive a new version, unless they have opted out of further participation. However, where only minor changes were requested this follow-up review might be done by the Section Editor. After these;

- Copyedit submission
- Layout
- Corrections
- Publishing the submissions on the web page as early print
- Creating issues
- Organize Table of Contents
- Publishing the issue on the web page and printing hardcopy

**We are applying the same steps on The Double-Blind Peer Review Process when we got the in-house submission.*

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