Original Article
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Can the De Nunzio Nomogram Reliably Predict Stone-Free Rates After Semirigid Ureteroscopy? A Retrospective External Validation Study

De Nunzio Nomogramı, Semirigid Üreteroskopi Sonrası Taşsızlık Oranlarını Güvenilir Şekilde Öngörebilir mi? Retrospektif Bir Eksternal Validasyon Çalışması

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ABSTRACT

Objective: To externally validate the De Nunzio nomogram for predicting stone-free outcomes after semirigid ureteroscopic lithotripsy (ULT) in patients with ureteral stones.

Materials and Methods: This retrospective study included 385 patients who underwent semirigid ULT for ureteral stones between December 2021 and October 2024. Demographic, clinical, and radiological data were collected. The De Nunzio nomogram score was calculated for each patient. Stone-free status was defined as the complete absence of residual fragments on imaging within 4–6 weeks postoperatively. Predictive performance of the nomogram was assessed using ROC curve analysis and decision curve analysis (DCA).

Results: The overall stone-free rate was 85.7%. There were no significant differences between the stone-free and non-stone-free groups regarding age, gender, or stone density. However, patients in the stone-free group more frequently had single stones, lower median stone length, and lower De Nunzio scores. Stones were more commonly located in the middle and distal ureter, while pyuria and hydronephrosis were less frequently observed in this group. The nomogram demonstrated high discriminative performance with an AUC of 0.866. DCA showed a net clinical benefit across a wide range of threshold probabilities.

Conclusions: The De Nunzio nomogram is a valid and clinically useful tool for predicting stone-free outcomes following semirigid ULT. Its implementation may enhance preoperative risk stratification and support individualized treatment planning in patients with ureteral stones.

Keywords: de Nunzio score, nomogram validation, semirigid ureteroscopy, stone-free rate, , ureteral stones, urolithiasis

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ÖZET

Amaç: De Nunzio nomogramının, üreter taşı bulunan hastalarda semirigid üreteroskopik litotripsi (ULT) sonrası taşsızlık sonuçlarını öngörme gücünün eksternal validasyonunu yapmak.

Gereç ve Yöntem: Bu retrospektif çalışmaya, Aralık 2021 ile Ekim 2024 tarihleri arasında üreter taşı nedeniyle semirigid ULT uygulanan 385 hasta dahil edildi. Demografik, klinik ve radyolojik veriler toplandı. Her hasta için De Nunzio nomogram skoru hesaplandı. Taşsızlık durumu, ameliyat sonrası 4–6 hafta içinde görüntülemede rezidü taş olmaması olarak tanımlandı. Nomogramın prediktif performansı ROC eğrisi analizi ve karar eğrisi analizi (DCA) ile değerlendirildi.

Bulgular: Genel taşsızlık oranı %85,7 idi. Taşsız ve rezidü kalan gruplar arasında yaş, cinsiyet veya taş dansitesi açısından anlamlı fark yoktu. Taşsız gruptaki hastalarda tek taş olma sıklığı daha fazlaydı. Ayrıca median taş uzunluğu ve De Nunzio skorları daha düşüktü. Taşlar daha çok mid ve distal üreterde lokalizeydi; piyüri ve hidronefroz bu grupta daha az sıklıkla izlendi. Nomogram, 0,866'lık AUC değeri ile yüksek ayırt edici performans gösterdi. DCA, geniş bir eşik olasılık aralığında nomogramın net klinik fayda sunduğunu ortaya koydu.

Sonuç: De Nunzio nomogramı, semirigid ULT sonrası taşsızlık sonuçlarını öngörmede geçerli ve klinik olarak faydalı bir araçtır. Bu nomogramın kullanımı, preoperatif risk sınıflandırmasını geliştirebilir ve üreter taşı olan hastalarda bireyselleştirilmiş tedavi planlamasını destekleyebilir.

Anahtar Kelimeler: de Nunzio skoru, nomogram doğrulama, semirigid üreteroskopi, taşsızlık oranı, üreter taşları, ürolitiyazis

INTRODUCTION

Urolithiasis is a common and increasing global health problem, with an estimated 106 million new cases reported in 2021, with a higher incidence observed in men compared to women (1). Among its subtypes, ureterolithiasis is also notably prevalent, with lifetime risk estimates suggesting that nearly one in eleven adults in the United States may be affected (2). In clinical practice, the mainstay of treatment for ureteral stones includes minimally invasive approaches such as extracorporeal shock wave lithotripsy (ESWL) and ureteroscopy (URS), with the choice of modality largely determined by stone size, location, composition, and patient-related factors. URS has emerged as a primary treatment modality for ureteral stones due to its high stone-free rates (SFR), often exceeding 90%, particularly when Holmium: YAG laser lithotripsy is used with high-energy settings (3).

Ureteroscopic lithotripsy (ULT) is widely regarded as a safe procedure for the treatment of ureteral stones. However, despite its favorable safety profile, certain complications may still occur, albeit infrequently. Reported complications include mucosal injury, ureteral perforation, stone migration, urinary tract infection, ureteral stricture, and, in rare cases, ureteral avulsion (4).

Although ULT generally yields high SFR, it remains important to identify patients who are at risk of treatment failure or who may require repeat intervention, so that they can be appropriately counseled in advance. Therefore, it is crucial to develop nomograms that are both easy to implement in clinical practice and have strong predictive performance. Until recently, such predictive tools were lacking for ULT, but in the past few years, three notable studies have addressed this gap. The first nomogram in this field was introduced by Imamura et al. in 2013 to predict stone-free status following transurethral ureterolithotripsy (5). This model was externally validated in 2019 by De Nunzio et al., confirming its predictive accuracy (6). Subsequently, in 2021, De Nunzio and colleagues developed their nomogram based on a Southern European cohort undergoing semirigid ULT [7]. Most recently, another nomogram was introduced in 2023 based on a Chinese cohort, marking the latest contribution to this evolving area of research (8).

Notably, the most recent two nomograms have not yet undergone external validation. Conducting such validation studies is essential to assess their generalizability and predictive accuracy across different clinical settings. In this

context, evaluating all three nomograms within the same patient population would provide valuable insights and could significantly contribute to their integration into routine clinical practice.

In light of these considerations, the present study aimed to externally validate the nomogram proposed by De Nunzio et al. for predicting stone-free status following semirigid ULT. By testing its performance in an independent patient cohort, this study seeks to contribute to the growing body of evidence regarding the clinical applicability and reliability of predictive tools in endourology.

MATERIALS AND METHODS

This retrospective observational study was conducted at a tertiary referral center and included 385 patients who underwent semirigid ULT for ureteral stones between December 2021 and October 2024. Ethical approval was obtained from the University of Health Sciences, Başakşehir Çam and Sakura City Hospital (KAEK/21.05.2025.165, Date: 2025-05-21). The study was conducted by the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The requirement for informed consent was waived by the ethics committee due to the retrospective design of the study and the use of anonymized patient data. All procedures were performed using a standardized technique by experienced endourologists. Patients with incomplete clinical data, anatomical abnormalities of the urinary tract, active urinary tract infection, pregnancy, or age under 18 years were excluded from the study.

Demographic and clinical parameters, including age, gender, stone location (distal, midureteral, proximal, or ureteropelvic junction), stone length, number of stones, presence of pyuria, degree of hydronephrosis, and stone density, were recorded for all patients. All stone-related measurements, including size, location, and density, were obtained from preoperative non-contrast computed tomography (CT) scans. Stone length was defined as the maximum diameter of the stone measured on axial or reconstructed images. Pyuria was considered present when the urine sediment contained ≥5 white blood cells per high-power field, or when the urine dipstick test yielded a positive result for leukocyte esterase and/or nitrite. Data were obtained retrospectively from medical records and operative reports. Body mass index (BMI) was calculated by dividing weight (kg) by the square of height (m^2). Stone volume was estimated using the ellipsoid formula: volume (mm^3) = $\pi \times$ length $\times$ width $\times$ depth / 6 [9]. For each patient, a total score was calculated based on the scoring system described in the De Nunzio nomogram (Figure 1), in order to evaluate its association with stone-free outcomes.

Surgical Technique

All procedures were performed under either general or spinal anesthesia, with the patient placed in the lithotomy position. A safety guidewire was inserted into the ureter under cystoscopic guidance. Ureteral access was achieved using a semirigid ureteroscope (6/7.5 Fr Ultrathin model, Richard Wolf GmbH, Knittlingen, Germany). Stone fragmentation was performed using a Holmium: YAG laser (Sphinx Jr., LISA Laser, Omniguide Company, Germany) with a 273-µm laser fiber. The dusting technique was used in all cases, with laser settings ranging from 0.5 to 0.8 Joules in energy and 15 to 20 Hertz in frequency. At the end of the procedure, the surgeon decided whether to place a double-J stent. Stents were typically removed 2 to 4 weeks postoperatively.

Outcomes:

Treatment outcomes were assessed 4 to 6 weeks after the procedure using non-contrast CT imaging. Patients were considered stone-free only if no residual fragments were visible on the scan. In cases where residual stone fragments were identified, patients were scheduled for an additional intervention such as repeat ureteroscopy, retrograde intrarenal surgery, ESWL, or mini-PCNL to achieve complete stone clearance.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA), except where otherwise stated. The normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed continuous variables were presented as mean ± standard deviation, while non-normally distributed continuous variables were presented as median (interquartile range). Categorical variables were presented as frequency (percentage). Continuous variables were compared between stone-free and non-stone-free groups using the Mann–Whitney U test for non-normally distributed data and the independent-samples t-test for normally distributed data. Categorical variables were compared using the chi-square test. Receiver operating characteristic (ROC) curve analysis was used to evaluate the discriminative ability of the De Nunzio score, and the area under the curve (AUC) was calculated. The optimal cut-off value was determined by maximizing the Youden Index. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated at the optimal threshold. Decision curve analysis (DCA) was performed in Python (version 3.11) to assess the clinical utility of the nomogram-derived predicted probabilities, based on the methodology described by Vickers and Elkin. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 385 patients were included in the study, with a median age of 45 years (IQR: 42–50), and 76.9% (n = 296) were male. Of these, 330 (85.7%) were stone-free after the procedure. There were no significant differences between the groups in terms of age, gender, or stone density. However, patients who were not stone-free had significantly greater stone length, higher De Nunzio scores, higher stone number, and higher rates of proximal ureter/UPJ stone location and pyuria (all $p < 0.001$), as well as hydronephrosis ($p = 0.018$). All demographic, preoperative, intraoperative, and postoperative characteristics of the patients are summarized in the Table.

ROC curve analysis was performed to assess the predictive performance of the De Nunzio score for stone-free status. The AUC was 0.866. The optimal cut-off value, determined by the Youden Index, was 9.0. At this threshold, sensitivity was 91.8%, specificity was 70.9%, PPV was 95.0%, and NPV was 59.1%. The ROC curve for this analysis is presented in Figure 2. DCA demonstrated a net clinical benefit for the use of the nomogram-derived predicted probabilities across a threshold probability range of approximately 15% to 65% (Figure 3).

DISCUSSION

In patients diagnosed with ureteral stones, the primary goal is to achieve complete stone clearance using minimally invasive techniques that offer high SFR with low morbidity. To determine the optimal surgical approach for each patient, several factors must be considered individually, including stone characteristics (such as location, laterality, size, burden, and density), patient-specific conditions (such as comorbidities or anatomical anomalies), the surgeon's experience with the procedure, and the availability of surgical equipment. Advances in the imaging quality and miniaturization of semirigid ureteroscopes, along with continuous improvements in laser technology, have contributed to making these procedures safer and more comfortable for both patients and surgeons (10).

In the management of urolithiasis, there is a clear need for clinically practical and validated scoring systems or nomograms with strong predictive performance. However, the number of studies addressing this need remains limited. Such predictive tools play a key role in patient counseling and in guiding individualized treatment decisions. Factors such as stone location, degree of hydronephrosis, larger stone size (11), stone impaction (12), number of stones, and stone density (13) have all been shown to influence stone-free outcomes following semirigid URS independently. Consequently, nomograms incorporating these parameters are increasingly being used in the field of urolithiasis, but further external validation in diverse patient populations is still warranted.

Table 1. Baseline characteristics of patients according to stone-free status.

	Overall	Stone-Free (n=330)	Not Stone-Free (n=55)	p-value
Age (years)	47 (IQR: 44–52)	45 (IQR: 41–50)	47 (IQR: 44–51)	0.715
Gender				
Female	142	124	18	0.548
Male	243	206	37	
Stone Length (mm)	10 (IQR: 8–13)	16 (IQR: 13–23)	11 (IQR: 8–16)	< 0.001
Stone Density (HU)	875.5 ± 244.8	924.3 ± 300.2	884.4 ± 254.1	0.187
De Nunzio Score	16.6 (IQR: 14.0–22.0)	7.9 (IQR: 3.0–11.0)	15.6 (IQR: 10.0–20.0)	< 0.001
De Nunzio Group				
1	173	127	46	
2	58	51	7	< 0.001
3	108	106	2	
4	46	46	0	
Number of Stones				
1	315	289	26	
2	56	37	19	
3	8	4	4	< 0.001
4	4	0	4	
6	2	0	2	
Stone Location				
Distal Ureter	221	204	17	
Middle Ureter	84	76	8	< 0.001
Proximal Ureter	47	30	17	
UPJ	33	20	13	
Pyuria				
Yes	319	289	30	< 0.001
No	66	41	25	
Hydronephrosis				
Yes	221	181	40	0.018
No	164	149	15	

Abbreviations: mm: milimeter, HU: hounsfield unit, UPJ: ureteropelvic junction.

Age, stone length, stone density, and De Nunzio score were compared using the Mann–Whitney U test.

Gender, number of stone, stone location, hydronephrosis, pyuria, and De Nunzio groups were compared using the chi-square test.

HU values were compared using the independent-samples t-test

The green curve represents the net benefit of using the nomogram-derived predicted probabilities to guide clinical decisions across a range of threshold probabilities. The blue and brown curves indicate the strategies of treating all or treating none, respectively.

In parallel with URS, predictive nomograms for other treatment modalities have also emerged. Among them, a recent 2024 study introduced a logistic regression–based nomogram to predict stone-free success after ESWL, reporting robust predictive accuracy and suggesting its potential use for patient selection and counseling (14). In the context of PCNL, although no nomograms have specifically targeted proximal ureter or ureteropelvic junction stones, research efforts continue in this field. For example, recent studies have explored predictive models for postoperative bleeding and residual stones following upper tract PCNL [15]. Moreover, nomogram-based prediction of stone-free outcomes and complications after ESWL and PCNL has gained traction, reflecting a broader trend toward personalized endourology. Importantly, the development of nomograms specific to URS in recent years not only underscores this shift but also highlights the growing emphasis on individualized treatment planning in endourologic stone management.

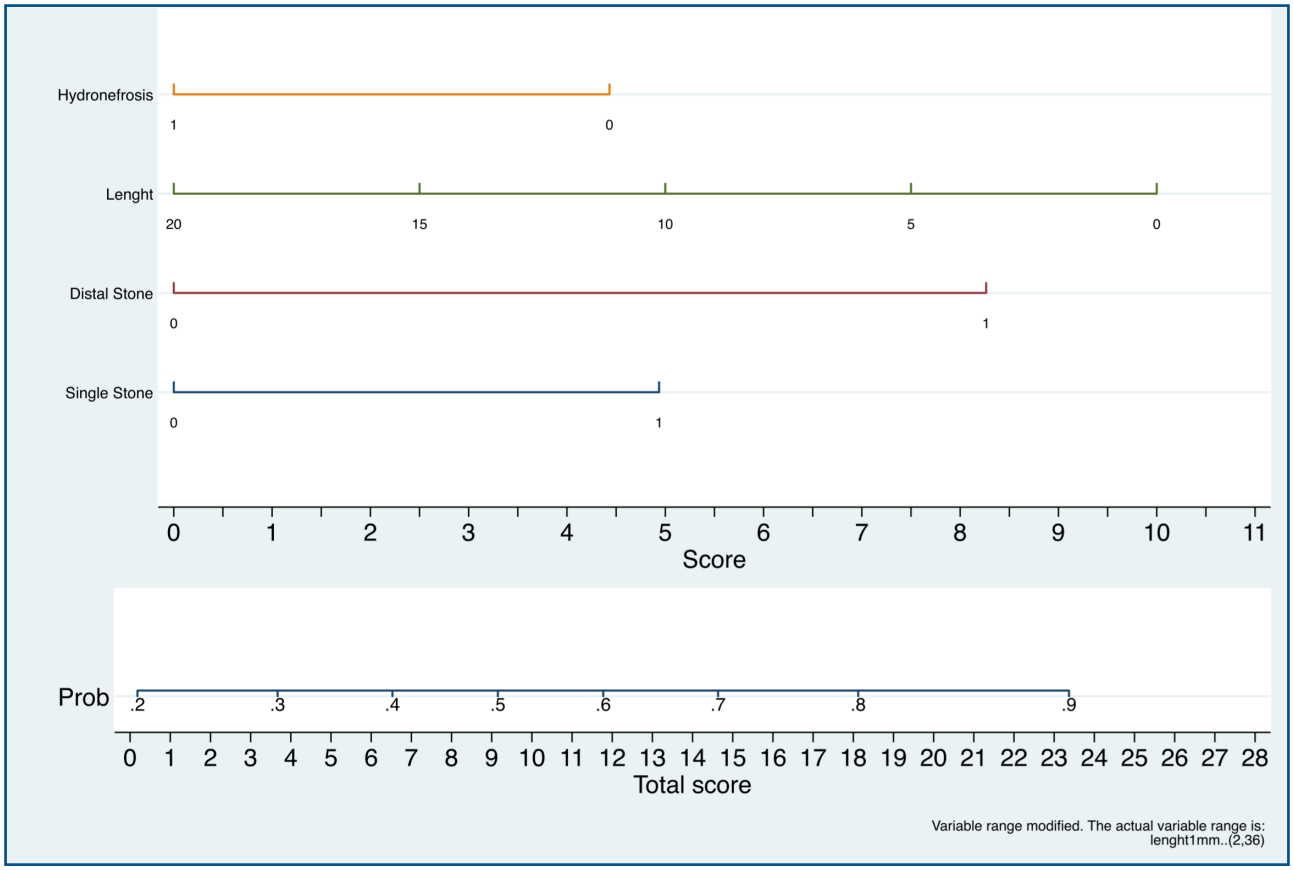

Figure 1. De Nunzio nomogram

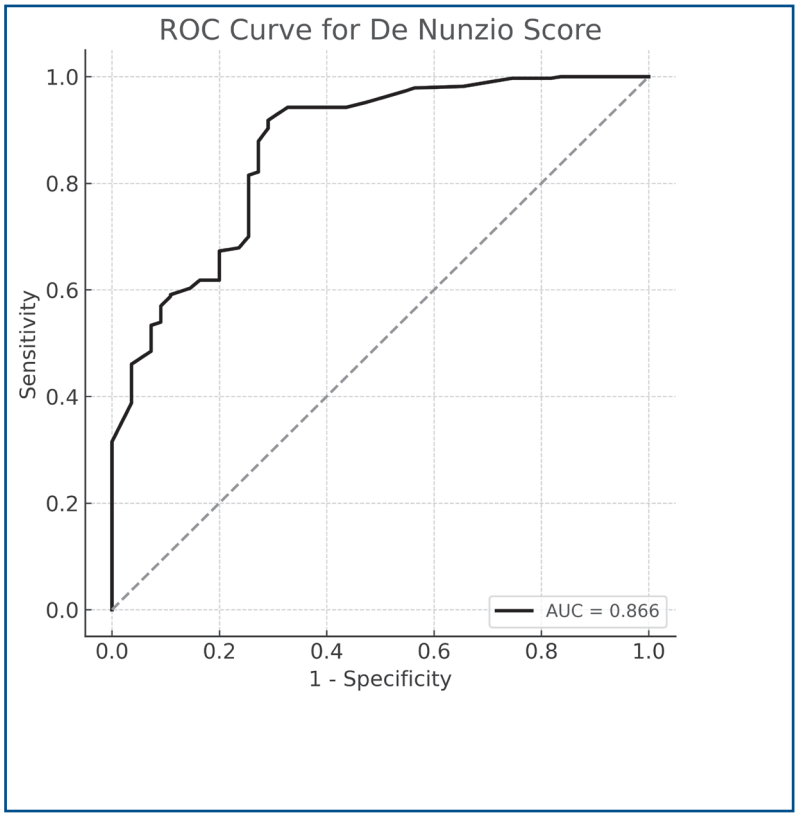

Figure 2. Receiver operating characteristic (ROC) curve for the De Nunzio score in predicting stone-free status.

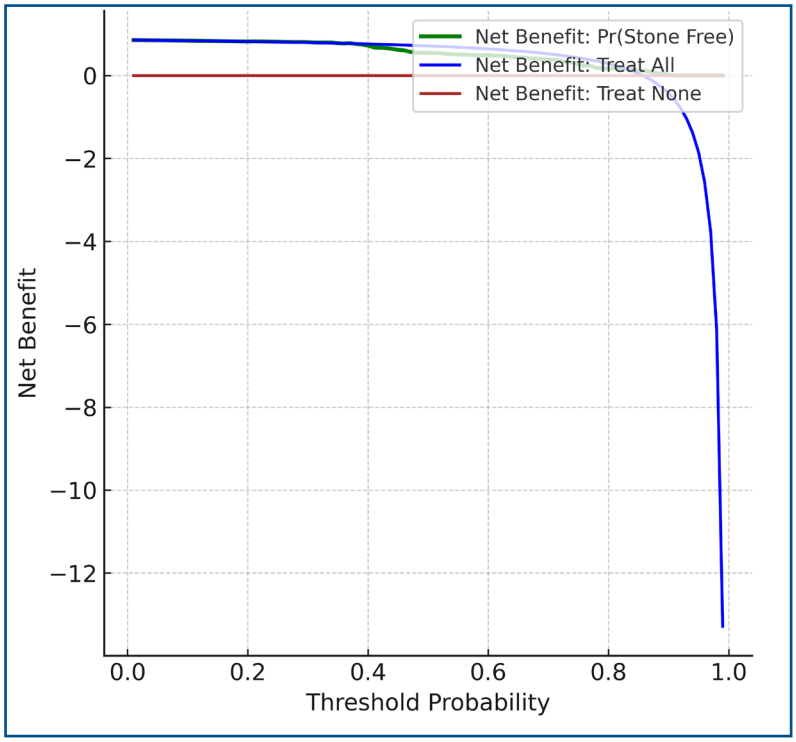

Figure 3. Decision curve analysis of the externally validated nomogram based on the De Nunzio score.

In this context, our study aimed to externally validate the De Nunzio nomogram, which was specifically developed to predict stone-free outcomes following semirigid ULT. To the best of our knowledge, this is the first study to validate the nomogram in an independent patient cohort externally. By applying the original scoring system to a contemporary real-world population, we assessed its discriminative performance and clinical applicability. Our findings, based on comprehensive statistical analyses including ROC curve and DCA, confirm the model's strong predictive accuracy and highlight its potential role in supporting individualized treatment decisions in endourologic stone surgery.

The AUC value obtained in our study (0.866) was notably higher than that reported in the original De Nunzio study (0.746). Several cohort-related factors may explain this difference. In our population, the median stone length was greater, and the distribution of stone locations was more concentrated in the distal ureter, which is typically associated with higher SFR [16]. In addition, our cohort included a wider range of De Nunzio scores, with a higher proportion of patients clustered at both the lower and upper ends of the scale. This may have enhanced the nomogram's capacity to discriminate between outcomes. Furthermore, key predictive variables such as pyuria and hydronephrosis showed stronger associations with stone-free status in our dataset, which likely contributed to the improved discriminative performance. These differences, taken together, may explain the higher AUC observed in our external validation.

The SFR observed in our cohort was 85.7%, which is consistent with previous large-scale studies evaluating semirigid ULT. In the original De Nunzio study, the reported SFR was 81.5%, while Imamura et al. and other contemporary series have documented rates ranging from 80% to 90%, depending on stone characteristics and surgical techniques (17,18). The increased SFR observed in our cohort relative to those reported by De Nunzio and Imamura may be attributable to the predominance of distal ureteral stones and a higher incidence of solitary calculi, both of which are well-established predictors of successful ULT (19–21). A recent nomogram-based study also reported a similar SFR of 84.9% (8), further supporting the generalizability of our findings. Therefore, our findings support the reliability of semirigid URS as an effective modality for ureteral stone management and confirm the external applicability of the De Nunzio nomogram across different patient populations.

The evaluation of a prediction model's performance should incorporate multiple dimensions, including discrimination, calibration, clinical utility, as well as internal and external validation, to ensure its reliability and applicability across diverse clinical settings (22). Numerous predictive models have been developed for urological cancers, and research in this area continues to expand with the publication of new studies (23–25). However, the development of reliable nomograms for ureterolithiasis presents several challenges, including the lack of consensus on the definition of residual fragments, variability in postoperative evaluation timing and imaging methods, ongoing debates regarding the optimal surgical approach (rigid vs. flexible ureteroscopy), differences in equipment used (laser alone vs. laser plus basket retrieval), and the presence or absence of a preoperative ureteral stent (26). The Imamura nomogram incorporated stone length, number, and location, as well as the presence of pyuria (5). Similarly, the De Nunzio nomogram included hydronephrosis, stone length, stone location, and number of stones (7). The Zhang nomogram, on the other hand, was based on hydronephrosis, hypertension, stone location, transverse diameter, and white blood cell count (8). All of these parameters remain open to discussion and further refinement. Notably, the inclusion of variables such as hypertension and white blood cell count in the most recent nomogram remains scientifically debatable, as their independent impact on stone-free outcomes has yet to be established through robust evidence.

This study has several limitations that should be acknowledged. First, its retrospective and single-center design may introduce selection bias and limit the generalizability of the findings. In addition, although the sample size was relatively large, certain potentially relevant variables, such as stone composition, operative time, and surgeon-specific factors, were not included in the analysis. Future prospective multicenter studies with standardized operative techniques are needed to validate and refine the De Nunzio nomogram. Moreover, comparative evaluations involving multiple nomograms within the same patient population would be valuable to determine the most accurate and clinically applicable model for predicting stone-free outcomes following ureteroscopic lithotripsy.

CONCLUSION

In conclusion, our study confirms the external validity of the De Nunzio nomogram in predicting stone-free outcomes after semirigid ureteroscopic lithotripsy. The findings support its use as a reliable clinical tool for preoperative risk assessment and personalized treatment planning. By demonstrating consistent predictive performance in an independent cohort, this study contributes to the growing body of evidence favoring the integration of nomogram-based models into routine endourological practice. Further prospective, multicenter validation studies are encouraged to strengthen the nomogram's applicability across diverse clinical settings.

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

Funding: The authors declare that they have no relevant financial interests.

Ethical Approval: The study was approved by the local ethics committee at University of Health Sciences, Başakşehir Çam and Sakura City Hospital (KAEK/21.05.2025.165, Date: 2025-05-21). All procedures performed in our study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards, and this study was designed according to the STROCSS 2021 criteria.

Author Contributions

MŞ: corresponding author, protocol and project development, data analysis, and manuscript writing.
EA: project development, data analysis, and manuscript writing
YNA: project development, data analysis, and manuscript writing,
YCF: project development, manuscript writing, and editing
TÖ: project development, manuscript writing, and editing

MS: project development, manuscript writing, and editing
HLC: project development and editing,

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