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ORIGINAL RESEARCH

Neutrophil Percentage-to-Albumin Ratio as a Predictor of Urinary Tract Infection in Patients with Urinary Stone Disease: Development a Novel User-Friendly Tool

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Background: Urinary stone disease (USD) is a prevalent condition, and associated urinary tract infections (UTIs) present significant risks, often leading to severe complications. Current diagnostic approaches for UTIs, such as urine culture, are time-consuming, while existing predictive models often lack dynamic biomarkers or are overly complex. The neutrophil-to-albumin ratio (NPAR), a readily available inflammatory marker, merits investigation as a predictor of UTIs in this patient population.

Objective: This study aimed to examine the relationship between NPAR and UTIs in patients with USD and to develop a novel, user-friendly predictive tool for assessing UTIs risk.

Methods: A retrospective cohort study was conducted at a single center, including 7000 participants with USD (January 2015 to January 2025). The cohort was randomly split into training and validation sets (7:3). The association between NPAR and UTIs was explored using restricted cubic splines (RCS) with three knots. Both traditional logistic regression and LASSO (Least Absolute Shrinkage and Selection Operator) regression were employed, and model performance was assessed via the area under the receiver operating characteristic (ROC) curve (AUC), calibration curves, and decision curve analysis (DCA).

Results: NPAR was independently associated with an increased risk of UTIs (adjusted odds ratio [OR] 1.34, 95% confidence interval [CI]: 1.07–1.69, $P < 0.001$). Restricted cubic spline analysis revealed a nonlinear relationship, with the risk increasing markedly when NPAR exceeded 1.21. A significant interaction by sex was observed (P for interaction < 0.001), with a stronger association in males (OR = 2.79, 95% CI: 2.20–3.52). The LASSO regression model demonstrated good discrimination, with AUC of 0.8016 in the training set and 0.8013 in the validation set, comparable to those of the logistic regression model (0.8015 and 0.8008). Additionally, the LASSO model showed better calibration and greater parsimony. A user-friendly, web-based tool was successfully developed. (https://utipredictor.streamlit.app).

Conclusion: NPAR is an independent, easily accessible predictor of UTIs in patients with USD. The developed web-based tool may enable rapid UTI risk stratification, with the potential to support timely intervention and personalized treatment. External validation is needed to confirm its generalizability.

Keywords: neutrophil-to-albumin ratio, urinary tract infection, urinary stone disease, predictive model, LASSO regression

Introduction

Urinary stone disease (USD), also known as urolithiasis, is a prevalent condition characterized by stone formation in the urinary tract, including the kidneys, ureters, bladder, and urethra.[1] It ranks among the most common urinary tract disorders, with incidence rates ranging from 7–13% in North America, 5–9% in Europe, and 1–5% in Asia, showing a continuous global rise.[2,3] Due to high rates of both new and recurrent stone formation, the management of USD incurs

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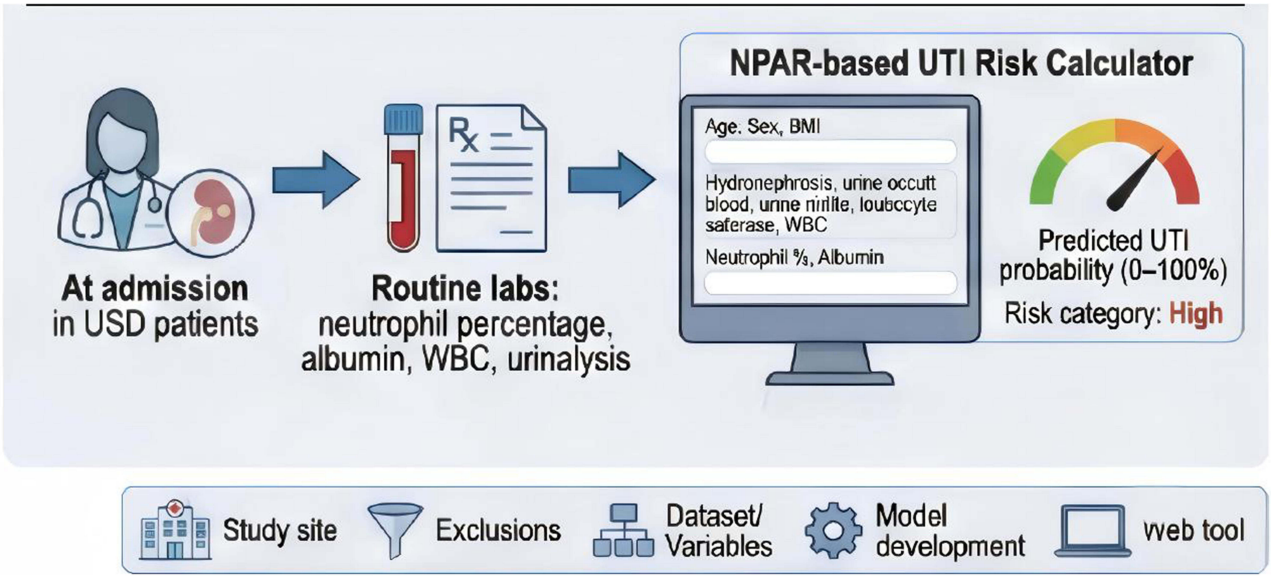
Graphical Abstract



substantial costs, exceeding $10 billion annually in healthcare expenditures in the United States.[4] In addition to causing severe pain and urinary obstruction, patients with USD are highly vulnerable to urinary tract infections (UTIs), a serious complication that can lead to sepsis, renal dysfunction, or even life-threatening conditions.[5,6] Up to 30% of stone patients experience postoperative UTIs, with 15% developing septicemia.[7] Identifying and predicting which patients with USD are at higher risk for UTIs is essential for enabling early clinical intervention, preventing complications, and improving patient outcomes.[8,9] While urine culture remains the gold standard for UTIs diagnosis, the process requires 24–72 hours, and improper sampling or storage may lead to false-positive results.[10] Recent attempts to predict UTIs have typically relied on static clinical data, often failing to integrate biomarkers that reflect real-time inflammatory and immune status, thereby limiting their predictive accuracy and dynamic assessment capabilities.[11–13] Thus, identifying objective, accessible biomarkers with strong predictive value and developing faster, more cost-effective predictive tools is critical for UTI prevention and management in patients with USD.[14]

Neutrophils are a key component of the innate immune response, playing a pivotal role in bacterial infections and inflammation.[15,16] In patients with USD presenting with concurrent UTIs, elevated neutrophil levels often reflect the body's response to pathogens.[17] High neutrophil counts may signal infection risk or severity.[18] However, neutrophil levels can also rise due to non-infectious factors, such as stress, trauma, or corticosteroid use, potentially reducing the specificity and accuracy of this marker in predicting UTIs risk in patients with USD.[18,19] Albumin, a plasma protein synthesized by the liver, maintains plasma colloid osmotic pressure and plays critical roles in anti-inflammatory, antioxidant, and immunomodulatory functions.[20,21] Low serum albumin levels are typically indicative of malnutrition, chronic inflammation, or hepatorenal dysfunction and are associated with poor prognosis in various diseases. In infectious conditions, reduced albumin levels may signal impaired immune function or increased inflammatory consumption, heightening susceptibility to infection and worsening clinical outcomes.[22,23] Among patients with USD, low albumin levels often reflect poor overall health, further elevating the risk of infection.[24] Like neutrophil counts, albumin levels are influenced by multiple factors, diminishing the reliability of this marker alone in predicting UTIs risk in patients with USD.[25,26]

Given the limitations of using either marker in isolation, composite indices that integrate multiple physiological pathways may offer superior predictive performance. The Neutrophil-to-Albumin Ratio (NPAR) is one such biomarker

that has garnered attention in recent years.[27–29] Its potential advantage lies in concurrently reflecting two critical aspects: the numerator (neutrophil count) represents the intensity of the acute inflammatory response, often directly triggered by infection, while the denominator (albumin level) serves as a proxy for the host's nutritional reserve, systemic inflammatory burden, and overall immunocompetence.[27,30] A high NPAR thus theoretically captures a state of both heightened inflammatory drive and diminished physiological reserve, which is particularly relevant for infection risk. This integrative property may make NPAR more robust and informative than either component alone, reducing misclassification caused by non-specific fluctuations in a single parameter. Furthermore, NPAR has demonstrated promising prognostic value in predicting outcomes in sepsis, community-acquired pneumonia, and postoperative infections, supporting its broader relevance in infectious contexts.[31–33] From a practical standpoint, NPAR is derived from routine complete blood count and biochemistry panels, making it rapidly available, cost-effective, and amenable to dynamic monitoring without additional testing.[34] However, the utility of NPAR in predicting UTIs occurrence in patients with USD remains to be fully elucidated.

Thus, this study explored the relationship between NPAR and UTIs development in patients with USD, with the aim of developing a novel, user-friendly predictive tool that offers healthcare professionals an objective and convenient reference for assessing UTIs risk. This tool could facilitate early risk stratification and preventive interventions.

Materials and Methods

Study Design and Setting

This single-center, retrospective observational cohort study was conducted in two phases, as depicted in Figure 1. The first phase focused on developing a UTIs prediction model for patients with USD, which involved training the model using a large dataset and validating it with an internal validation set to ensure its generalizability. The second phase centered on creating a user-friendly bedside tool to ensure clinical applicability. The study adhered to the TRIPOD checklist for reporting standards.

Participants

Data were retrospectively collected from 7548 patients with USD treated at Jiangmen Central Hospital between January 2015 and January 2025. The complete participant screening and inclusion process is detailed in Figure 1. Inclusion Criteria: Age $\geq$ 18 years; Diagnosis of USD confirmed by CT, X-ray, or ultrasound examination. Exclusion criteria included: (1) cases with contaminated urine culture results; (2) cases with missing critical data exceeding 10%. For patients with multiple hospitalizations, only data from the first hospitalization episode were considered. Following screening, 7000 patients were included in the study. The data were randomly split into training and validation sets in a 7:3 ratio using the Python random function.

Data Collection

This study primarily focused on NPAR as the key predictor variable, calculated as: NPAR = neutrophil count / albumin concentration. Other inflammatory ratios were calculated as follows: NLR = neutrophil count / lymphocyte count; PLR = platelet count / lymphocyte count; MLR = monocyte count / lymphocyte count. The following variables were collected: (1) General Information: Age, sex, and body mass index (BMI). (2) Clinical Parameters: Occult blood in urine, hydronephrosis. (3) Laboratory Indicators: White blood cell count, neutrophil count, lymphocyte count, monocyte count, hemoglobin, platelet count, Serum creatinine, urea, Urine pH, urine glucose, urine ketones, urine leukocytes, urine leukocyte esterase, urinary nitrite, urinary protein, uric acid crystals.

Trained research personnel extracted objective data from medical records regarding demographics, clinical features, and laboratory results, and developed a standardized data dictionary. All data were collected from patients' first examination upon admission to minimize the impact of subsequent treatments on various parameters. To ensure data integrity, the principal investigator conducted random audits on 10% of the data. Weekly meetings between the principal investigator and data collectors were held during the data collection period to review any discrepancies identified in the audits and address any questions regarding the data review process.

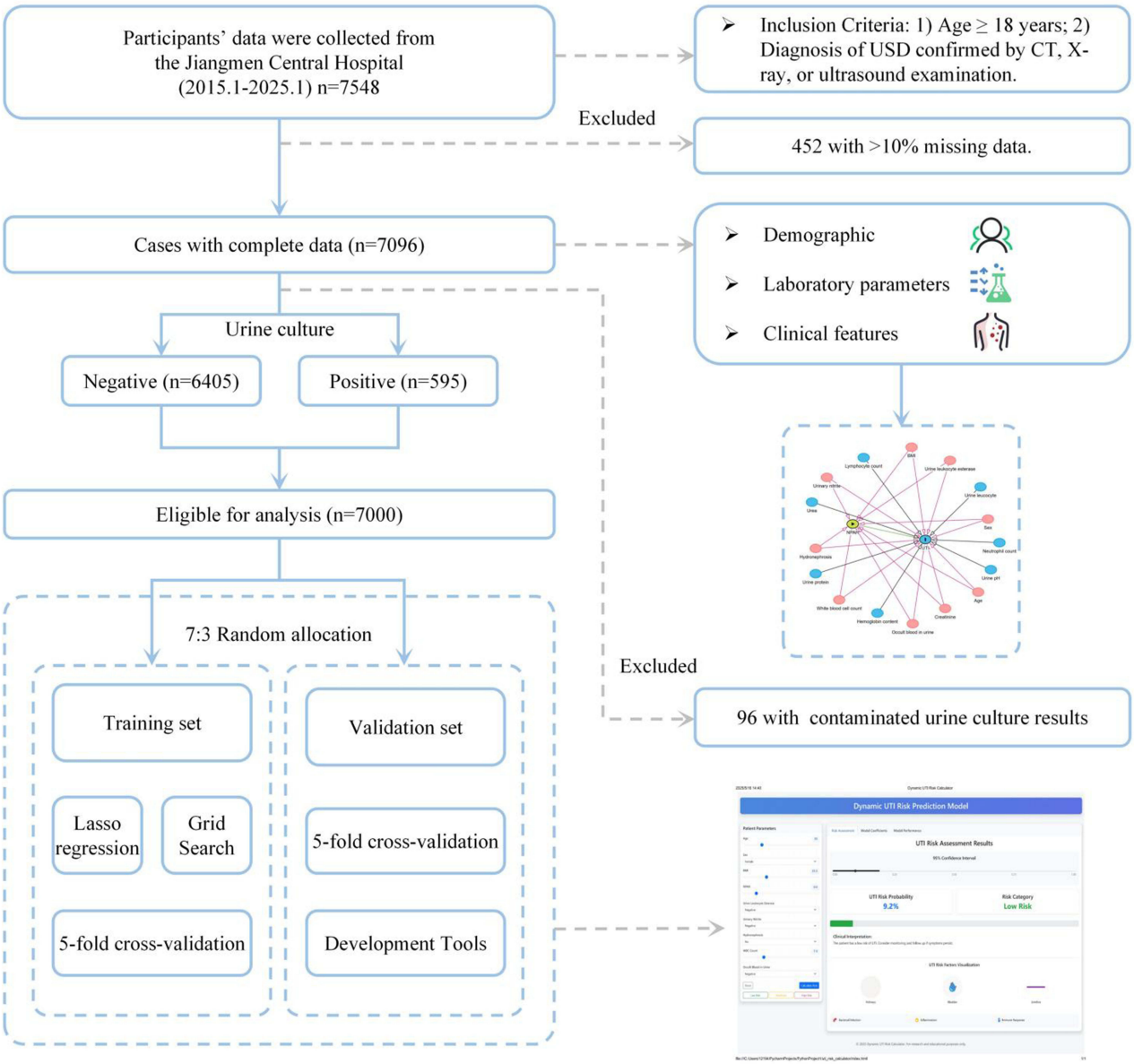


Figure 1 Flow chart of participant recruitment and data analysis methods.

Outcomes

The primary outcome, "UTIs", was defined as bacterial growth > 100,000 colony-forming units per milliliter (CFU/mL) in the urine of patients with USD, or the presence of at least two of the following conditions without other causes: fever, hypotension, nausea or vomiting, rigors, delirium, or trauma causing bleeding or new urologic obstruction.[35] For the purpose of this study, UTIs were those diagnosed based on clinical and laboratory findings from the patient's first examination upon admission.

Sample Size Calculation

Sample size calculation was based on an expected total of 9 independent variables, with the standard requirement of at least 10 events per variable (EPV).[36] Historical data indicated a UTIs incidence rate of approximately 10%, and with a 70% training set proportion, the required sample size for the training set was 1286 participants.[37] Factoring in

a potential 10% data inefficiency rate, the final required total sample size was 1429 participants. This study ultimately included 7000 patients, exceeding the minimum requirement and providing sufficient statistical power.

Statistical Analysis

Data analysis was performed using Python (v3.13.2). The analysis proceeded in sequential phases: (1) Description and Comparison:

Normally distributed variables were presented as mean ± standard deviation, while non-normally distributed data were expressed as median and interquartile range (IQR). Categorical variables were summarized as counts and percentages. For continuous variables, independent *t*-tests were applied to compare differences between groups for normally distributed data, while the Mann–Whitney *U*-test was used for non-normally distributed data. Categorical data were analyzed using chi-square tests or Fisher's exact tests. (2) Exploring the Primary Relationship: To avoid assuming a simple linear relationship between NPAR and UTI, this study employed restricted cubic spline (RCS) fitting to model the underlying association between the two variables. This method flexibly reveals and visualizes nonlinear patterns among continuous variables while quantitatively assessing the statistical significance of nonlinearity through likelihood ratio tests.[38] The three nodes of the RCS were positioned at the 10th, 50th, and 90th percentiles of the NPAR distribution.[39] (3) Sensitivity analyses: Missing data were analyzed using Little's MCAR test, which yielded a χ^2 value of 5.560 ($P > 0.05$), indicating the data were likely missing completely at random (MCAR).[40] Based on this, samples with more than 10% missing data were excluded, and the Markov Chain Monte Carlo (MCMC) method was employed for multiple imputation. Ten complete datasets were generated, and the results were summarized to reduce bias and enhance the reliability of subsequent analyses.[41,42] A directed acyclic graph (DAG) was constructed using DAGitty software based on literature evidence[12,43] and univariate analysis results to identify potential confounders and determine the minimal sufficient adjustment set for multivariate regression models,[44] as shown in Figure 2. Three progressive models were built: Model 1 was unadjusted; Model 2 included demographic and clinical covariates (age, sex, BMI); and Model 3 incorporated key laboratory indicators (occult blood in urine, hydronephrosis, urinary nitrite, urine leukocyte esterase, and white blood cell count) in addition to the variables in Model 2. Subgroup analyses by sex, age, BMI, and NPAR tertiles (NPAR < 1.37; 1.37 ≤ NPAR < 1.84; NPAR ≥ 1.84) were also conducted to assess the consistency of predictive performance across different subpopulations. 4) Model Development and Validation: To mitigate risks of multicollinearity and overfitting in multivariate prediction, sparse learning methods were employed. LASSO, a renowned sparse learning technique,[45] was used to obtain sparse solutions for coefficients associated with the most important predictors. LASSO has demonstrated superior performance in predictive model selection compared to traditional regression methods.[46] In the training dataset, the optimal hyperparameters for base learners were determined using grid search and 5-fold cross-validation.[47,48] The hyperparameter C yielded the highest area under the receiver operating characteristic (ROC) curve (AUC) and was selected as the final training condition. The Synthetic Minority Over-sampling Technique (SMOTE) was applied to address class imbalance in UTIs-positive samples, aiming to increase the model's sensitivity to underrepresented positive cases.[49] Model performance was evaluated using ROC curve analysis, with AUC values computed separately for the training and validation sets (AUC = 0.5 indicating no discriminative ability, AUC = 1 indicating perfect discrimination).[50] Accuracy, sensitivity, specificity, and brier score were also assessed. Additionally, the Hosmer–Lemeshow test was used to evaluate model calibration, and decision curve analysis (DCA) was applied to assess clinical utility. Based on the best-performing model, a user-friendly, web-based bedside prediction tool was developed to facilitate clinical application.

Results

Baseline Demographic and Clinical Characteristics

Table 1 presents the baseline characteristics of participants. Patients in the UTI group were significantly older (60.90 ± 12.93 vs. 56.36 ± 13.74 years, $P < 0.001$) and had a higher proportion of females (56.30% vs 36.03%, $P < 0.001$). Regarding urinary indicators, the UTI group exhibited significantly higher rates of positive urinary leukocyte esterase (particularly +++: 63.72% vs 19.91%, $P < 0.001$) and positive urinary nitrite (64.03% vs 9.99%, $P < 0.001$). For occult

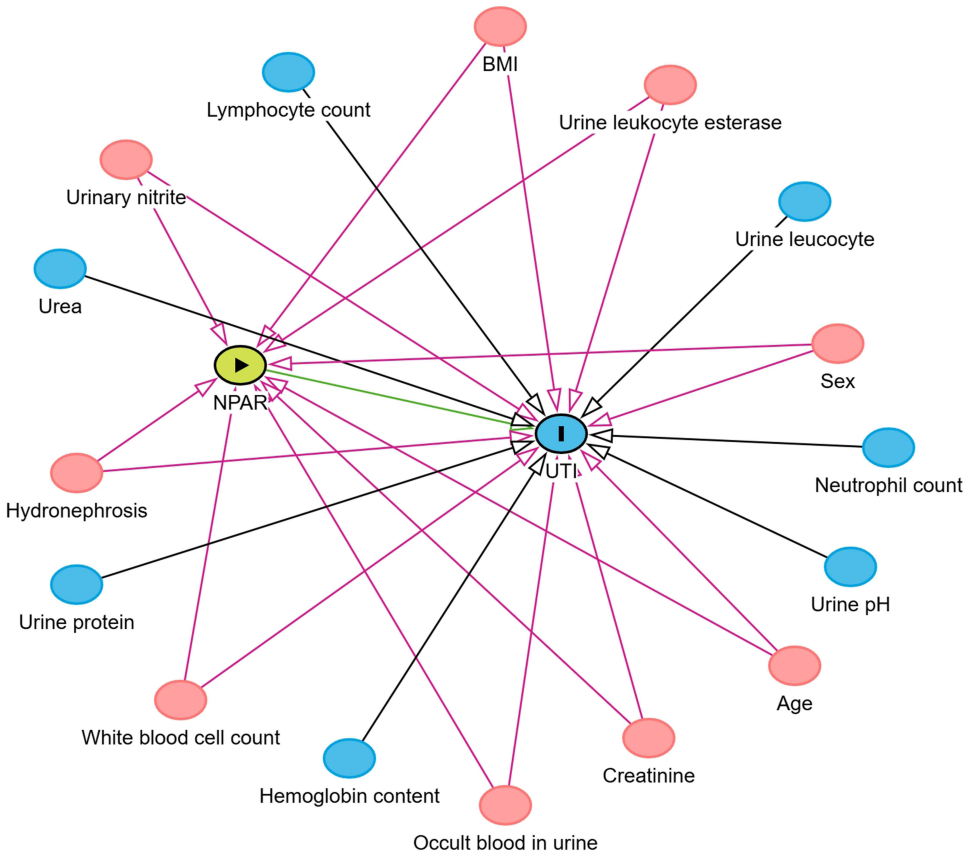


Figure 2 Directed acyclic graph of NPAR and UTIs.

blood in urine, the UTI group showed a markedly higher proportion of patients with strongly positive results (+++: 39.32% vs 14.22%), whereas the non-UTI group had a higher proportion of negative results (−: 33.22% vs 14.28%) ($P < 0.001$). Urine leukocyte counts were significantly elevated in the UTI group (1489.48 ± 3575.13 vs 436.39 ± 2490.01 /

Table 1 Comparison of Baseline Characteristics Between Urine Culture-Negative and Urine Culture-Positive Groups

Variables	Total (n = 7000)	Negative Urine Culture (n = 6405)	Positive Urine Culture (n = 595)	*P*-value	Reference Range
Demographic variables					
Age (years)	56.74 ± 13.73	56.36 ± 13.74	60.90 ± 12.93	< 0.001	
Sex, n(%)				< 0.001	
Males	4357 (62.24)	4097 (63.97)	260 (43.70)		
Females	2643 (37.76)	2308 (36.03)	335 (56.30)		
BMI	23.66 ± 3.56	23.67 ± 3.56	23.60 ± 3.67	0.66	
Clinical Parameters					
Occult blood in urine, n(%)				< 0.001	
–	1811 (25.9)	2128 (33.22)	85 (14.28)		

(*Continued*)

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Table 1 (Continued).

Variables	Total (n = 7000)	Negative Urine Culture (n = 6405)	Positive Urine Culture (n = 595)	*P*-value	Reference Range
+	1801 (25.7)	1726 (26.94)	161 (27.05)		
++	1026 (14.7)	1640 (25.60)	115 (19.32)		
+++	2362 (33.7)	911 (14.22)	234 (39.32)		
Hydronephrosis, n(%)				< 0.001	
Yes	1610 (22.93)	1523 (23.78)	152 (25.54)		
No	5390 (77.00)	4882 (76.22)	443 (77.45)		
Laboratory indicators					
White blood cell count	7.85 ± 3.50	7.83 ± 3.49	8.12 ± 3.57	0.05	3.5–9.5 $\times 10^9$/L
Neutrophil count	5.22 ± 3.46	5.18 ± 3.44	5.67 ± 3.62	< 0.001	1.8–6.3 $\times 10^9$/L
Lymphocyte count	1.86 ± 0.73	1.87 ± 0.73	1.70 ± 0.74	< 0.001	1.1–3.2 $\times 10^9$/L
Monocyte count	6.67 ± 2.00	6.67 ± 2.01	6.61 ± 1.94	0.48	0.1–0.6 $\times 10^9$/L
Creatinine	129.25 ± 154.97	126.61 ± 152.21	157.66 ± 179.70	< 0.001	Males: 59–104 μmol/L Females: 45–84 μmol/L
Urea	7.08 ± 5.46	6.93 ± 5.24	8.72 ± 7.28	< 0.001	2.9–8.2 mmol/L
Hemoglobin content	127.41 ± 21.30	128.39 ± 20.97	116.85 ± 21.95	< 0.001	Males: 130–175 g/L Females:115–150g/L
Uric Acid Crystals	0.21 ± 6.08	0.19 ± 5.64	0.46 ± 9.60	0.31	0–2 /HPF
Urine pH	6.03 ± 0.50	6.02 ± 0.50	6.09 ± 0.51	< 0.001	4.5–8.0
Urine Glucose, n(%)				0.23	
Negative	6093 (90.41)	5588 (90.67)	505 (87.67)		
+	213 (3.16)	189 (3.07)	24 (4.17)		
++	89 (1.32)	79 (1.28)	10 (1.74)		
+++	248 (3.68)	222 (3.60)	26 (4.51)		
++++	96 (1.42)	85 (1.38)	11 (1.91)		
Urine Leucocyte	525.90 ± 2616.12	436.39 ± 2490.01	1489.48 ± 3575.13	< 0.001	0–10 /μL
Urine Leukocyte Esterase, n(%)				< 0.001	
Negative	3321 (49.28)	3227 (52.36)	94 (16.32)		
+	912 (13.53)	868 (14.08)	44 (7.64)		
++	912 (13.53)	841 (13.65)	71 (12.33)		
+++	1594 (23.65)	1227 (19.91)	367 (63.72)		
Urinary Protein, n(%)				< 0.001	
Negative	2028 (30.09)	1812 (29.40)	216 (37.50)		
+ ~ ++++	4711 (69.91)	4351 (70.60)	360 (62.50)		

(*Continued*)

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Table 1 (Continued).

Variables	Total (n = 7000)	Negative Urine Culture (n = 6405)	Positive Urine Culture (n = 595)	*P*-value	Reference Range
Urinary Nitrite, n(%)				< 0.001	
Negative	5979 (85.41)	5765 (90.01)	214 (35.96)		
Positive	1021 (14.58)	640 (9.99)	381 (64.03)		
Urine Ketone Body, n(%)				0.08	
Negative	6387 (94.78)	5832 (94.63)	555 (96.35)		
Positive	352 (5.22)	331 (5.37)	21 (3.65)		
Inflammation index					
NPAR	1.67 ± 0.47	1.65 ± 0.46	1.82 ± 0.55	< 0.001	
NLR	3.87 ± 6.29	3.83 ± 6.22	4.36 ± 6.94	0.05	
PLR	160.22 ± 108.51	159.47 ± 108.37	168.23 ± 109.87	0.06	
MLR	4.29 ± 2.94	4.29 ± 2.93	4.31 ± 2.96	0.91	

Notes: *t*: *t*-test, χ^2: Chi-square test. NPAR: Neutrophil-to-albumin ratio = percentage of neutrophils / albumin concentration; NLR: Neutrophil-to-lymphocyte ratio = neutrophil count / lymphocyte count; PLR: Platelet-to-lymphocyte ratio = platelet count / lymphocyte count; MLR: Monocyte-to-lymphocyte ratio = monocyte count / lymphocyte count.
Abbreviations: SD, standard deviation; BMI, body mass index.

μL, $P < 0.001$), far exceeding the normal reference range (0–10 /μL). Although the data are presented as mean ± SD, the extremely large standard deviations indicate a highly right-skewed distribution. The current mean ± SD is shown solely for consistency with other continuous variables in Table 1. Hydronephrosis was higher prevalent in the UTI group (25.54% vs 23.78%, $P < 0.001$). Neutrophil counts were significantly elevated in UTI patients (5.67 ± 3.62 vs 5.18 ± 3.44 $\times 10^9$/L, $P < 0.001$), approaching the upper limit of normal (1.8–6.3 $\times 10^9$/L), while lymphocyte counts were significantly reduced (1.70 ± 0.74 vs 1.87 ± 0.73 $\times 10^9$/L, $P < 0.001$), falling within the lower-normal range (1.1–3.2 $\times 10^9$/L). Creatinine and urea levels were both significantly elevated in the UTI group (157.66 ± 179.70 vs 126.61 ± 152.21 μmol/L; 8.72 ± 7.28 vs 6.93 ± 5.24 mmol/L, respectively; both $P < 0.001$), with mean values exceeding the upper normal limits (Cr: >104 μmol/L in males, >84 μmol/L in females; Urea: >8.2 mmol/L). Conversely, hemoglobin levels were significantly lower in the UTI group (116.85 ± 21.95 vs 128.39 ± 20.97 g/L, $P < 0.001$), falling below the normal range (male: <130 g/L, female: <115 g/L). NPAR was significantly elevated in the UTI group (1.82 ± 0.55 vs 1.65 ± 0.46, $P < 0.001$).

No significant differences were observed in missing variables between the training and validation sets, both before and after multiple imputation (Table 2). As shown in Table 3, the baseline clinical characteristics of the training and validation sets were comparable, with no significant differences across all measured variables ($P > 0.05$).

NPAR is an Independent Risk Indicator for UTIs

In univariate and multivariate logistic regression analyses of the association between NPAR and UTIs (Table 4), unadjusted NPAR (Model 1) was significantly associated with UTIs (unadjusted OR, 1.85; 95% CI, 1.59–2.15; $P < 0.001$). After adjusting for age, sex, and BMI (Model 2), NPAR remained a significant risk predictor for UTIs (adjusted OR, 1.48; 95% CI, 1.25–1.75; $P < 0.001$). Furthermore, Model 3, which included additional adjustments for urine leukocyte esterase, urinary nitrite, hydronephrosis, occult blood in urine, and white blood cell count based on Model 2, confirmed that NPAR was an independent risk indicator for UTIs (adjusted OR, 1.34; 95% CI, 1.07–1.69; $P < 0.001$). RCS analysis (Figure 3) was performed for NPAR to visualize the relationship between NPAR and UTIs. The analysis showed a significant association ($P < 0.001$), though no non-linear trend was detected ($P = 0.469$). When NPAR was

Table 2 Comparison of Continuous Variables Before and After Multiple Imputation

Variables	Before Interpolation	After Interpolation	*P*-values
Demographic variables			
Age	58.00 (48.00, 67.00)	58.00 (48.00, 67.00)	0.925
Sex	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.999
BMI	23.50 (21.30, 25.80)	23.50 (21.20, 25.80)	0.837
Clinical Parameters			
Occult blood in urine	1.00 (0.00, 3.00)	1.00 (0.00, 3.00)	0.835
Hydronephrosis	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.999
Laboratory indicators			
White blood cell count	7.12 (5.85, 8.84)	7.17 (5.83, 8.92)	0.760
Neutrophil count	4.32 (3.35, 5.83)	4.35 (3.33, 5.96)	0.678
Lymphocyte count	1.80 (1.37, 2.28)	1.81 (1.37, 2.29)	0.847
Monocyte count	6.50 (5.50, 7.70)	6.50 (5.50, 7.70)	0.980
Creatinine	90.00 (73.00, 119.85)	90.00 (72.50, 125.00)	0.516
Urea	5.59 (4.51, 7.28)	5.61 (4.50, 7.49)	0.478
Hemoglobin content	130.00 (116.00, 142.17)	130.00 (115.00, 142.00)	0.606
Uric acid crystals	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.822
Urine pH	6.00 (5.50, 6.50)	6.00 (5.50, 6.42)	0.896
Urinary glucose	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.999
Urine leucocyte	33.00 (8.00, 181.00)	35.00 (7.00, 216.00)	0.390
Urine leukocyte esterase	1.00 (0.00, 2.00)	1.00 (0.00, 2.00)	0.041
Urinary protein	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.999
Urinary nitrite	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.999
Urine ketone body	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	0.999
Inflammation index			
NPAR	1.56 (1.37, 1.84)	1.57 (1.37, 1.86)	0.595
NLR	2.31 (1.67, 3.63)	2.33 (1.65, 3.84)	0.469
PLR	133.77 (103.19, 181.04)	134.79 (102.68, 184.91)	0.594
MLR	3.58 (2.64, 5.00)	3.61 (2.63, 5.09)	0.683

Table 3 Demographic and Clinical Characteristics of the Training and Validation Sets

Variables	Total (n = 7000)	Training Set (N = 4900)	Validation Set (N = 2100)	*P*-value
Demographic variables				
Age (years)	56.74 ± 13.73	56.71 ± 13.77	56.83 ± 13.66	0.737

(*Continued*)

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Table 3 (Continued).

Variables	Total (n = 7000)	Training Set (N = 4900)	Validation Set (N = 2100)	*P*-value
Sex (female/male)	0.38 ± 0.48	0.38 ± 0.49	0.37 ± 0.48	0.455
BMI	23.66 ± 3.56	23.67 ± 3.56	23.60 ± 3.67	0.360
Clinical Parameters				
Occult blood in urine	1.56 ± 1.21	1.56 ± 1.22	1.57 ± 1.20	0.964
Hydronephrosis	0.23 ± 0.42	0.23 ± 0.42	0.23 ± 0.42	0.995
Laboratory indicators				
White blood cell count	7.85 ± 3.50	7.83 ± 3.49	7.87 ± 3.37	0.836
Neutrophil count	5.22 ± 3.46	5.22 ± 3.53	5.21 ± 3.31	0.830
Lymphocyte count	1.86 ± 0.73	1.85 ± 0.73	1.88 ± 0.75	0.124
Monocyte count	6.67 ± 2.00	6.68 ± 1.98	6.63 ± 2.06	0.308
Creatinine	7.08 ± 5.46	7.05 ± 5.40	7.16 ± 5.61	0.433
Urea	129.25 ± 154.97	128.24 ± 156.67	131.61 ± 150.94	0.405
Hemoglobin content	127.41 ± 21.30	127.43 ± 21.22	127.37 ± 21.49	0.916
Uric acid crystals	0.21 ± 6.08	0.24 ± 6.87	0.14 ± 3.62	0.500
Urine pH	6.03 ± 0.50	6.02 ± 0.49	6.04 ± 0.51	0.143
Urinary glucose	0.23 ± 0.77	0.23 ± 0.78	0.21 ± 0.75	0.413
Urine leucocyte	525.90 ± 2616.12	546.18 ± 2801.76	478.58 ± 2120.57	0.322
Urine leukocyte esterase	1.12 ± 1.25	1.13 ± 1.25	1.11 ± 1.25	0.747
Urinary protein	0.30 ± 0.46	0.30 ± 0.46	0.31 ± 0.47	0.911
Urinary nitrite	0.09 ± 0.29	0.09 ± 0.29	0.09 ± 0.29	0.986
Urine ketone body	0.05 ± 0.22	0.05 ± 0.22	0.05 ± 0.22	0.466
Inflammation index				
NPAR	1.67 ± 0.47	1.67 ± 0.47	1.67 ± 0.46	0.981
NLR	3.87 ± 6.29	3.88 ± 6.63	3.87 ± 5.39	0.969
PLR	160.22 ± 108.51	159.89 ± 112.11	160.98 ± 99.64	0.700
MLR	4.29 ± 2.94	4.31 ± 3.05	4.26 ± 2.66	0.511

Notes: *t*: *t*-test, χ^2: Chi-square test.
Abbreviations: SD, standard deviation; BMI, body mass index; NPAR, neutrophil-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio.

Table 4 Univariate and Multivariate Logistic Analyses of the Association Between NPAR and UTIs

Variables	Model 1		Model 2		Model 3	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
NPAR	1.85 (1.59 ~ 2.15)	< 0.001	1.48 (1.25 ~ 1.75)	< 0.001	1.34 (1.07 ~ 1.69)	0.001

Notes: Model 1: Crude. Model 2: Adjust for sex, age, and BMI. Model 3: Adjust for sex, age, BMI, urine leukocyte esterase, urinary nitrite, hydronephrosis, occult blood in urine, and white blood cell count.
Abbreviations: OR, Odds Ratio; CI, Confidence Interval.

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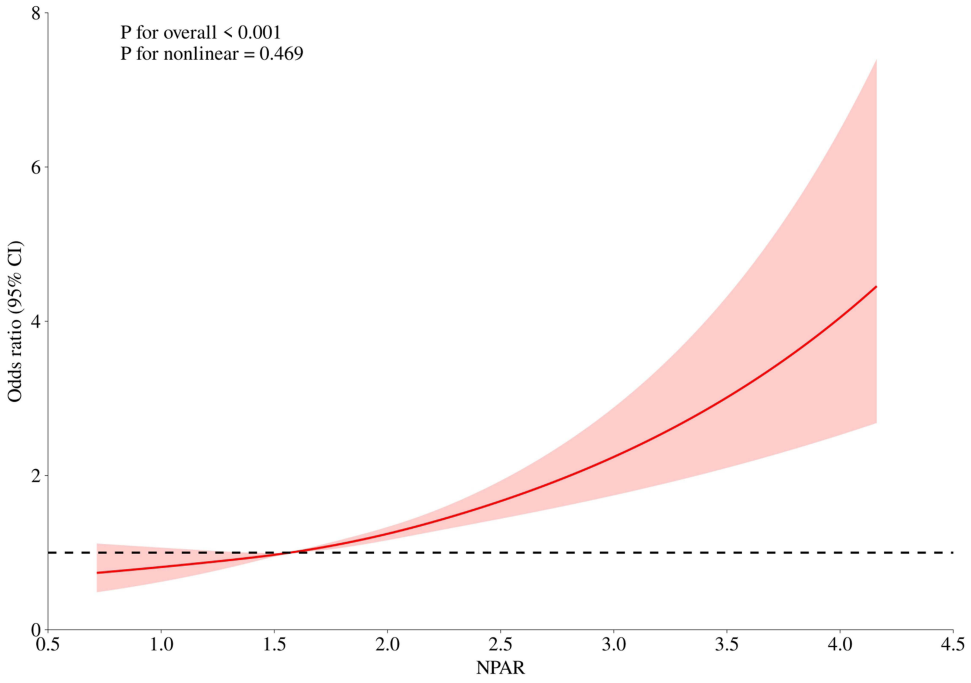

Figure 3 Restricted cubic spline curve for the association of NPAR and UTIs.

below 1.21, the risk change was relatively flat; however, between the median NPAR (1.57) and the 90th percentile (2.28), the risk of UTIs increased significantly with higher NPAR values. This suggests a potential threshold effect for NPAR, with clinical monitoring becoming particularly crucial in the higher NPAR range (> 1.21).

Subgroup Analysis

Subgroup analysis revealed sex-specific differences in the relationship between NPAR and UTIs (interaction $P < 0.001$). In males, each unit increase in NPAR was associated with a 2.79-fold increase in the odds of UTIs (OR = 2.79, 95% CI: 2.20–3.52), which was significantly higher than the 1.22-fold increase observed in females (OR = 1.22, 95% CI: 1.00–1.50). While interaction effects for BMI stratification ($P = 0.542$), age groups ($P = 0.486$), and NPAR tertiles ($P = 0.210$) were not statistically significant, all subgroups demonstrated a positive association between elevated NPAR and increased UTIs risk (OR range: 1.22–2.80). Notably, the highest risk was observed in the moderate NPAR group (1.37–1.84) (OR = 2.80, 95% CI: 1.07–7.36), suggesting a potential local non-linear effect. However, the main analysis, based on continuous variables ($\beta = 0.62$, $P < 0.001$), still supports a consistent linear trend (Figure 4).

The performance of different models was evaluated using ROC curve analysis. As shown in Figure 5A and B (Model A constructed using LASSO and Model B using logistic regression), both models demonstrated strong discrimination of outcome events in the training and validation cohorts. The AUCs for the training set were 0.8016 and 0.8015, respectively, while the AUCs for the validation set were 0.8013 and 0.8008. In the training set data, the optimal C was 0.05 (Supplementary Figure 1). The AUC, specificity, sensitivity, and accuracy for each model in the validation set are presented in Table 5.

Figure 5C and D illustrates the calibration curves for the LASSO regression model (Model A) and the logistic regression model (Model B) in both the training and validation sets. The results indicated that in the training set, the Hosmer–Lemeshow test *P*-value for the LASSO regression model was 0.842, and for the logistic regression model, it was 0.161. In the validation set, the *P*-values for both models were 0.432 (LASSO) and 0.129 (logistic regression). All models had *P*-values greater than 0.05, suggesting acceptable calibration consistency. Moreover, the LASSO regression model outperformed the logistic regression model in calibration, particularly in the low-risk range, indicating superior risk stratification capabilities. To further assess the clinical utility of these models, DCA was performed for the LASSO

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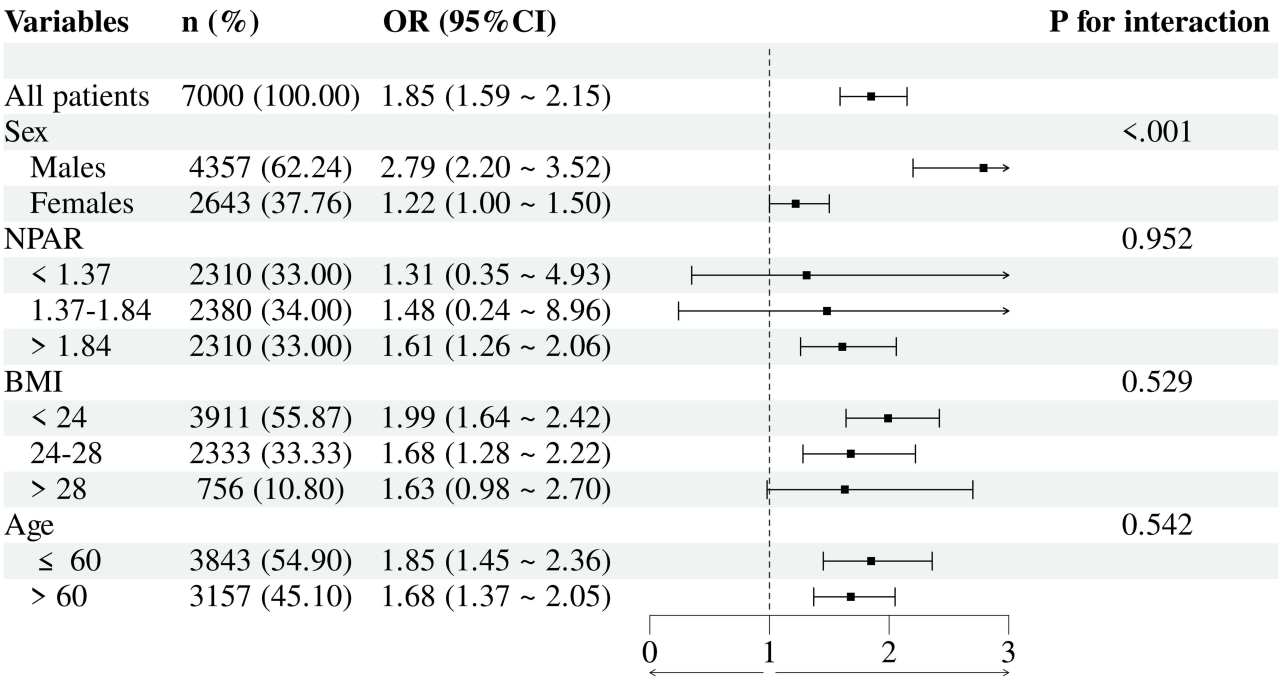

Figure 4 Subgroup analysis for the association between NPAR and UTIs.
Notes: Forest plot showing the adjusted odds ratios (ORs) and 95% confidence intervals (CIs) across different strata, with P values for interaction.

model in both the training and validation sets (Figure 5E and F). DCA results confirmed that the LASSO regression model provided a significant net clinical benefit.

New User-Friendly Prediction Tool

Although nomograms are practical and cost-effective, they cannot provide exact values for calculations. To address this limitation, a web-based, user-friendly prediction tool was developed to simplify the calculation process and generate more accurate predictive values (https://utipredictor.streamlit.app). This tool enables the automatic calculation of UTIs risk based on straightforward numerical inputs, offering real-time predictive insights for clinicians. After entering the required parameters on the left side, clicking the "Calculate Risk" button initiates the model calculation. The system then displays the risk assessment results in the right panel, which includes UTIs risk probability (ranging from 0% to 100%) and risk classification. Model coefficients and performance metrics are accessible via the top tabs (Supplementary Figure 2).

Discussion

UTIs are a prevalent and potentially severe complication in patients with USD, with reported incidence rates ranging from 10–15%. These infections can lead to sepsis, renal dysfunction, and even life-threatening conditions.[6,7,37] Early and accurate identification of high-risk individuals for UTIs in patients with USD holds significant clinical value for guiding preventive measures, optimizing treatment strategies, and improving patient outcomes.[8,9] While urine culture remains the gold standard, it requires stringent operational standards and is time-consuming. The challenge remains how to quickly and accurately identify UTIs in patients with USD who often require prompt and aggressive antibiotic treatment.[12] Although recent advancements in sensitive and rapid technologies for predicting urine culture results, such as multiplex recombinase polymerase amplification,[51] plasmonic nanosensors,[52] and molecular diagnostics with microfluidic technologies,[53] show promise, these innovations are still in development and not yet ready for widespread clinical use.[12] Prediction models based on traditional clinical data offer a more immediate solution.[12] To our knowledge, this

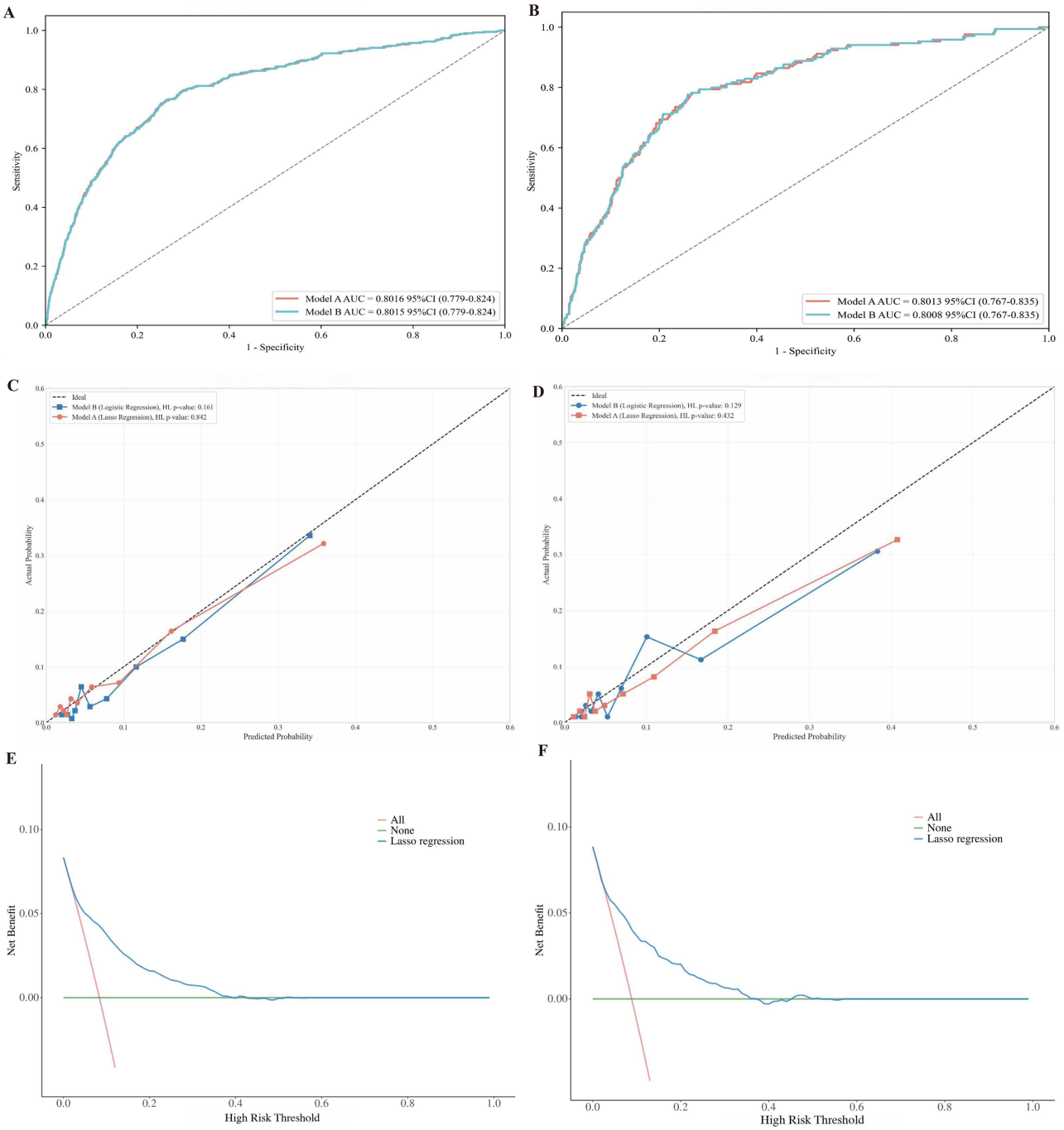

Figure 5 Assessment of the predictive performance of Model A and Model B.
Notes: (**A** and **B**) Receiver operating characteristic (ROC) curves for Model A and Model B in the training (**A**) and validation (**B**) sets. (**C** and **D**) Calibration curves for Model A and Model B in the training (**C**) and validation (**D**) sets. (**E** and **F**) Decision curve analysis (DCA) for Model A in the training (**E**) and validation (**F**) sets.

study is among the first to explore the potential of NPAR as a biomarker for predicting UTIs in patients with USD and to develop a web-based, bedside, user-friendly prediction tool.

NPAR was independently associated with UTI risk, and patients with NPAR > 1.21 had a markedly higher odds of UTI. Neutrophils, critical components of the innate immune system, increase in response to the acute inflammatory reaction to pathogens.[15] In contrast, albumin, a marker of nutritional status and liver function, typically decreases in conditions of impaired immune function.[21] Neutrophil count or albumin levels alone lack specificity in predicting infection risk due to various non-infectious factors.[18,26] By combining these two indicators, NPAR may mitigate some

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Table 5 Summary of AUC, Accuracy, Sensitivity, and Specificity of Different Models in the Validation Set

	Accuracy	Sensitivity (%)	Specificity (%)	Brier	AUC	95% CI
Model A	0.760	0.735	0.762	0.067	0.801	0.767–0.835
Model B	0.757	0.735	0.759	0.068	0.800	0.767–0.835

Notes: Model A = LASSO regression model; Model B = Logistic regression model; Brier = Brier score (measures the accuracy of probabilistic predictions, with lower values indicating better calibration); Sensitivity and Specificity are presented as percentages. All performance metrics were calculated using the validation dataset.
Abbreviations: AUC, Area Under the Curve; CI, Confidence Interval.

of these confounding factors, thereby enhancing predictive accuracy. Notably, significant sex differences were observed in the relationship between NPAR and UTIs risk. The risk increase in males (OR = 2.79) was significantly higher than in females (OR = 1.22), which may reflect sex-specific differences in immune responses.[54,55] This sex difference may be attributable to unmeasured confounders, such as prostatic hyperplasia or chronic prostatitis in older men, which were not available in this dataset.[56,57] These conditions may lead to urinary obstruction, require instrumentation, and are associated with more persistent infections, potentially eliciting a more pronounced systemic inflammatory response and a greater catabolic state, thereby resulting in a higher NPAR and strengthening its association with UTI diagnosis in this subgroup.[58,59]

Although several clinical prediction tools have been developed to assess UTIs risk in patients with USD, their universal applicability and immediate effectiveness in widespread clinical use remain challenging. For example, Shen et al[60] developed a nomogram achieving high discrimination (AUC 0.960), but its reliance on urine culture results limits its applicability in settings where rapid decision-making is required.

Machine learning approaches have also been extensively explored in this area, showing considerable promise. For instance, the machine learning prediction model developed by Wu et al,[43] which achieved an AUC of 0.772, demonstrated relatively low sensitivity (0.522), potentially leading to missed diagnoses in high-risk patients and delayed treatment. In other studies applying machine learning to predict UTIs risk in patients with USD, although some models exhibit high predictive performance, they often face challenges related to model complexity or data collection burdens. For example, He et al[12] constructed a GBDT model in a multicenter study with 2054 participants, achieving a slightly higher AUC than this study (0.831, 95% CI: 0.823–0.840). However, such complex models require extensive feature engineering and computational resources, and their reported MCC and F1 scores (0.460 and 0.588, respectively) suggest there is room for improvement in balancing precision and recall. On the other hand, Chen et al[61] reported excellent performance (AUC 0.951) using 15 variables, though the number of predictors may increase data collection burden in busy clinical environments. Furthermore, a common challenge in UTIs prediction studies using machine learning is the relatively small sample sizes for model training and rigorous external validation.[13] This limitation may affect the generalizability and clinical robustness of the models.[62]

Compared with these studies (which included 2054, 2565, and 462 participants, respectively), the present study had a larger sample size (n = 7000). Additionally, it integrates the novel inflammatory biomarker NPAR, which was validated through a series of sensitivity analyses, establishing its value as a key predictor of UTIs in patients with USD. Furthermore, a web-based, user-friendly prediction tool was developed based on the optimal model, which enables rapid UTI risk estimation using routinely available laboratory parameters. This prediction tool may have several potential applications in clinical practice. In emergency or admission settings, clinicians or triage nurses could input routine laboratory parameters to obtain an estimated UTI risk score. Previous studies suggest that similar point-of-care decision tools may help reduce assessment time and support emergency triage.[28] By incorporating the NPAR threshold (>1.21) and the observed sex-specific risk estimate (OR for males = 2.79), the tool might assist in prioritizing urine cultures, imaging studies, or initial antibiotic therapy for high-risk patients.[63] For hospitalized patients, serial NPAR and risk score calculations could offer a more objective basis for deciding whether to repeat urine cultures or to evaluate response to empirical therapy. This approach may contribute to more individualized infection management during hospitalization.[29]

However, this study has several limitations. First, as a single-center retrospective study, selection bias is a potential concern, and the model's external validation remains insufficient, particularly in terms of its applicability across diverse regions and populations. Second, data on the use of antimicrobial agents prior to admission was not systematically available, and thus its potential confounding effect could not be adjusted. Third, this study defined UTIs at the index hospitalization and did not distinguish between recurrent and nonrecurrent infections due to inconsistent data on prior UTI history. Fourth, while multiple confounding factors were adjusted for, residual confounding cannot be entirely excluded. Future studies should focus on externally validating this model through multicenter, prospective research, with rigorous collection of data on antimicrobial exposure and UTI history, and examine its practical impact on improving patient outcomes in clinical settings.

Conclusion

In conclusion, this study identifies the NPAR as an independent predictor of UTIs in patients with USD, with a markedly stronger association observed in males (OR=2.79) than in females (OR=1.22). The risk of UTIs increased sharply when NPAR exceeded 1.21, identifying a potential threshold for clinical monitoring. Leveraging this readily available biomarker, this study developed and validated a user-friendly, web-based tool that enables rapid, bedside risk stratification upon admission. This tool may serve as a potential resource to inform the prioritization of diagnostic workup and support early therapeutic decision-making in the management of USD. Future research should focus on the external validation of this model, prospective evaluation of its impact on clinical outcomes and workflows, and investigation into the biological mechanisms underlying the observed sex difference.

Overall, by quantifying the predictive value of NPAR and embedding it into an accessible clinical tool, this work provides a practical foundation for improving risk-stratified care and reducing infectious complications in patients with USD.

Data Sharing Statement

Prof. Liu had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Ethics Statement

The study adhered to the ethical principles outlined in the Declaration of Helsinki and received approval from the Ethics Committee of the Jiangmen Central hospital (approval number: [2025]199A). All participants were fully informed about the study's purpose, procedures, and their rights, including anonymity and confidentiality of responses, voluntary participation, and the right to withdraw at any time without penalty. Written informed consent was obtained from all participants prior to their involvement.

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Author Contributions

Each author made a significant contribution to the work reported, including the conception, study design, execution, data acquisition, analysis, and interpretation, or in all these areas. They participated in drafting, revising, or critically reviewing the manuscript, provided final approval of the version to be published, agreed on the journal to which the article was submitted, and take full responsibility for all aspects of the work.

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Disclosure

No conflict of interest has been declared by the authors.

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