

Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you **“NU Rounds”** which contains latest and interesting news in the field of Urology.

Inside This Issue:

- Progression of Disease after Bacillus Calmette-Guerin Therapy: Refining Patient Selection for Neoadjuvant Chemotherapy before Radical Cystectomy
- Efficacy and tolerability of the hexanic extract of Serenoa repens compared to tamsulosin in moderate-severe LUTS-BPH patients
- Development and validation of a preoperative nomogram for predicting patients with impacted ureteral stone: a retrospective analysis

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

Progression of Disease after Bacillus Calmette-Guerin Therapy: Refining Patient Selection for Neoadjuvant Chemotherapy before Radical Cystectomy

Introduction

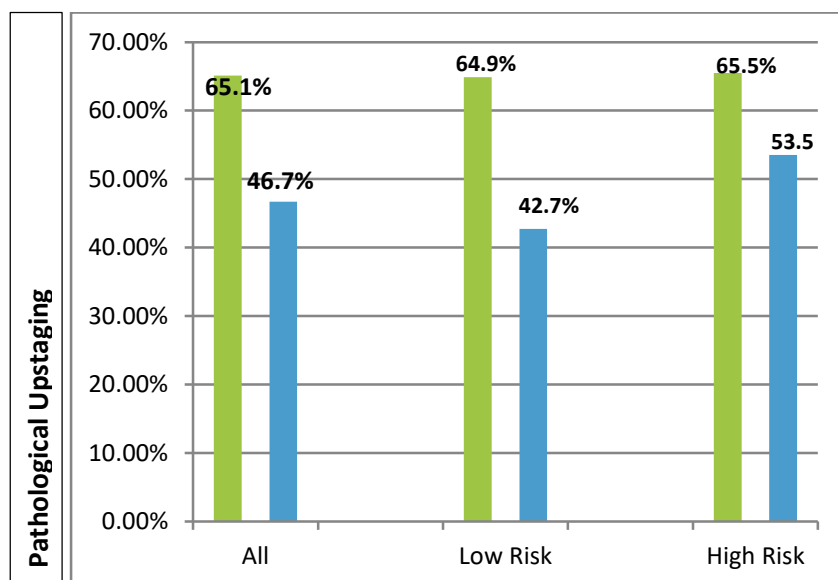
For all the subjects with muscle invasive bladder cancer (MIBC), while neoadjuvant chemotherapy (NAC) is recommended prior to cystectomy. Large proportion of subjects do not receive it for a various reasons. Bacillus Calmette-Guerin or BCG is the common intravesical immunotherapy for treating early-stage bladder cancer. Subjects who progress on bacillus Calmette-Guerin (BCG) to muscle-invasive bladder cancer (P-MIBC) exhibit worse outcomes compared to de novo muscle-invasive bladder cancer MIBC (D-MIBC). This data was suggested from the pre-neoadjuvant chemotherapy (NAC) era. Various efforts and trials are underway for appropriately selecting the subjects who benefit from neoadjuvant chemotherapy. The published criteria include: lymphovascular invasion, variant histology, hydronephrosis and cT3 + disease. This study evidence suggest that the subjects who progress to MIBC after bacillus Calmette-Guerin therapy for non-MIBC (P-MIBC) are at high risk compared to de novo MIBC (D-MIBC). Therefore, in clinical stage T2-3 P-MIBC subjects, this study assessed whether MIBC after bacillus Calmette-Guerin therapy should be included in risk-adapted approaches to NAC patient selection.

Aim: To investigate whether P-MIBC is an independent poor risk factor in the setting of contemporary NAC use.

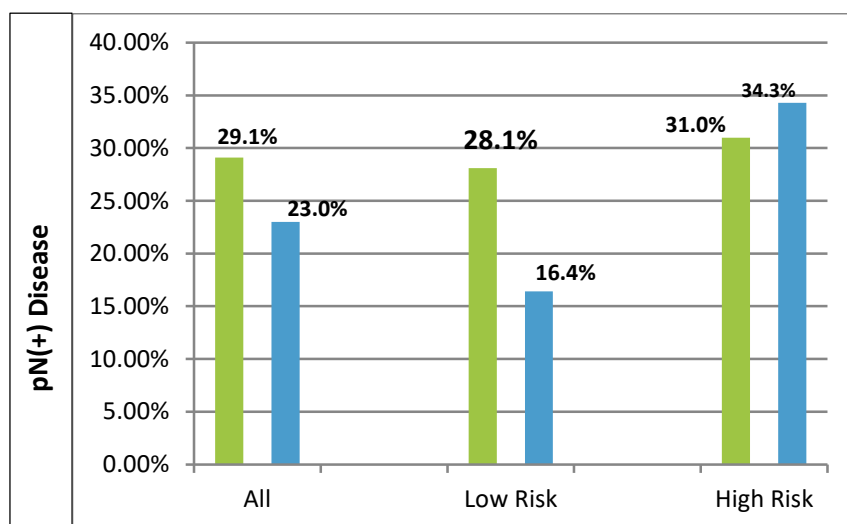
Methods: A review of patients who underwent radical cystectomy (RC) for cT2-3 MIBC was performed. Patients were stratified into high risk (lymphovascular invasion, variant histology, hydronephrosis, cT3b) vs low risk (no risk factors) and P-MIBC ($\leq$ pT1 treated with at least induction BCG who progressed to $\geq$ cT2) vs D-MIBC.

Results: Out of the 801 subjects who underwent radical cystectomy (RC) 163 (20.3%) had P-MIBC and 638 (79.7%) had D-MIBC; 77 (47.2%) P-MIBC patients and 368 (57.7%) D-MIBC patients were treated with a median 4 cycles of NAC. NAC regimen was cisplatin-based in 79.2% and 79.6% of P-MIBC and D-MIBC patients. Higher rates of variant histology, LVI,

hydronephrosis, palpable tumors on bimanual examination, and clinical stage T3 disease was observed in subjects who received NAC. P-MIBC status revealed poor survival outcomes to subjects who did not receive NAC compared to D-MIBC without NAC. However this did not remain a negative prognostic factor in the setting of NAC.

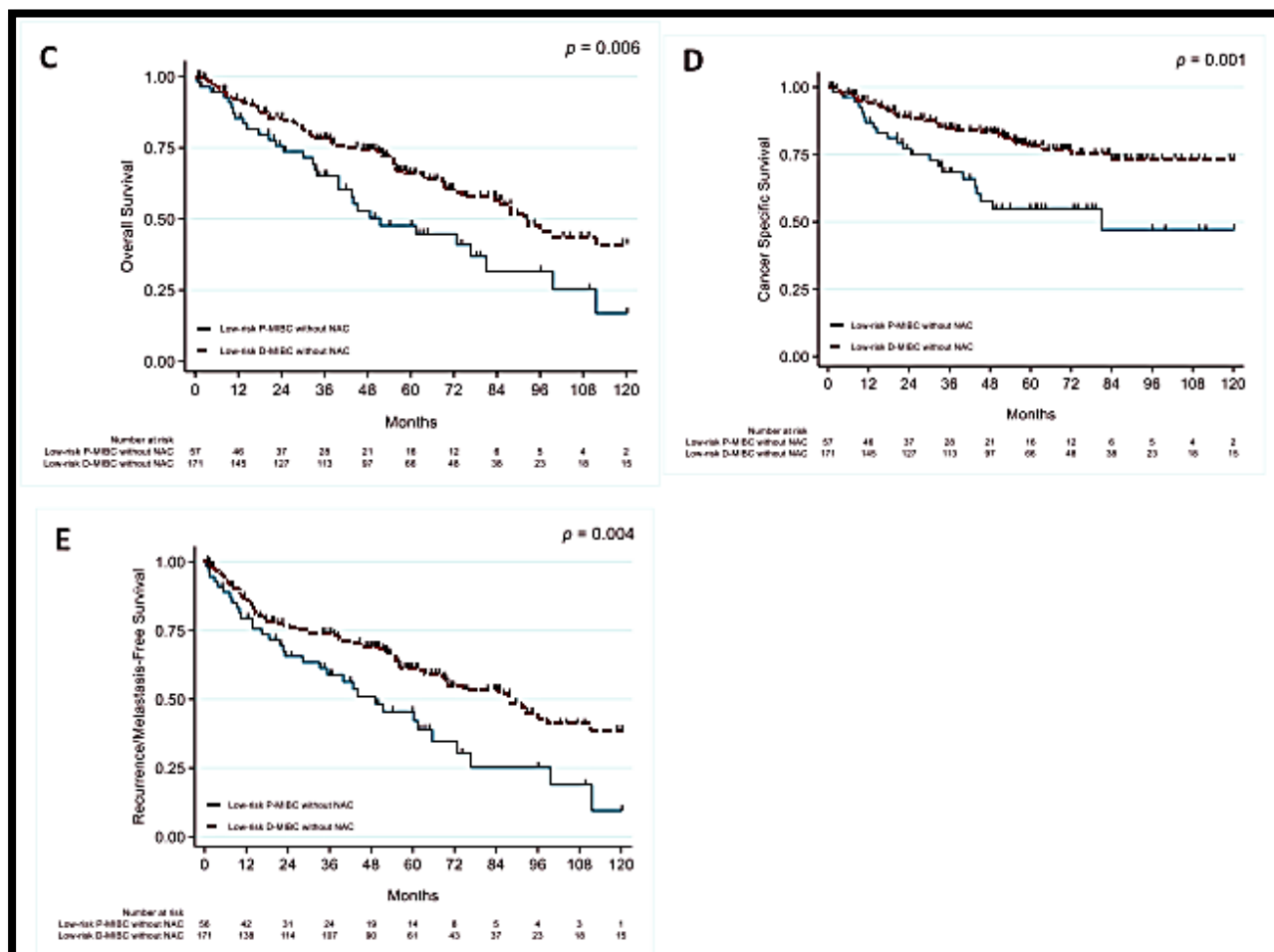


Pathological upstaging rates (A) and pathological nodal positive rates



(B) on final radical cystectomy (RaC) pathology.

Clinical outcomes in patients with P-MIBC and D-MIBC managed without NAC



Conclusion: When managed with radical cystectomy alone P-MIBC confers a poor prognosis. Treatment with Neoadjuvant chemotherapy (NAC) showed equivalent pathological response and survival outcomes compared to D-MIBC. These data suggest that a comparable window of cure exists in BCG progressive subjects with contemporary use of NAC and P-MIBC should be included in risk-stratified approaches to NAC selection.

Reference: Hensley PJ, et al. Progression of Disease after Bacillus Calmette-Guérin Therapy: Refining Patient Selection for Neoadjuvant Chemotherapy before Radical Cystectomy. J Urol. 2021 Nov;206(5):1258-1267.

*Efficacy and tolerability of the hexanic extract of *Serenoa repens* compared to tamsulosin in moderate-severe LUTS-BPH patients*

Introduction

Benign prostatic hyperplasia (BPH) is a common condition in aging men and a common cause of lower urinary tract symptoms (LUTS). Prevalence of the disease has been shown to increase with advancing age. Prevalence of BPH at autopsy is as high as 50% to 60% for males in their 60's, increasing to 80% to 90% of those over 70 years of age. According to the European Association of Urology (EAU) guidelines on the management of LUTS symptoms can be divided into three types, one is the storage, second is voiding and third post-micturition symptoms. Several clinical studies have showed that LUTS/BPH can have a significant impact on subjects quality of life (QoL). The hexanic extract of *Serenoa repens* (HESr) is a phytotherapeutic treatment for LUTS/BPH which has been shown to have anti-inflammatory, antiandrogenic, and antiproliferative effects.

Objective: To compare the changes in urinary symptoms and QoL in men with moderate to severe LUTS/BPH receiving tamsulosin or HESr as monotherapy using two different matching approaches to optimize comparability of the treatment groups. Treatment tolerability was also evaluated and compared.

Methods: Data for this analysis was from the QUALIPROST study to evaluate change in symptoms and quality of life in subjects with moderate to severe LUTS/BPH. This was a longitudinal, prospective, non-interventional design in which participants were followed up for a period of 6-months. Subjects were excluded if they had received a medical treatment for BPH in the 6 months prior to inclusion, received any drug with a known effect on BPH symptoms, any time in the 4 weeks prior to inclusion or if the subject had undergone surgery of the lower urinary tract. Subjects ≥ 40 years of age with a diagnosis of LUTS/BPH and an IPSS score of > 7 points who were receiving either tamsulosin 0.4 mg/day or HESr as monotherapy were included in this study. Change in LUTS evaluated by means of the International Prostate Symptom Score (IPSS) and impact on QoL assessed using the Benign Prostatic Hyperplasia

Impact Index (BII). Sociodemographic data was collected. Adverse effects associated with treatment were recorded at follow-up. Haynes-Sackett questionnaire was used to assess treatment compliance.

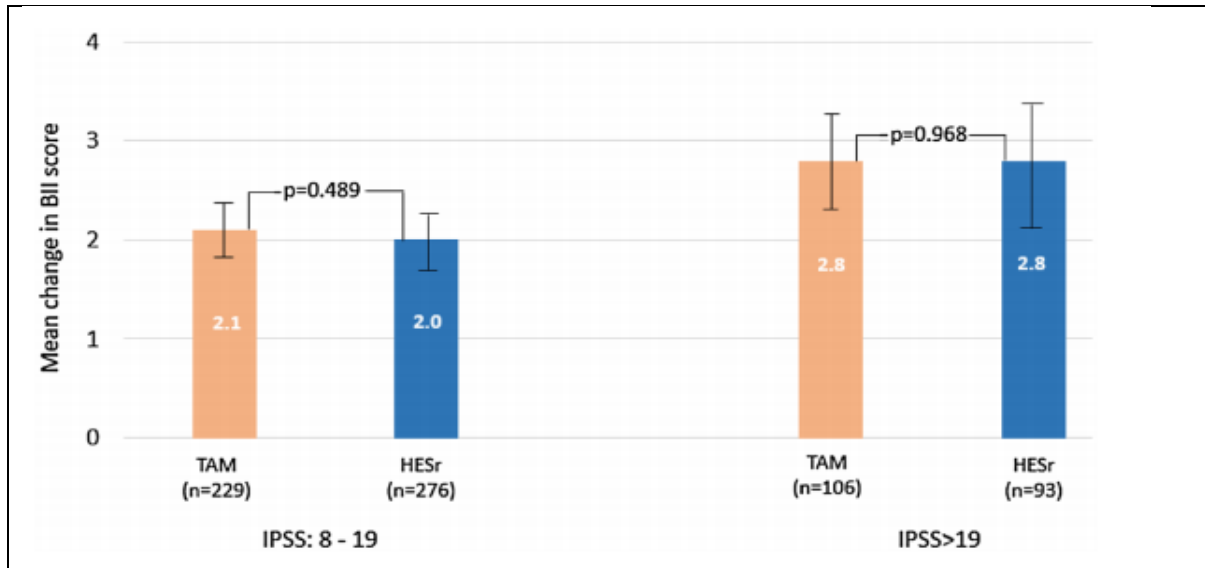
Results: After 6 months, International Prostate Symptom Score improved by a mean (SD) of 5.0 (4.3) points in the TAM group and 4.5 (4.7) points in the HESr group. Quality of Life was equivalent in both the groups. Adverse effects were seen more in Tamsulosin subjects than HESr patients (14.7% vs 2.1%), particularly ejaculation dysfunction and orthostatic hypotension. These results revealed that for the patients with moderate/severe LUTS/BPH, HESr is a valid option. Urinary symptoms improvement and QoL was similar to those observed for tamsulosin with fewer adverse effects.

	TAM		HESr		p value
	n	Mean (SD)	n	Mean (SD)	
IPSS total	335	5.0 (4.3)	369	4.5 (4.7)	0.117
IPSS voiding sub-score	335	2.9 (2.8)	369	2.5 (3.1)	0.051
IPSS storage sub-score	335	2.1 (2.1)	369	2.0 (2.3)	0.527
Nocturia	335	0.6 (0.9)	369	0.6 (1.0)	0.539
BII total	335	2.3 (2.4)	369	2.2 (2.5)	0.417
IPSS 8 (QoL)	335	1.3 (1.2)	369	1.1 (1.2)	0.129

Improvements from baseline to 6-month follow-up in symptoms and quality of life by treatment group (TAM: tamsulosin; HESr)

	TAM		HESr		p value
	n*	Mean (SD)	n*	Mean (SD)	
PSA total (ng/ml)	116	-0.2 (1.3)	128	-0.1 (0.8)	0.771
Qmax (ml/sec)	62	3.2 (3.4)	79	3.1 (3.6)	0.849
Prostate volume (cm ³)	61	-2.6 (9.3)	89	-2.7 (11.6)	0.961

Change from baseline to 6-month follow-up in PSA, Qmax and prostate volume for the study groups. (TAM: tamsulosin; HESr)



Mean improvement (95% CI) in mean BII total score by baseline symptom severity and treatment group, baseline to 6 months. (TAM: tamsulosin; HESr)

Conclusion: In the present analysis, the hexanic extract of *S. repens* appears to have similar efficacy to tamsulosin but with better tolerability which likely makes it a good first-line treatment choice for many patients.

Reference: Alcaraz A, et al. Efficacy and tolerability of the hexanic extract of *Serenoa repens* compared to tamsulosin in moderate-severe LUTS-BPH patients. *Sci Rep.* 2021 Sep 29;11(1):19401

Development and validation of a preoperative nomogram for predicting patients with impacted ureteral stone: a retrospective analysis

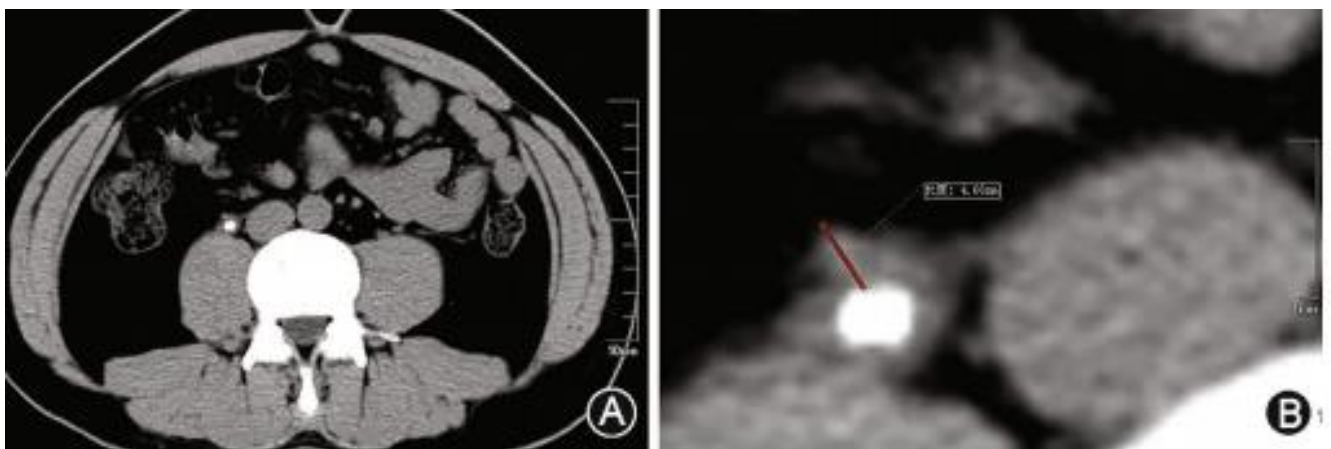
Introduction: Impacted ureteral stones are the stones that stay in the same location for a prolonged time and causing ureteral obstruction. In the clinical practice stone impaction is common and often lead to obstructive hydronephrosis. Intra-operative and postoperative complications are common with impacted stones because of the longer operation time and more complicated surgical procedures compared with non-impacted ones. Hence there is a need of developing a tool to predict stone impaction prior to surgery.

Objective: To develop and validate a practical nomogram for predicting the probability of subjects with impacted ureteral stone.

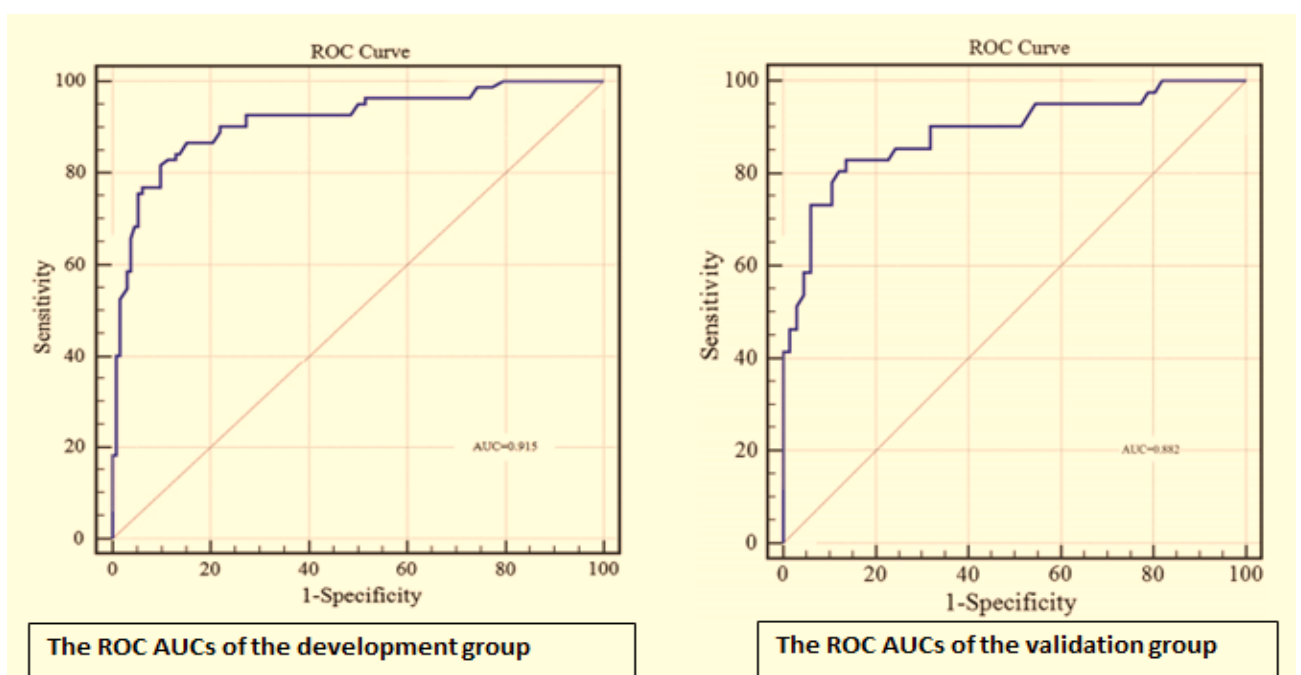
Methods: This was a retrospective study in which 214 single ureteral stones received ureteroscopy lithotripsy (URSL) were selected in development group and 82 single ureteral stones received URSL in validation group were included. By using univariate and multivariate logistic regression analysis independent factors for predicting impacted ureteral stone was screened. Medical records were reviewed to assess patients baseline characteristics, laboratory values and radiological investigations. Subjects were divided into 2 groups : Group1: impacted and Group2: Non impacted stones. Using an 8/9.5 F semi-rigid ureteroscope, a holmium laser lithotripsy system, and a pressure controlled irrigation pump all URSL procedures was performed in the lithotomy position after spinal or general anesthesia. Preoperative factors and stone impaction was modeled according to the regression coefficients. Area under the receiver operating characteristic (AUROC) curve and calibration curve was used to estimate discrimination and calibration.

Results: 296 subjects were included in the present study. The stone-free rate was 97.7% (non-impacted subjects) in development group and 89.0% (impacted subjects) stone-free rate in validation group was 98.0% (non-impacted patients) and 87.5% (impacted patients). In development and validation groups comparison of factors showed that there was no significant difference between subjects in both the groups. Independent predictors for impacted stone were age, ipsilateral stone treatment history, hydronephrosis and maximum ureteral wall

thickness at the portion of the stone. Area under the receiver operating characteristic (AUROC) curve of development was 0.915 and validation group was 0.882. Strong concordance between the predicted and actual probabilities was revealed by Calibration curve for both the groups. Predictive nomogram had a superior net benefit than maximum ureteral wall thickness (UWTmax) for all examined probabilities.



A) The ureteral calculus is demonstrated in axial section. B) UWT max is calculated by the imaging software. Maximal (8 ×) magnification is used to facilitate



Conclusion: This was the first attempt at developing a Nomogram to predict using preoperative parameters the possibility of impacted stones. This study concluded that through this prediction model urologists can select an optimal treatment method and decrease intraoperative and postoperative complications for the subjects with impacted ureteral calculus.

Reference: Wang C, Jin L, Zhao X, Xue B, Zheng M. Development and validation of a preoperative nomogram for predicting patients with impacted ureteral stone: a retrospective analysis. BMC Urol. 2021 Oct 8;21(1):140.



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