A simple predictive model with internal validation for assessment of stone-left after ureteroscopic lithotripsy in upper ureteral stones

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Background: Stone free rate in upper ureteral stones is not as high. We sought to identify easily accessible risk factors attributing to stones left in the ureteroscopy in the treatment of upper ureteral calculi, and to build a simple and reliable predictive model.

Methods: Patients treating only for upper ureteral stones in 2018 were retrospectively analyzed. Correlations between factors and the stone free rate were analyzed using bidirectional stepwise regression, curve fitting and binary logistic regression. Stone shape was judged by the gap between length and width in the two-dimensional section. A predictive nomogram model was built based on those selected variables ($P<0.05$). The area under the receiver operator characteristic curve (AUC) and calibration curve were used to access its discrimination and calibration. Decision curve analysis (DCA) was conducted to test the clinical usefulness.

Results: Totally, 275 patients with 284 stones were enrolled in this research. Bidirectional stepwise regression showed that stone length had a significant effect on stone free, instead of width or burden. Stone shapes were also found playing a big role. Curve fitting showed that quasi-circular stones had a high risk of retropulsion, and eventually led to stone left. Finally, stone length, shape, modality, and the distance of stones to the ureteropelvic junction were enrolled in the model. Among them, the distance of the stone to the ureteropelvic junction showed a noticeable impact on stone left. AUC was 0.803 (95% CI: 0.730–0.876), and the calibration curve showed good calibration of the model (concordance index, 0.792). DCA indicated the model added net benefit to patients.

Conclusions: The present predictive model based on those factors, stones length, shape, modality, and distance of the stone to the ureteropelvic junction was easy, reliable and useful.

Keywords: Ureteroscopy; stone free; nomogram; risk factors; ureteral calculi

Submitted Jan 19, 2022. Accepted for publication Apr 17, 2022.
doi: 10.21037/tau-22-22
View this article at: https://dx.doi.org/10.21037/tau-22-22

Introduction

Urolithiasis is a common disease around the world. Ureteroscopy has been as first line surgical option for ureteral stones for decades (1). It is more effective compared with shock wave lithotripsy (SWL), and less invasive than percutaneous nephrolithotomy (PCNL) or laparoscopic ureterolithotomy (2,3). However, the stone-free rate (SFR) in upper ureteral calculi has always been smaller than that in the middle or distal ureteral location (4).

Stone size, location, impaction, density, ureteral wall

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thickness, lithotripter devices, etc. are reported risk factors (5,6). However, there is no need to take all factors into consideration every time. Predictive models based on these factors are complicated. Moreover, lots of factors depend on digging into non-contrast-enhanced computed tomography (NCCT). Clinical application is limited. It is of great clinical significance to screen out those common clinical indicators leading to postoperative residual stones.

Therefore, in the present study we revealed four easily accessible factors leading to stone left in upper ureteral stones, investigated the weight of each factor, and built a simple but useful model. We then conducted an internal validation. We present the following article in accordance with the TRIPOD reporting checklist (available at https://tau.amegroups.com/article/view/10.21037/tau-22-22/rc).

Methods

Patients

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Review Board of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (No. TJ-IRB20191205) and individual consent for this retrospective analysis was waived. All patients underwent ureteroscopy in treating only upper ureteral stones in 2018 were enrolled. Patients with multiple stones on each side or whose surgery failed due to objective reasons like narrow ureter were excluded.

Definitions

Clinical data were recorded from medical records anonymously. Upper ureter extends from the ureteropelvic junction (UPJ) to the upper margin of the sacroiliac joint (or the lower margin of the fourth lumbar vertebra). Stone shape was determined in the two-dimensional section. Length was the maximum diameter of the stone in any measurable axis and width was its orthogonal maximum diameter. Quasi-circular shape was defined as the gap between stone length and width not over 2 mm. The rest was named oval. Figure S1 presented each profile roughly. Stone free was defined as no fragment present or fragment ≤4 mm judged by plain film of kidney-ureter-bladder (KUB) or NCCT image 1 month later. Surgery methods were judged by primary attempt. Stones parameters were judged from pre-treatment NCCT images. The judgements were finished by a radiologist and a urologist. Any disagreement was resolved by a consultation. Distance of stone to the UPJ was the measured vertical difference from the stone center to the UPJ which was determined at the narrowest part of the lower part of the renal pelvis in appearance. Retropulsion meant stone migrated up into the kidney out of design before disintegration. Stone duration meant the period between the first stone symptoms date and the day of surgery.

Surgery

All procedures were finished by professors or fellowship trained attending urologists under standard process.

Semirigid ureteroscopy

General anesthesia, lithotomy position, patients were placed a guide wire through the ureteroscope under aseptic conditions. The 9.8-F ureteroscope went along the wire to the stone. Pump irrigation pressure was as small as possible, usually 50–150 cmH_2O. Lumenis holmium: YAG laser with 550-µm fiber, settings of 1–1.5 J, 15–20 Hz were used to disintegrate the stones. A double J stent was placed, and removed 1 month later.

Semirigid ureteroscopy with anti-retropulsive device

Anti-retropulsive device N-trap was used to prevent stone migration (7). Large stone fragments were swept out from the ureter. Other steps were as described above.

Flexible ureteroscopy

Placement of the guide wire and the steps before it were the same. Ureteral access sheath was inserted, along the guide wire to the stone. Olympus digital flexible ureteroscope reached the stone through the sheath. Pump irrigation pressure was as small as possible, usually 50–200 cmH_2O. Lumenis holmium: YAG laser with 200-µm fiber, settings of 0.7–1.5 J, 20–40 Hz were used. The kidney was examined for fragment and retrieval basket was used to remove it. A double J stent was placed, and removed 1 month later.

Factors screening and model building

Based on clinical experience and hypothesis, several factors including stones length, width, burden, duration,

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Table 1 Patient and stone baseline characteristics

Characteristics	Stone free	Stone residual	P
Gender, n (%)			0.091
Male	168 (70.6)	21 (56.8)	
Female	70 (29.4)	16 (43.2)	
Age (years), mean ± SD	49.5±13.8	47.4±14.8	0.389
BMI (kg/m^2), mean ± SD	24.7±3.4	24.4±3.5	0.599
Stone duration (days), n (%)			0.725
7	43 (18.1)	8 (21.6)	
14	65 (27.3)	11 (29.7)	
30	64 (26.9)	11 (29.7)	
30+	66 (27.7)	7 (18.9)	
Stone laterality†, n (%)			0.210
Left	135 (57.0)	17 (45.9)	
Right	102 (43.0)	20 (54.1)	
Stone length (mm), mean ± SD	11.5±4.2	12.0±4.3	0.511
Stone width (mm), mean ± SD	7.3±2.4	7.7±2.2	0.346
Stone burden (mm^2), mean ± SD	71.5±45.8	78.2±43.4	0.403
Stone number	247	37	–
Stone density, mean ± SD	1,239.6±301.6	1,265.8±324.7	0.684
Hydronephrosis (I/II/III/IV)††, n	5/141/59/33	0/24/8/5	0.817
Surgery (URS/URSard/fURS), n	99/86/53	26/6/5	0.004
Stone to UPJ (mm)			0.016
≤30	55	14	
31–90	137	22	
>90	46	1	
Stone shape (quasi-circular/oval), n	76/153	18/17	0.039

†, one missing data; ††, none/mild/moderate/severe. BMI, body mass index; SD, standard deviation; URS, ureteroscopy; URSard, ureteroscopy with anti-retropulsive device; fURS, flexible ureteroscopy; UPJ, ureteropelvic junction.

shape, distance from UPJ, and hydronephrosis, surgical options, operators were selected. Multicollinearity test and bidirectional stepwise regression were used to identify the most appropriate factors. Curve fitting was used to identify the relationship between length and stones left. Further analysis about the relationship between shape and retropulsion was conducted. Then, a model was built based on binary logistic regression results. Finally, a nomogram was plotted.

Model checking and validation

Firstly, Hosmer-Lemeshow test was used to evaluate the goodness-of-fit of the model. Secondly, discrimination performance was assessed by the area under the receiver operator characteristic curve (ROC) calculation (AUC). Thirdly, calibration curve was plotted to evaluate the model calibration. Finally, decision curve analysis (DCA) was conducted to test the clinical usefulness.

Statistical analysis

All statistical analyses were performed by R software (v. 4.1.0) and SPSS (v. 26). All P values were two-tailed, and <0.05 was considered as statistically significant. Normality test was performed among all numerical data before Student's *t*-tests. Missing data were small and discarded.

Results

Totally, 275 patients with 284 stones matched our criteria. Patient baseline data shown in *Table 1* showed that patients between groups were comparable. Length, width, and burden did not pass multicollinearity test and length was selected by bidirectional stepwise regression. Length, shape, procedure, and stone from UPJ had an independent effect on SFR after adjustment for potential confounding factors, including hydronephrosis, operators in the multivariate regression model.

Analysis indicated that retropulsion rate and stone left differed a lot between stone shapes, presented in *Table 2*. When length was restricted to ≤1.5 cm (the largest diameter of quasi-circular stones), results showed that most of stone

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Table 2 Impact of stone shapes on retropulsion and stone left

Variables	Stone length ≤1.5 cm		Total†	
	Retropulsion (n=24)	Stone left (n=27)	Retropulsion (n=24)	Stone left (n=35)
Quasi-circular, n (%)	15 (14.9)	18 (19.1)	15 (14.9)	18 (19.1)
Oval, n (%)	9 (6.5)	9 (6.6)	9 (5.2)	17 (10.0)
OR	0.400	0.299	0.317	0.469
95% CI	0.168–0.955	0.128–0.699	0.133–0.753	0.229–0.962
P	0.034	0.004	0.007	0.036

†, two missing data. OR, odd ratio; CI, confidence interval.

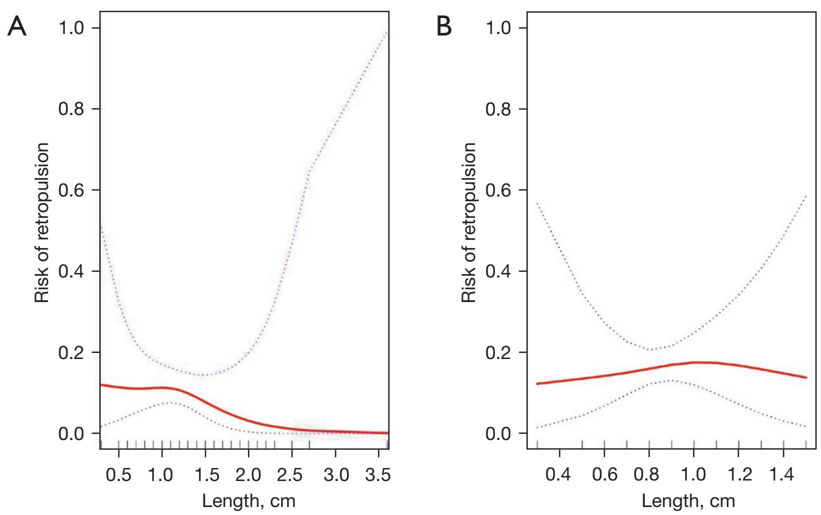

Figure 1 The relationship between stone length and the risk of retropulsion. (A) In all stones, a nonlinear relationship in all stones between length and retropulsion was observed after adjusting for operators and hydronephrosis. (B) In quasi-circular stones, a high incidence of retropulsion was observed after adjusting for operators and hydronephrosis.

left attributed to retropulsion. Curve fitting outcomes shown in *Figure 1* manifested that there were nonlinear relationships between stone length and retropulsion risk. The risk started to be stable, and turned to decrease with the stone length up. The cut-off was 1.4 cm. Further curve fitting showed that the risk of retropulsion in the shape of quasi-circular had been at a high incidence all the length.

Odds ratios (ORs) of each factor were shown in *Figure 2*. Stone locations demonstrated a noticeable impact on stone left. The nomogram was plotted in *Figure 3*. Hosmer-Lemeshow test showed that the model had a goodness of fit (χ^2=3.341, P=0.911), and the ROC curve yielded an AUC of 0.803 (95% CI: 0.730–0.876), showing a goodness of discrimination. The calibration curve showed good calibration of the nomogram model. The concordance index (C-index) of the curve was 0.792 (95% CI: 0.717–0.867, P=0.734). The nomogram might overestimate the probability of stone left when the threshold was over 30%. Moreover, the DCA curve suggested that using the nomogram model to predict the rate of stone left added net benefit to patients. The above results were placed in *Figure 4*.

Discussion

For upper ureteral stones, ureteroscopy is an often-used procedure. However, the SFR is not as high as that of other locations (4,6). Figuring out the risk factors attributed to the stone left shows a magnificent sense in improving SFR. However, the factors are so many. In this study, only four factors were screened out, while the model worked well

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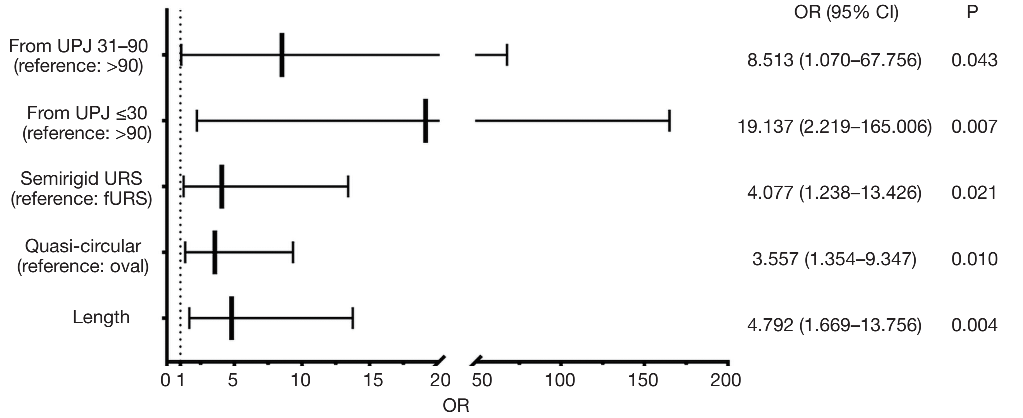

Figure 2 ORs of factors on residual stones in binary logistic regression. CI, confidence interval; UPJ, ureteropelvic junction. URS, ureteroscopy; fURS, flexible ureteroscopy; ORs, odds ratio.

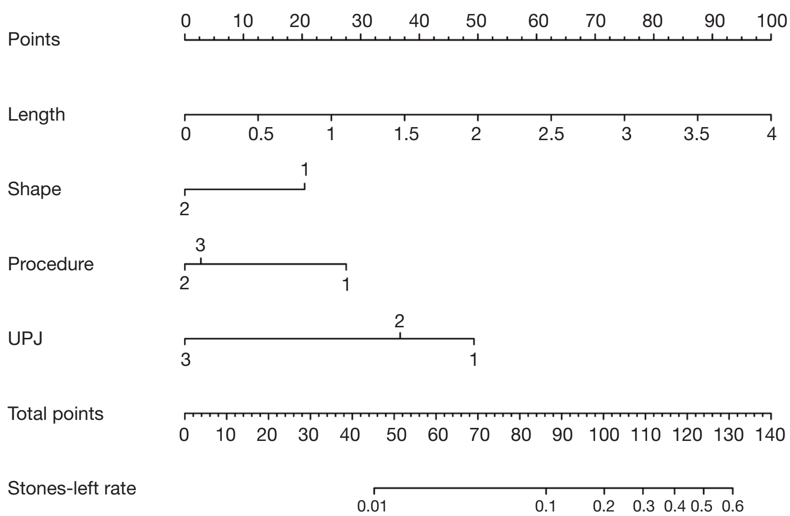

Figure 3 Nomogram model for predicting stone left based on length, shape, procedure, and distance from UPJ. Length, cm. Shape: 1, quasi-circular; 2, oval. Procedure: 1, semirigid ureteroscopy alone; 2, semirigid ureteroscopy with anti-retropulsive device; 3, flexible ureteroscopy. UPJ: 1, the distance of stone from UPJ ≤30 mm; 2, the distance of stone from UPJ 31–90 mm; 3, the distance of stone from UPJ >90 mm. UPJ, ureteropelvic junction.

in calibration and inspection. Urologists will use simple clinical data to evaluate the SFR in the model. When the SFR cannot be improved by adjusting the surgical method anyway, PCNL might be an alternative (2). Moreover, the model did not rely on NCCT results. All the four factors length, shape, procedure, stone to UPJ could be obtained from routine check. That is to say the model has a board range of use.

The effect of stone length on the SFR seemed reasonable. Many other similar models also incorporate the size factor (8). Zhang *et al.* found same effect among pediatric upper urinary calculi (9). It is worth noting that ureteroscopy extended to large stone does not mean that the ureteroscopy could ignore the size negative effect (10). Inversely, a study conducted by Goldberg *et al.* by collecting recent 15 years data about flexible ureteroscopy demonstrated that the stone size still had a significant effect on SFR and complication (11). Though the conclusion was drawn from renal stones.

To our knowledge, the effect of stone shape on SFR

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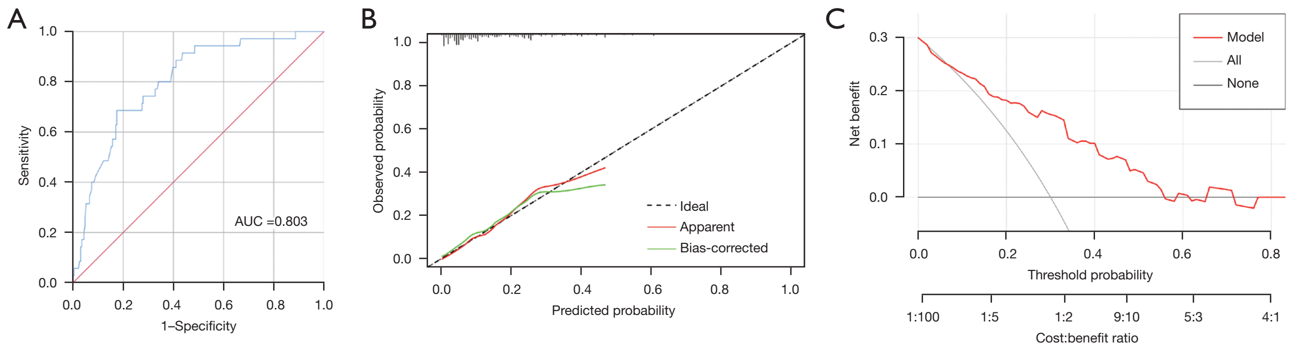

Figure 4 Calibration and inspection of the model. (A) The area under the receiver operator characteristic curve (AUC) of the model. (B) Calibration curve of the nomogram model. Internal validation was performed using 1,000 bootstrap resamples, mean absolute error =0.019, mean squared error =0.00088. (C) Decision curve analysis for the nomogram model. The red line represents the nomogram model. The gray line represents the hypothesis that all patients had residual stones. The black line represents the hypothesis that no patients had residual stone.

was firstly reported. The criteria for stone shape were a preliminary attempt. The difference greater than 2 mm was significant in appearance. We found that stone shape affected the SFR by influencing the risk of retropulsion (definition shown in Methods section). The shape of quasi-circular was found a high incidence of retropulsion, no matter the stone size. The reason for the vast difference between the two shapes was unknown. Probably, stone in quasi-circular shape blocked the ureter more thoroughly. A more increased inner pressure pushed the stone at the same level of irrigation. In addition, taking the length into consideration, the quasi-circular stones had a bigger stones volume. The larger the stone burden was, the lower the SFR was (8).

There were three ureteroscopic procedures in this study. Combined with anti-retropulsive device, the SFR of semirigid ureteroscopy raised a lot, which was consistent with prior studies (7). However, regarding to the retropulsion defined in this paper, the anti-retropulsive device could not provide any help. Because it had not been placed yet. For those small quasi-circular stones, which were suspected to have a higher incidence of retropulsion, flexible ureteroscopy is worthy of consideration. The ability of able to reach renal space accounted for the high SFR of flexible ureteroscopy.

The present study found that the location of the stone had a substantial influence on SFR. It was reasonably straightforward. The closer the stone to the kidney, the bigger the likelihood of stones or fragments left in the renal. Even though flexible ureteroscopy was able to reach the kidney, a paper reported that the debris and dust needed several months to clear (12).

Legemate *et al.* demonstrated the ureteroscopy for impacted ureteral stones led to a lower stone free rate (5). We do not deny it. However, impaction diagnosis is based on the judgment of the surgeon or NCCT (13). The information is difficult to obtain before surgery. The diagnosis method is complex with lots of subjectivity. Density is another risk factor. The criterion of the maximum Hounsfield unit is hard to reflect the overall situation. The convincing parameter is the three-dimensional mean stone density, however the diagnosis method is also complex (14). There were also many other prediction models. However, most of them were limited to one type of surgery, rigid or flexible ureteroscopy (15). Studies have demonstrated that the surgical methods can greatly affect the outcomes, four times of stone-left incidence of flexible ureteroscopy less than ureteroscopy in this paper. In addition, there were also lots of researches that includes all ureteral stones, which in our opinion was meaningless (16). Unless those rare stones, nearly all distal and middle ureteral stones can reach a high SFR under standard skilled procedures. Details were shown in Table S1.

The major limits of this research were that there were too many confounding factors but small samples. The procedures involved and the nature of the stones were quite different. Although we focused on upper ureteral stones, the sizes and locations of the stones still varied. In addition, subtle difference existed between different operators in standard ureteroscopy procedure, even though we adjusted

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confounding factors. Stone free was partly judged by KUB, which might misdiagnose. Moreover, NCCT and KUB had a difference in sensitivity of residual fragments. The information about the preoperative ureteral stent was unknown. Last but not least, stones are three-dimensional. It was undoubtable that there was a bias in the judgment of the shape.

Conclusions

Stones length, shape, modality, and distance of the stone to the UPJ were good prognostic factors. Among them, the distance of the stone to the UPJ showed a noticeable impact on stone left. The nomogram model based on those factors was easy, reliable and useful.

Acknowledgments

Thanks to all selfless online course sharers.
Funding: This work was supported by the National Natural Science Foundation (No. 82170780).

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-22-22/rc

Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-22-22/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-22-22/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Institutional Review Board of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (No. TJ-IRB20191205) and individual consent for this retrospective analysis was waived.

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Cite this article as: Wu W, Zhang J, Yi R, Li X, Wan W, Yu X. A simple predictive model with internal validation for assessment of stone-left after ureteroscopic lithotripsy in upper ureteral stones. Transl Androl Urol 2022;11(6):786-793. doi: 10.21037/tau-22-22

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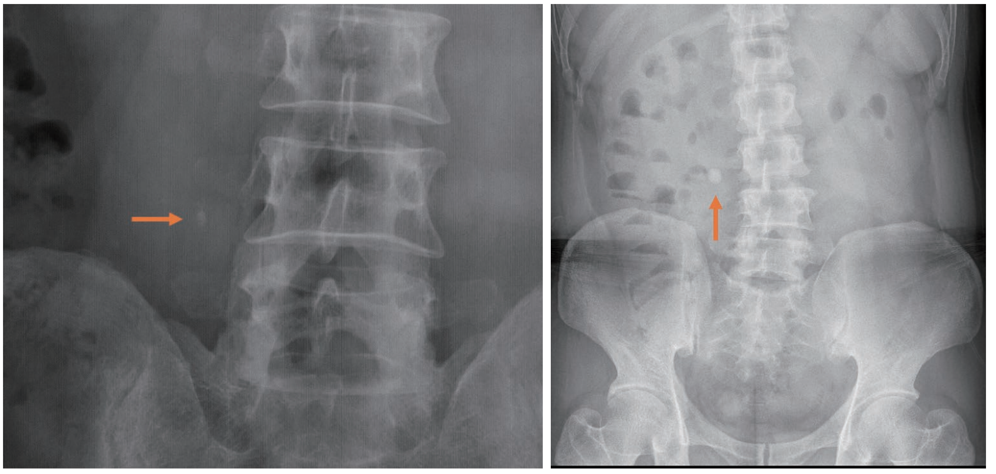

Figure S1 Profile of the two stone shapes. Oval (horizontal arrow) and quasi-circular stone (vertical arrow).

Table S1 Comparisons between the model with others

Item	Case	Center	Object	Surgery	Predictors	AUC	Validation
This model	275	Single	Upper ureteral	URS, URSard, fURS	Length, location, shape, surgery	0.803	Internal
Imamura Y *et al.*	412	Single	All ureteral	URS	Length, number, location, pyuria	0.743	Internal
Zhang Y *et al.*	348	Single	All ureteral, renal	fURS, miniPCN, microPCN	Surgery, location, irrigation, operation duration, stone mass	0.810	Internal
Hori S *et al.*	586	Single	All ureteral, renal	fURS	Length, Hounsfield unit, location	0.845	Internal
De Nunzio C *et al.*	356	Double	All ureteral	URS	Number, size, distal ureteral location, hydronephrosis	0.750	Internal

URS, ureteroscopy; URSard, ureteroscopy with anti-retropulsive device; fURS, flexible ureteroscopy; miniPCN, mini-percutaneous nephrolithotomy; microPCN, micro-percutaneous nephrolithotomy; AUC, area under the receiver operator characteristic curve.

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