Evaluation of Nephrolithometric Scoring Systems to Predict Outcomes of Retrograde Intrarenal Surgery

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Purpose: The aim of the study was to evaluate the predictive value of nephrolithometric scoring systems used to predict the complexity of renal stones for the outcomes of retrograde intrarenal surgery (RIRS).

Materials and Methods: A total of 81 patients who underwent RIRS for nephrolithiasis between January 2013 and October 2017 were reviewed in this retrospective study. Guy's Stone Score (GSS), the S.T.O.N.E., Clinical Research Office of the Endourologic Society (CROES), and Seoul National University Renal Stone Complexity (S-ReSC) nephrolithometry scores were assessed by same researcher for each patient from preoperative non-contrast enhanced computed tomography scans. These nephrolithometric scores, stone characteristics and complications were compared in patients with/without residual stone.

Results: The median (IQR) age of patients (37 female/44 male) was 45 (20) years. The median (IQR) stone burden was 139.4 (125.4) mm² and the mean Hounsfield unit (HU) value was 1034.46 \pm 239.56. The stone burden, S.T.O.N.E. and S-ReSC scores were statistically significantly higher and the CROES score was significantly lower in patients with a residual stone (p < 0.001, for all). The incidence of residual stones was statistically significantly higher in patients with Grade 3 GSS (p = 0.018). While S.T.O.N.E., S-ReSC and CROES were significantly correlated with stone-free rates, GSS failed to correlate with stone-free status. According to the receiver operating characteristic (ROC) curve analysis, the predictive value of stone burden was higher for residual stones, compared to S-ReSC scoring (p < 0.05).

Conclusion: Nephrolithometric scoring systems nomograms used to predict the PCNL success were not superior to stone burden in predicting the RIRS success.

Keywords: percutaneous nephrolithotomy; kidney stone; nephrolithiasis; retrograde intrarenal surgery; flexible ureteroscopy

INTRODUCTION

Urinary system stone disease is the third most common disorder following urinary tract infections and prostate diseases in urological complaints. Its incidence varies between 2 and 20% with a lifelong risk of

12% in men and 6% in women.⁽¹⁾ With the technological advances in the field of medicine, urinary system stone disease can be treated using non-invasive or minimally invasive methods. According to the European Association of Urology (EAU) guidelines, extracorporeal shock wave lithotripsy (SWL), ureteroscopic lithotripsy (URS-L), retrograde intrarenal surgery (RIRS), and percutaneous nephrolithotomy (PCNL) are the first-line treatment methods for the removal of kidney stones with varying sizes and localization.⁽²⁾ The EUA guidelines state that stones smaller than 2 cm can be effectively treated using RIRS, although there are several studies reporting favorable results for stones larger than 2 cm, as well.^(3,4) Over the past few decades, RIRS has become widespread thanks to sophisticated flexible ureterorenoscopes and other instruments and increased experience.

Currently, RIRS is an alternative to SWL and PCNL with high stone-free status and low morbidity rates in the treatment of urinary system stone disease.⁽⁵⁾ In addition, RIRS has been shown to be a safe method with minimal complication rates.^(6,7)

The stone-free rate is the most significant factor of successful nephrolithotomy. To date, several scoring systems have been developed to predict the success of PCNL and to minimize procedure-related complications including Guy's Stone Score (GSS), the S.T.O.N.E. nephrolithometry score, Clinical Research Office of the Endourologic Society (CROES) nephrolithometric nomogram, and Seoul National University Renal Stone Complexity (S-ReSC) score.⁽⁸⁻¹¹⁾

The Resorlu-Unsal Stone Score (RUUS) is the first scoring system described in the literature for predicting the stone-free rate after RIRS.⁽¹²⁾ Moreover, the S-ReSC scoring system has been modified for predicting RIRS success.⁽¹³⁾ In this context, the Xiao et al. developed the R.I.R.S. scoring system to estimate the stone-free rate after RIRS.⁽¹⁴⁾ However, these scoring systems has not been externally validated.

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Variable		n (%)
Age (year)	Median (IQR)	45 (20)
Sex	Female	37 (45.7)
	Male	44 (54.3)
Stone features and scoring systems		
Side	Right	48 (59.3)
	Left	33 (40.7)
Stone localizations	Upper pole	7 (8.6)
	Middle pole	5 (6.2)
	Lower pole	10 (12.3)
	Renal pelvis	17 (21.0)
	Kidney + proximal ureter	20 (24.7)
	Multiple calyces	22 (27.2)
Stone burden (mm ²)	Median (IQR)	139.4 (125.4)
Hounsfield unit	Mean \pm SD	1034.46 ± 239.56
Residual stone	Yes	21 (25.9)
	No	60 (74.1)
GSS	Grade 1	42 (51.9)
	Grade 2	36 (44.4)
	Grade 3	3 (3.7)
S.T.O.N.E. score	Mean±SD	6.48 ± 1.00
S-ReSC score	Median (IQR)	1(1)
S-ReSC risk group	Low	73 (90.1)
	Middle	7 (8.6)
	High	1 (1.2)
CROES score	Mean ± SD	194.64 ± 49.71
CROES probability of stone-free status (%)	Mean \pm SD	82.23 ± 10.38
Complication	No	78 (96.3)
-	Pyelonephritis	2 (2.5)
	DJS migration to bladder	1 (1.2)

Table 1. Demographic characteristics of patients, baseline stone status, and scores of scoring systems.

Abbreviations: Min, minimum; Max, maximum; SD, standard deviation; GSS, Guy's Stone Score; S.T.O.N.E. stone size (S), tract length (T), obstruction (O), number of involved calices (N), and essence or stone density (E); CROES, Clinical Research Office of the Endourologic Society; S-ReSC, Seoul National University Renal Stone Complexity; DJS, double J stent.

To the best of our knowledge, there is no study or headto-head comparison evaluating the predictive value of common nephrolithometric scoring systems for RIRS success. In the present study, therefore, we aimed to evaluate the predictive value of nephrolithometric scoring systems which are commonly used in PCNL for RIRS success.

PATIENTS AND METHODS

Study Population

In this retrospective study, a total of 102 patients who underwent RIRS for kidney stones between January 2013 and October 2017 were analyzed. All steps of the study were planned and performed according to the World Medical Association Declaration of Helsinki. All patients signed the informed consent demonstrating the permission of the patients to usage of their clinical data in future clinical studies.

Patients with urinary system anomalies and bleeding diatheses, need for anticoagulants, pregnant patients and patients under 18 years old were excluded from the study. Twenty-one patients whose preoperative computed tomography (CT) scans were not available were excluded. Finally, a total of 81 patients were included in the study.

Preoperative Evaluation and Calculation of Scoring Systems

When the preoperative urine culture of the patients was positive, the patients were treated preoperatively with appropriate antibiotic on the basis of antimicrobial susceptibility test for no less than 7 days. The patients whose control urine cultures were found to be sterile were scheduled for RIRS. Data including preoperative routine biochemistry analysis, complete blood count, coagulation tests, urine culture, and non-contrast CT scans were retrospectively analyzed. Non-contrast CT scans were reviewed by the same researcher who was blind to the patients' characteristics. He analyzed the stone volume, Hounsfield units (HU), and location of the stones. In case of multiple stones, total stone volume was the sum of each stone volume. The mean HU value was calculated from non-contrast enhanced CT scans showing maximum axial diameter of the stone on bone window using maximum diameter in the elliptic plane.⁽¹⁵⁾ The GSS, S.T.O.N.E. nephrolithometry score, CROES nephrolithometric nomogram, and S-ReSC scores were also calculated using preoperative non-contrast CT scans described by their authors.

Surgical Procedure

All patients received prophylactic single-dose intravenous antibiotherapy (cefazolin sodium 1 g) preoperatively. Surgery was performed under general anesthesia. The patient was placed in the semi-lithotomy position on the operating table with a fluoroscope depending on the affected side. The operation was initiated in a standard fashion using semi-rigid ureteroscopy (URS) and a 0.038-inch polytetrafluoroethylene-coated guidewire was advanced through the upper urinary system under the visual and fluoroscopic guidance. A ureteral access sheath compatible with the ureter diameter was placed over the guidewire (10/12-Fr or 12/14-Fr, Re-trace Ureteral Access Sheath, Coloplast, Humlebaek, Denmark). The 7.5-Fr flexible URS device (Karl Storz Endoskope, FLEX-X2, Tuttlingen, Germany) was used in all patients. During lithotomy, holmium-yttrium aluminum

		Residual Stone		p-value
		No (n,%=60, 74.1%)	Yes (n,%=21, 25.9%)	
Stone burden (mm ²)	Median (IQR)	97.02 (104.77)	266.35 (232.41)	°0.001**
Hounsfield units	Mean \pm SD	1013.58 ± 229.28	1094.10 ± 263.51	°0.099
GSS (n,%)	Grade 1	34 (56.7)	8 (38.1)	^d 0.018*
	Grade 2	26 (43.3)	10 (47.6)	
	Grade 3	0 (0)	3 (14.3)	
S.T.O.N.E. score	Mean \pm SD	6.17 ± 0.83	7.38 ± 0.92	°0.001**
S-ReSC score	Median (IQR)	1(1)	2(2)	°0.004**
S-ReSC risk group (n,%)	Low	58 (96.7)	15 (71.4)	°0.003**
	Middle/High	2 (3.3)	6 (28.6)	
CROES score	Mean ± SD	207.13 ± 43.76	158.95 ± 49.30	°0.001**
CROES probability of stone-free status (%)	Median (IOR)	90 (9)	72 (22)	°0.001**

Table 2. Relationship of stone types and scoring systems with residual stones.

^cMann-Whitney U Test, ^dFisher-Freeman-Halton Exact Test, ^eFisher's Exact Test. *p < 0.05, **p < 0.01

Abbreviations: Min, minimum; Max, maximum; SD, standard deviation; GSS, Guy's Stone Score; S.T.O.N.E. stone size (S), tract length (T), obstruction (O), number of involved calices (N), and essence or stone density (E); CROES, Clinical Research Office of the Endourologic Society; S-ReSC, Seoul National University Renal Stone Complexity.

garnet (YAG) laser using 270 μ m or 365 μ m fiber at an energy of 0.6 to 0.8 Joule and frequency of 8-10 Hertz was applied. Pieces of stones were removed using stone basket, if applicable. Surgery was terminated, once the absence of opacity was confirmed through fluoroscopy. A 4.8-Fr double-J stent was inserted in all patients at the end of surgery.

Postoperative Period

On the next day of surgery, all patients underwent ultrasonography (USG) and kidney- ureter- bladder graphy (KUB). Double J-stent was retrieved under local anesthesia one month after surgery in all patients.

The stone-free status was defined as no evidence of opacity on KUB or stones or the presence of clinically insignificant residual fragment stones <4 mm on CT.⁽¹⁶⁾ The treatment success was evaluated using KUB at one month postoperatively. The presence of hydronephrosis was assessed using non-contrast enhanced CT, if KUB showed no opacity but hydronephrosis in USG.

Statistical Analysis

Statistical analysis was performed using the Number Cruncher Statistical System (NCSS) 2007 statistics software (NCSS, LLC, Kaysville, UT, USA). The Kolmogorov-Smirnov test was used to analyze the normality of the distribution of variables. The Student's t-test was used to compare normally distributed quantitative data, while the Mann-Whitney U test was used to compare non-normally distributed quantitative data between the groups. The Pearson chi-square test, Fisher-Freeman-Halton exact test, and Fisher's exact test were used to compare qualitative data between the groups. The Spearman correlation analysis was performed to evaluate relationships between the variables. The receiver operating characteristic (ROC) curve analysis was conducted to estimate optimal cut-off values including sensitivity, specificity, positive predictive value, and negative predictive value. The ROC curve analysis was used to predict the presence of residual stones and the results were compared using binomial exact test. Chi-square test was performed to evaluate the consistency between the presence of residual stones and stone-free status according to the CROES. A *p* value of <0.05 was considered statistically significant.

RESULTS

Of the patients, 37 were females and 44 were males with a median (IQR) age of 45 (20) years. Right-sided operation was performed in 48 patients (59.3%) and left-sided operation in 33 patients (40.7%). The median (IQR) stone burden was 139.4 (125.4) mm² and the mean Hounsfield unit (HU) value was 1034.46 \pm 239.56. Demographic characteristics of the patients, baseline stone status, and scores of the scoring systems are shown in **Table 1**.

The incidence of residual stones was statistically significantly higher in the patients with increased stone burden (P < 0.05). However, there was no significant relationship between the presence of residual stones and HU (P > 0.05) (**Table 2**). The incidence of residual stones was statistically significantly higher in patients with grade 3 GSS (P < 0.05). The stone burden, S.T.O.N.E. and S-ReSC scores were statistically significantly higher and the CROES score was significantly

Table 3. Diagnostic screening tests and ROC curve analysis for stone burden, S.T.O.N.E., S-ReSC, and CROES scoring systems.

	Cut-off	Sensitivity	Diagnostic S Specificity	Screening Positive Predictive Value	Negative predictive valu	ROC Curve e		^a p
								0.00444
Stone burden (mm ²)	≥166.2	80.95	71.67	50.00	91.49	0.866	0.783-0.949	0.001**
S.T.O.N.E. score	≥ 7	95.24	70.00	52.63	97.67	0.837	0.737-0.937	0.001**
S-ReSC score	≥ 2	61.90	68.33	40.63	83.67	0.687	0.544-0.829	0.011*
CROES score	≤ 191	76.19	70.00	47.06	89.36	0.767	0.640-0.894	0.001**

^aComparisons of cut-off values of each nomograms and stone-burden separately, *p < 0.05, **p < 0.01

Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; S.T.O.N.E. stone size (S), tract length (T), obstruction (O), number of involved calices (N), and essence or stone density (E); CROES, Clinical Research Office of the Endourologic Society; S-ReSC, Seoul National University Renal Stone Complexity.

Table	4.	Pairwise	comparisons	of AUC	of I	ROC	curve	and	stone
			bu	rden.					

	Pairwise Comparison of AUC		
	AUC	р	
Stone burden - S.T.O.N.E.	0.866 - 0.837	0.594	
Stone burden - S-ReSC	0.866 - 0.687	0.008**	
Stone burden - CROES	0.866 - 0.767	0.099	
S.T.O.N.E S-ReSC	0.837 - 0.687	0.057	
S.T.O.N.E CROES	0.837 - 0.767	0.335	
S-ReSC - CROES	0.687 - 0.767	0.117	

Binomial Exact test. **p < 0.01

Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve; S.T.O.N.E. stone size (S), tract length (T), obstruction (O), number of involved calices (N), and essence or stone density (E); CROES, Clinical Research Office of the Endourologic Society; S-ReSC, Seoul National University Renal Stone Complexity.

lower in patients with a residual stone (P < 0.05, for all). The incidence of residual stones was also statistically significantly higher in patients with an intermediate/high S-ReSC risk and a low CROES stone-free rate (P < 0.05, for both) (**Table 2**).

No residual stone was observed in 60 patients (74.1%) with \geq 90% stone-free rate according to the CROES, while 21 patients (25.9%) with <90% stone-free rate had residual stones. According to the CROES stone-free rate estimation. 31 patients were at no risk for residual stone development with \geq 90% probability and no residual stone was observed in 28 of these patients while residual stone was present in three patients. According to the CROES stone-free rate estimation, 50 patients were at risk for residual stone development with < 90%probability; however, residual stones were observed in only 18 patients, while no residual stone was observed in 32 of these patients. These findings revealed no statistically significant consistency between the actual residual stone rate and CROES stone-free rate (P < 0.05). Stone burden and S.T.O.N.E., S-ReSC and CROES scoring systems according to the ROC curve analysis are presented in Figure 1. A cut-off value of \geq 166.2 mm² was calculated for the stone burden according to the presence of residual stones. The odds ratio (OR) for residual stones was 10.75 (95% CI 3.15 to 36.61) in patients with a stone burden of \geq 166.2 mm² (**Table 3**). A cut-off value of \geq 7 was calculated for the S.T.O.N.E. scoring system according to the presence of residual stones. The OR for residual stones was 46.66 (95% CI 5.81 to 374.62) in patients with \geq 7 S.T.O.N.È. scores (**Table 3**). A cut-off value of \geq 2 was calculated for the S-ReSC scoring system according to the presence of residual stones. The OR for residual stones was 3.50 (95% CI 1.24 to 9.87) in patients with \geq 2 S-ReSC scores (Table 3). A cut-off value of \leq 191 was calculated for the CROES scoring system according to the presence of residual stones. The OR for residual stones was 7.46 (95% CI 2.374 to 23.486) in patients with \leq 191 CROES scores (Table 3).

The ROC curve analysis revealed that the predictive value of stone burden was higher for residual stones, compared to S-ReSC scoring (P < 0.05). There was no statistically significant difference between the other variables (P > 0.05) (**Table 4**).



Figure 1. ROC curve analysis of stone burden and nomograms according to residual stone.

DISCUSSION

In our study, we found a statistically significant relationship between the scoring systems used to predict the PCNL success and stone-free status following RIRS. However, ROC curve analysis revealed that these nomograms were not superior to stone burden in predicting the RIRS success and that even the predictive value of S-ReSC was lower than stone burden for the postoperative stone-free status.

In the present study, we evaluated the predictive value of percutaneous nephrolithotomy scoring systems which are commonly used in PCNL for RIRS success. The PCNL is the gold standard treatment for complex kidney stones and stones larger than 2 cm; however, it is associated with certain minor and major complications including intra- or postoperative urinary extravasation, bleeding requiring transfusion, postoperative fever, sepsis, or colon or pleural injury.^(17,18) The addition of new ports to the new-generation flexible URS devices with thinner device size and sophisticated optical systems allows clearer visualization and RIRS, therefore, has become an alternative to PCNL for the treatment of kidney stones larger than 2 cm.⁽¹⁹⁾ On the other hand, compared to PCNL, the main disadvantage of RIRS is the requirement for a additional sessions.

In recent years, predicting stone-free rate and possible complications before surgery has generated great interest in endourology and several nomograms have been developed to predict the success rate of SWL, URS, PCNL, and RIRS.^(8-14,20,21) The GSS which is a simple and reliable tool for predicting success rate considers location of the stone and renal anatomy. Higher scores indicate low stone-free rates. The stone-free rate is also independent on the stone burden, experience of the surgeon, age, body weight and comorbidities of the patient.⁽⁸⁾ In a review including PCNL scoring systems, the stone-free rate ranged from 0 to 100% for GSS.⁽²²⁾In our study, the incidence of residual stones was higher in patients with Grade 3 GSS. However, we believe that GSS is not useful to predict the success rates following RIRS. Using the GSS, it is likely to classify a stone as grade 1 in the lower pole and as grade 2 in the upper pole of the kidney. During RIRS, it is more difficult to reach the stone localized in the lower pole using a flexible URS due to the deflection angle. În addition, RIRS is not a feasible alternative for Grade 4 staghorn stones.

The significant relationship found in our study can be attributed to the small sample size with Grade 3 GSS. The S.T.O.N.E. nephrolithometry score, which is a simple tool for predicting the success rate of PCNL, considers stone size (S), tract length (T), obstruction (O), number of involved calices (N), and essence or stone density (E).⁽¹¹⁾ The scores vary from 5 to 13 and lower scores indicate less complex stone, while higher scores indicate more complex scenario. In the present study, we found a statistically significant relationship between the S.T.O.N.E. scores and stone-free status. However, we observed no significant relationship between the HU, one of the parameters used in this scoring system, and stone-free status. In addition, tract length is not a helpful measure to predict the success rate of RIRS. Nonetheless, the area under the ROC curve for the S.T.O.N.E. scoring system in terms of the stone burden was the closest compared to the area under the ROC curve for other scoring systems. Thus, this finding suggests that the S.T.O.N.E. scoring system is superior to the other scoring systems in predicting stone-free status following RIRS and that modified version of the system can be used for this purpose.

The CROES nephrolithometric nomogram in predicting PCNL outcomes is an also reliable tool which incorporates several variables such as stone burden, location of the stone, the presence of staghorn stones, previous surgery due to urolithiasis, and case volume per year of the center. Higher scores indicate higher stone-free rates.⁽⁹⁾ In our study, we considered that all these variables were helpful in predicting RIRS outcomes and found statistically significantly lower CROES scores in patients with residual stones. However, we found no statistically significant consistency between the actual residual stone rate and CROES stone-free rate. This can be attributed to the fact that our sample size is small and that scoring based on the location of the stone using CROES system is not feasible for RIRS.

The S-ReSC scoring system, which is also useful in predicting the post-PCNL stone-free rate, is solely based on stone distribution as assessed by the cumulative number of calyces involved.⁽¹⁰⁾ It is a 9-point system with 1 point assigned to 9specific locations. A score of 1 to 2 is considered low, 3 to 4 is medium, and \geq 5 is high. In a study involving 327 patients undergoing PCNL, the stone-free rate was found to be 65.4%, indicating that the S-ReSC scoring system is useful in predicting the post-PCNL outcomes.⁽²³⁾ In our study, the incidence of residual stones was also statistically significantly higher in patients with an intermediate/high or high S-ReSC risk compared to low-risk patients. However, the ROC curve analysis revealed that the S-ReSC is the least sensitive scoring system in predicting stonefree status, compared to other nomograms. This can be explained by the fact that the S-ReSC nomogram considers equal scoring for all calyces and lacks higher scores for hard-to-reach calyces in the lower pole during RIRS.

Nonetheless, this study has some limitations, which have to be pointed out. First, it was a retrospective study with a relatively small sample size and the inherent retrospective and non-randomized nature might have led to selection bias. Second, non-contrast CT scan was not used in all patients to detect the clinically insignificant residual stones and to evaluate the outcomes of RIRS. Third, all nomograms evaluated in this study were originally designed to predict the PCNL success. Hence, these nomograms may not be useful in predicting RIRS outcomes. Despite all these limitations, the present study is the first study in the literature which demonstrates that all these nomograms may be helpful in predicting RIRS success with established cut-off values, although stone burden is still the most significant predictor. Further, well-designed, large scale, prospective studies are required to confirm the results of this study and to establish definite conclusion.

CONCLUSIONS

Nomograms which are used to predict the PCNL success are not superior to stone burden in predicting the RIRS success. Of note, the deflection angle of the flexible URS should be given particular consideration. In addition to the stone burden, nomograms used to predict the RIRS success should also encompass lower pole stones and lower pole infundibulopelvic angle.

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