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Investigation of Factors Related to Percutaneous Nephrolithotomy Failure in Horseshoe Kidneys and Comparison of Three Stone Scoring Systems in Prediction of Outcomes

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Keywords
Percutaneous nephrolithotomy · Horseshoe kidney · Stone-free status

Abstract
Introduction: We aimed to identify factors affecting percutaneous nephrolithotomy (PNL) outcomes among patients with horseshoe kidney (HSK) and assess the predictive accuracy of the Clinical Research Office of the Endourological Society (CROES), Guy's Stone Score (GSS), and S.T.O.N.E. scoring systems. ***Methods:*** Data from 98 patients with HSK who underwent PNL between November 2010 and January 2020 were evaluated. Patients were divided into the stone-free (SF) and non-SF groups and compared according to demographic data, stone and surgical characteristics, and stone scoring systems. Multivariate logistic regression analysis was performed to identify factors associated with SF status. ***Results:*** Among the included patients, 87 were male and 11 were female (mean age: 47.37 ± 14.42 years). The SF rate was 84.7% (83 patients). Group analysis identified GSS ($p < 0.001$), CROES score ($p < 0.001$), S.T.O.N.E. score ($p = 0.014$), stone burden ($p = 0.045$), and multiplicity ($p < 0.001$) as factors associated with SF status. Among our cohort, 10 patients developed complications. All scoring systems were significantly correlated with SF status (CROES: $r = -0.442$, $p < 0.001$; GSS: $r = 0.442$, $p < 0.001$; S.T.O.N.E.: $r = 0.250$, $p = 0.013$), while CROES score was identified as an independent factor associated with SF status (95% CI: 0.937–0.987; $p = 0.003$). ***Conclusions:*** PNL is an effective method for treating nephrolithiasis among patients with HSK. Moreover, stone-related factors, such as larger size, multiplicity, and complexity, were associated with procedural failure. Finally, the CROES nomogram was a better predictor of SF status compared with other scoring systems.

Introduction

Horseshoe kidney (HSK), first described by Carpi in 1522, is the most common renal fusion abnormality, with a reported incidence of 1 in 400–666 individuals among the general population [1]. HSK is caused by the abnormal fusion of the metanephric blastema during the embryonic period [2]. The high ureter insertion limits the drainage ability of the renal collecting system. As such, individuals with HSK are more prone to urinary stasis, ureteropelvic obstruction, infection, and urolithiasis [3]. Studies have reported that nephrolithiasis is the most common complication of HSK, with incidence rates ranging from 21 to 60% [2]. Considering the anatomical fea-

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tures of HSK, the treatment of nephrolithiasis has been a cause for concern among urologists. Currently, minimally invasive techniques, such as shock wave lithotripsy (SWL) and retrograde intrarenal surgery (RIRS), have been widely performed for the treatment of nephrolithiasis among individuals with HSKs [4]. Among such alternatives, SWL has been found to be well tolerated with reported stone-free rates (SFRs) ranging from 31 to 72% [5, 6]. Though minimally invasive, most of the patients require repeat SWL sessions to achieve higher SFRs, which have been shown to decrease significantly with larger stones [7]. Meanwhile, studies have shown that utilizing RIRS for the treatment of nephrolithiasis among patients with HSK produced SFRs ranging from 70 to 88.2% [8, 9]. Despite the seemingly sufficient efficacy of RIRS for nephrolithiasis in HSK, stones should theoretically be split into smaller fragments and extracted. Otherwise, the probability for ancillary procedures may increase. Considering the benefits of adequate pelvicalyceal system drainage for the success of SWL and RIRS, percutaneous nephrolithotomy (PNL), which can be performed relatively independent of anatomic features, may be advantageous.

The current European Association of Urology guidelines recommend PNL as an alternative treatment for stones ranging from 1 to 2 cm and as the first-line therapy for larger stones, regardless renal anatomical features [10]. Accordingly, previous studies had revealed that PNL was an effective modality for patients with HSK, with success rates ranging from 65.8 to 86.5% [11–17]. Although various studies have evaluated the efficacy of PNL among patients with HSK, the number of studies systemically investigating factors affecting outcomes of PNL and the predictive value of stone scoring systems have been, to the best of our knowledge, lacking. The success of PNL is primarily dependent on the patient (surgical history, body mass index, comorbidities, and anatomical abnormalities), stone (size, density, and location), and surgery-related factors (access number, access site, tract length, operative time, and surgeon's experience) [18–20]. Recently, different stone scoring systems consisting of various combinations have been developed to assist surgeons in predicting the surgical outcomes of PNL [21–23]. Accordingly, Guy's Stone Score (GSS), S.T.O.N.E. score, and the Clinical Research Office of the Endourological Society (CROES) nomogram have been the most widely used scoring systems. While GSS accounts for anatomical abnormalities as factors increasing PNL complexity, the CROES and S.T.O.N.E. scoring systems do not consider the same as factors affecting procedural outcomes. Considering our clinical experience in the field, the present study aimed to identify factors affecting PNL outcomes among patients with HSKs and assess the predictive value of the 3 aforementioned stone scoring systems.

Methods

After institutional review board approval, data from 98 patients with HSK who underwent PNL between November 2010 and January 2020 were evaluated. The procedure was performed on patients with stones larger than 2 cm, those with SWL-resistant stones, and those who opted for PNL after receiving information regarding treatment alternatives.

Preoperative Evaluation

Detailed physical examinations, history taking, blood count, blood biochemistry assays, urine analysis, and urine culture were performed. All patients underwent kidney-ureter-bladder radiography, ultrasonography, and computed tomography (CT). Stone size was calculated using CT images. Stone burden was determined by multiplying the 2 largest diameters. All calculations (stone size, GSS, S.T.O.N.E. score, and CROES score) were performed by the same surgeon, while all stone scoring systems were divided into 3 groups for detailed investigation (<150, 150–220, and >220 for CROES; 5–6, 7–8, and ≥9 for S.T.O.N.E.; and 2, 3, and 4 for GSS). Demographic characteristics (i.e., age, gender, stone number, and surgical history) and perioperative parameters (i.e., presence of upper calyx access, access number, operative time, anesthesia time, type of anesthesia, complications, and length of hospitalization) were noted.

Surgical Procedure

All procedures, which were performed in the prone position, started with cystoscopy for ureteral catheter insertion. A contrast agent was then injected through the catheter to visualize the renal collecting system. Access was performed under fluoroscopic guidance, after which a guidewire was inserted into the collecting system. Serial dilators were used for tract dilation, and a 30F Amplatz sheath was positioned. Stone fragmentation was performed using a pneumatic lithotripter. The fragments were then extracted using a grasper. Smaller fragments were extracted through irrigation. After the procedure, antegrade pyelography was performed to check for stone clearance and a nephrostomy tube was inserted under fluoroscopic guidance.

Stone clearance was assessed through CT 3-4 weeks after the procedure. The procedure was categorized as SF when no stone fragments were observed upon imaging. Patients were then divided into 2 groups according to the presence (non-SF group) and absence (SF group) of residual fragments. PNL-associated complications were recorded and classified according to the Clavien-Dindo classification [18].

Statistical Analysis

Comparisons between groups were performed using Pearson's χ^2 test for categorical variables and the Mann-Whitney U test for continuous variables. Logistic regression analysis was performed to identify factors independently associated with outcomes. Rela-

Table 1. Total cohort and the association of factors with residual stone rate in univariate analysis

	Total cohort (n = 98)	Patients with no residual stone (n = 83)	Patients with residual stone (n = 15)	p value
Mean age, years	46.87±14.56	47.37±14.42	44.07±15.55	0.471
Gender				
Male	87/88.8	73/87.95	14/93.3	0.543
Female	11/11.2	10/12.05	1/6.7	
Preoperative hemoglobin, g/dL	14.54±1.59	14.53±1.62	14.63±1.52	0.937
Preoperative creatinine, mg/dL	0.98±0.26	0.98±0.26	0.99±0.29	0.901
Stone burden, mm^2	509.2±477.8	452.07±402.55	825.47±711.58	0.043
CROES	237.02±56.87	247.74±53.40	177.73±35.59	<0.001
GSS	2.63±0.56	2.52±0.50	3.27±0.46	<0.001
S.T.O.N.E.	7.55±1.34	7.39±1.27	8.47±1.41	0.014
Hounsfield unit	893±294.2	884.6±290.9	905.4±303.6	0.869
Previous surgery				
+	69/70.4	60/72.3	9/60	0.337
–	29/29.6	23/27.7	6/40	
Stone, *n*				
Single	40/40.8	40/48.2	0/0	<0.001
Multiple	58/59.2	43/51.8	15/100	
Access, *n*				
Single	70/71.4	61/73.5	9/60	0.287
Multiple	28/28.6	22/26.5	6/40	
Upper calyx access				
+	53/54	44/53	9/60	0.617
–	45/46	39/47	6/40	
Anesthesia type				
General	61/62.2	50/60.2	11/73.3	0.336
Regional	37/37.8	33/39.8	4/26.7	
Complication				
+	10/8.4	7/8.3	3/20	0.173
–	88/91.6	76/91.7	12/80	
Hb drop	1.17±1.12	1.14±1.02	1.35±1.21	0.988
Operation time, min	66.53±35.03	62.35±31.50	89.67±45.02	0.019
Hospitalization, days	3.44±2.62	2.95±1.70	6.13±4.66	0.014

CROES, Clinical Research Office of the Endourological Society; GSS, Guy's Stone Score. Data are shown as mean±SD, or *n*/%.

tionships between the variables were analyzed using the Pearson correlation and Spearman correlation coefficients. All statistical analyses were performed using SPSS 16.0 for Windows (SPSS, Inc., Chicago, IL, USA) with $p < 0.05$ being considered significant.

Results

Among the 98 patients who underwent PNL, 87 were male and 11 were female with a mean age of 47.37 ± 14.42 years. After a single session, the SF rate was 84.7% (83 patients). Group analysis identified GSS ($p < 0.001$), CROES score ($p < 0.001$), S.T.O.N.E. score ($p = 0.014$), stone burden ($p = 0.045$), and multiplicity ($p < 0.001$) as factors associated with SF status. A comparison of the pre-, intra-, and postoperative data between both groups is presented in Table 1.

Among the included patients, 10 developed complications. Accordingly, 9, 4, and 1 grade I, II, and III complications were noted (Table 2). Fever observed in 9 patients was treated conservatively, while transfusion was required in 2 patients. One patient who developed perirenal hematoma received antibiotics with no surgical intervention required.

Associations between the stone scoring systems and SF status are presented in Table 3. Accordingly, SF status was significantly associated with both GSS and CROES score ($p < 0.001$ for both) but not S.T.O.N.E. ($p = 0.051$). Mul-

Table 2. Postoperative complications according to Clavien-Dindo classification, *n*/%

Grade 1	
Transient fever	9/9.2
Grade 2	
UTI	1/1
Transfusion	2/2
Cellulitis	1/1
Grade 3	
Perirenal hematoma	1/1
Grade 4	None
Grade 5	None

Table 3. The effect of both nephrolithometry scoring systems on the SF status

	n	SF status, *n*/%	*p* value
CROES			
Grade 1–2	6	3/33.3	<0.001
Grade 3	23	16/69.6	
Grade 4	69	65/94.2	
S.T.O.N.E.			
5–6	24	24/100	0.051
7–8	53	43/81.1	
≥9	21	16/76.2	
GSS			
2	40	40/100	<0.001
3	54	43/79.6	
4	4	0/0	

SF, stone-free; CROES, Clinical Research Office of the Endourological Society; GSS, Guy's Stone Score.

tivariate analysis identified CROES nomogram as the only independent factor associated with SF status (Table 4). All stone scoring systems were significantly correlated with SF status (Table 5). Receiver operating characteristic analysis revealed an area under curve (AUC) of 0.854 (95% confidence interval [CI]: 0.769–0.939), 0.810 (95% CI: 0.708–0.912), and 0.695 (95% CI: 0.563–0.827) for CROES, GSS, and S.T.O.N.E., respectively (Fig. 1).

Discussion

The treatment of nephrolithiasis among patients with HSK has continued to be a challenge for urologists. Given the anatomical variations and poor drainage, SWL and

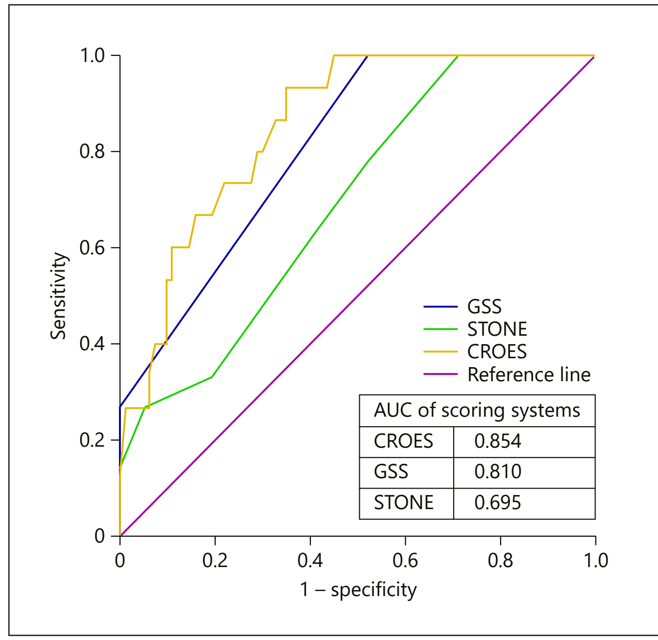

Fig. 1. ROC curves and AUC for GSS, S.T.O.N.E., and CROES nomogram in predicting SF status. ROC, receiver operating characteristic; AUC, area under curve; CROES, Clinical Research Office of the Endourological Society; GSS, Guy's Stone Score; SF, stone-free.

RIRS have limited efficacy in HSK. To date, PNL has been the treatment of choice for large stones regardless of the anatomical features of the kidney. Given that HSK is a relatively rare abnormality, surgery for patients with HSK may be a concern even for surgeons practicing in referral centers where PNL is frequently applied. Consistent with the previous literature, the initial SFR obtained herein was 84.6%. However, our definition of SF differed from those utilized in previous studies. Accordingly, studies performed by Skolarikos et al. [15], Ozden et al. [14], and Gupta et al. [13] defined SF as the complete clearance of stones with corresponding SFRs of 65.5, 80, and 86.5%, respectively [13–15]. Moreover, Etemadian et al. [17] and Shokeir et al. [15] defined fragments smaller than 4 mm as clinically insignificant residual fragments (CIRF) and obtained success rates of 82 and 71.4%, respectively [11, 17]. Considering the limited pelvicalyceal drainage, the presence of CIRFs after PNL among patients with HSKs may increase the risk for new stone formation. Among the patients included herein, 7 had CIRFs with a corresponding success rate of 91.8%. However, we believe that the presence of CIRFs should not be described as a successful result, especially among those with HSK.

Table 4. Multivariate analysis of factors affecting SF status

	p value	OR	95% CI
CROES	0.003	0.958	0.937–0.987
GSS	0.499	0.608	0.338–1.225
S.T.O.N.E.	0.975	0.868	0.450–2.168
Stone burden	0.574	0.999	0.998–1.001

SF, stone-free; CROES, Clinical Research Office of the Endourological Society; GSS, Guy's Stone Score; OR, odds ratio; CI, confidence interval.

Table 5. Correlation analysis between SF status and stone scoring systems

	r	*p* value
CROES	–0.442	<0.001
GSS	0.442	<0.001
S.T.O.N.E.	0.250	0.013

SF, stone-free; CROES, Clinical Research Office of the Endourological Society; GSS, Guy's Stone Score.

After evaluating the data from 58 patients with HSK who underwent PNL at 2 centers, Skolarikos et al. [15] found that stone-related factors, such as size >5 cm^2, staghorn form, multiple stones, and complex stones, were significantly associated with failure on univariate analysis ($p = 0.013$, $p < 0.001$, $p = 0.006$, and $p = 0.01$, respectively). Moreover, logistic regression analysis in the same study revealed that staghorn stone was the only factor that significantly predicted SF status ($p = 0.002$). Another study by Tepeler and coworkers [16], who retrospectively evaluated the data of 54 patients with HSK who underwent PNL at 3 centers, found that stone complexity and multiplicity, but not stone size, were associated with SF status ($p = 0.026$ and 0.043, respectively) upon univariate analysis [16]. Our findings differ from those presented previously considering that this was a single-center study with more patients. Accordingly, we did not divide our cohort according to simplicity and complexity of the stones given that stone scoring systems created from multiple parameters were used to determine complexity. The current study achieved an SFR of 84.7%, which was higher than that in Skolarikos et al. [15] (65.5%) and comparable with that in Tepeler et al. [16] (85.2%). Skolarikos et al. [15] associated lower SFR with a higher number of staghorn stones (19 patients, 32.7% of total cohort) and greater mean stone burden (7.62 ± 7.18 cm^2), with stone clearance being achieved in only 21% of the patients with staghorn stones. On the other hand, 4 patients included in the present study had complete staghorn stones, none of whom were able to achieve total stone clearance. In fact, the study by Tepeler et al. [16] also achieved a higher rate of complete staghorn stone clearance compared with our series (22.2%). The use of flexible nephroscope during the procedure, which was reported as a reason for higher SFR in this study, may have caused comparable SFR with our study. A similar study had reported that the use of flexible nephroscope during the procedure may promote higher SFR [12]. Although we believe that the use of flexible devices may promote better stone clearance, especially in abnormal kidneys, this had not been routinely used in our practice. Consistent with the aforementioned studies, we showed that the presence of multiple and larger stones was associated with failure ($p < 0.001$ and $p = 0.045$, respectively).

Despite its known safety, PNL may cause several complications, including fever, urinary tract infections, hemorrhage, neighboring organ injury, and chest complications [24]. Among the patients included herein, 2 required blood transfusion. In a normal kidney, PNL performed via an upper calyx access (UCA) increases the probability of chest complications given that a supracostal puncture is required in a considerable number of patients. Accordingly, 53 of the patients included herein underwent PNL via an UCA, majority of whom required a subcostal puncture due to the lower position associated with HSK. We believe that an UCA can decrease transfusion requirement by providing a direct access to the entire calyces, pelvis, and isthmus, thereby facilitating instrument movement and shortening operative time. Only 1 patient with UCA in our series required transfusion related to low preoperative hemoglobin levels. Moreover, none of our patients developed chest complications. Miller et al. [12], who suggested prescribing antibiotics 2 weeks before PNL among patients with HSK, reported an urosepsis rate of 2.85%. The present study administered antibiotics to 3 patients: 1 for urinary tract infection, 1 for perirenal hematoma, and 1 for cellulitis. We believe that early antibiotic administration is not needed unless a tubeless procedure, which may limit drainage, is planned.

Owing to advancements in technology, technique refinement, and increased experience, PNL has been widely performed today even in special conditions, such as in pediatric patients and those with anatomical abnormalities or a solitary kidney. Recently, applicable and practical stone scoring systems have been developed to assist surgeons in decision-making, patient counseling, and prediction of surgical outcomes. Accordingly, GSS consists of 4 grades based on stone burden, stone location, and anatomical features of the kidney [21]. The CROES nomogram considers variables, such as stone characteristics (size, number, location, and presence of staghorn stones), surgical history, and number of cases treated per year in each institution [22]. S.T.O.N.E. nephrolithometry involves 5 parameters, including stone size, density, location, tract length, and level of obstruction [23]. Overall, PNL complexity can be considered to be directly proportional to GSS and S.T.O.N.E. score and inversely proportional to CROES score. Labadie et al. [25], who compared S.T.O.N.E., CROES, and GSS in 246 patients, found that all 3 stone scoring systems were able to predict PNL success ($p = 0.004$, $p < 0.001$, and $p = 0.02$, respectively) on univariate analysis, although such results were not analyzed using multivariate analysis. In a similar study, Tailly and coworkers demonstrated the predictive utility of CROES ($p = 0.004$ with an AUC of 0.646), S.T.O.N.E. ($p < 0.001$ with an AUC of 0.671), and GSS ($p = 0.019$ with an AUC of 0.629) on multivariate logistic regression analysis [26]. Recent studies evaluating the predictive value of stone scoring systems among special patient groups, such as pediatric patients and those with obesity, staghorn stones, and chronic kidney disease, revealed controversial results [27–30]. Taking this into account, we believe that the efficacy of stone scoring systems differs among patients with special conditions. To the best of our knowledge, only 1 study had evaluated the efficacy of these stone scoring systems among patients with anatomical abnormalities, with the current study being the first to compare the same among those with HSK. Kocaaslan et al. [31] retrospectively evaluated the data from 137 cases with anatomical abnormalities, 46 of whom had HSKs. Accordingly, they found that the CROES nomogram and GSS ($p < 0.001$ and $p = 0.001$, respectively), but not S.T.O.N.E. score ($p = 0.168$), were significantly associated with SF status on univariate analysis, with the CROES nomogram having the strongest predictive accuracy for SF status (odds ratio: 1.01, 95% CI: 1,005–1,021; $p = 0.001$). The current study showed that all 3 stone scoring systems were associated with SF status on univariate analysis ($p < 0.001$ for CROES and GSS; $p = 0.014$ for S.T.O.N.E.) and were significantly correlated with SF status. However, multivariate analysis revealed that only the CROES score was independently associated with SF status. Although GSS considers anatomical variations in the measurement of stone complexity, we found that the CROES nomogram, which assesses patient- and stone-related factors in more detail, had a better predictive accuracy.

The current study has 2 limitations worth noting. First was the retrospective nature of the study data, and second was our single-center design, which limited the generalizability of our results.

Conclusion

The present study showed that PNL is an effective method for the treatment of nephrolithiasis among patients with HSK. Moreover, stone-related factors, such as larger size, multiplicity, and complexity, had been found to be associated with failure. Our results also revealed that compared with other scoring systems, the CROES nomogram was a better predictor of SF status among patients with HSK who are candidates for PNL. Further studies are nonetheless needed to evaluate the efficacy of nephrolithometric scoring systems in predicting surgical outcomes after PNL among patients with HSK.

Statement of Ethics

This study was approved by the Local Ethics Committee (2011-KAEK-25 2020/03/02).

Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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Author Contributions

Sinan Avci: writing and analysis; Volkan Caglayan: data collection, writing, design, and analysis; Metin Kilic: data collection; Sedat Oner: design and analysis.

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