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RESEARCH

Can additional variables be used to predict stone-free rates following retrograde intrarenal surgery? Anticoagulants and parenchyma thickness: a detailed examination

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Abstract

The purpose of this article is to identify the factors that predict the success of retrograde intrarenal surgery (RIRS), with a focus on the effect of renal parenchymal thickness and anticoagulant use on stone-free rates. From February 2014 to April 2022, cases of kidney stones treated with RIRS at our clinic were retrospectively screened. The study included 642 cases meeting all inclusion and exclusion criteria. The patients who were observed to be stone free after a single session of RIRS were assigned to Group F, while those with residual fragments were assigned to Group R. Group F comprised 472 patients, while Group R included 170 patients. The two groups have compared certain preoperative and postoperative laboratory and radiological parameters. The infundibulopelvic angle was significantly more acute in Group R (45.63 ± 16.25 vs. 49.28 ± 15.36, $p = 0.011$) while patients in Group F tended to have thicker parenchyma (27.39 ± 8.38 vs. 22.88 ± 5.56, $p < 0.001$). In our analysis of multivariate logistic regression, stone size (OR: 1.074, 1.037–1.113; $p < 0.001$), lower calyceal location (OR: 0.550, 95% CI 0.364–0.831; $p = 0.005$), multiple numbers of stones (OR 0.254, 95% CI 0.166–0.389; $p = < 0.001$), the value of parenchymal thickness (OR 0.911, 95% CI 0.882–0.941; $p = < 0.001$) and more importantly use of anticoagulants/antiplatelets (OR 0.557, 95% CI 0.333–0.933; $p = 0.026$) appeared to be independent predictors of stone-free status after RIRS. Further evaluation of the data revealed that the cut-off value of the renal parenchymal thickness for an effective stone-free status in a ROC curve analysis was 24.5 with 62.9% sensitivity and 56.8% specificity (area under curve value: 0.654 [95% CI 0.608–0.699, $p < 0.001$]). The endourologist may be able to make more informed decisions by evaluating renal parenchymal thickness in addition to patient-related factors like anticoagulant use, which we find significantly affects outcomes, along with the stone and renal anatomy-related factors.

Keywords Kidney stones · Retrograde intrarenal surgery · Anticoagulants · Parenchymal thickness

Introduction

The prevalence of urinary system stone disease has increased in recent years [1]. This increase has brought the technological development of the tools used in the minimally invasive treatment of urinary stones together [2]. As a result of these tremendous technological advancements, retrograde intrarenal surgery (RIRS) has become a valuable alternative for the successful and safer management of moderate-sized stones (10–20 mm) due to its minimally invasive nature [3]. SWL and RIRS are equally effective treatment modalities according to the European Association of Urology (EAU) Urolithiasis Guidelines for kidney stones smaller than 20 mm in diameter, whereas PCNL remains the treatment of choice for stones larger than 20 mm due to its higher stone-free rates after a single session [4]. In addition, PCNL

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results are less affected by stone size than those of ESWL and RIRS. However, it is well known that PCNL is more invasive than the other two methods, and the risk of severe complications (bleeding, sepsis) is unquestionably greater than RIRS [5].

Achieving a stone-free status in a single session with RIRS is one of the primary objectives of current endourologic stone management. Several stone and patient-related factors have been evaluated to predict the final success of this procedure [6]. In this regard, the RIRS depends heavily on good visualization, which may be adversely impacted by the presence of any bleeding [7]. It is crucial at this time to study the potential impact of anticoagulant medications on stone-free status after RIRS. Residing fragments following successful endoscopic stone surgery (RIRS, PCNL) are accepted as a distressing "headache" that affects the patient's life quality and necessitates additional intervention, incurring additional costs to the health system [8]. A small number of studies focused on the effect of renal parenchyma thickness (PT) as a potential predictive factor for stone-free rates following minimally invasive stone removal procedures [9]. Based on the results of these studies and our clinical observations, it appears that the thickness of the renal parenchyma and anticoagulants and/or antiplatelet agents may play a role in the stone-free rates after RIRS. In light of this, the purpose of the present study was to determine the potential predictive value of these factors on the final success rates following the RIRS application.

Patients and methods

Kidney stone cases treated with RIRS in our clinic were screened from February 2014 to April 2022 retrospectively. Our study was approved by the ethics committee of our institute, and all ethical rules in the Declaration of Helsinki were complied with. Inclusion criteria were defined as patients undergoing uncomplicated RIRS to treat kidney stones. The exclusion criteria were determined as preoperatively placed ureteral stent, detection of ureteral stenosis, solitary kidney, ectopic kidney, and other anatomical anomalies, and patients with ureteral rupture or avulsion during the operation. 642 cases meeting all inclusion and exclusion criteria were included in the study.

Kidney–ureter–bladder graphy (KUB) and non-contrast computerized tomography (NCCT) were performed in all cases to evaluate the stone specifications and anatomical features of the renal collecting system. In the pre-treatment, radiological evaluation procedures and urinary ultrasonography (USG) were performed when necessary. Stone size was assessed with its largest diameter in the KUB for opaque stones and the NCCT for lucent stones. The technique previously described by El-Bahnasy as the inner angle between the ureteropelvic axis and the central axis of the lower pole infundibulum was utilized to estimate the infundibulopelvic angle [10]. Parenchymal thickness (PT) was obtained by measuring the thickest region on transverse sections on preoperative NCCT. Our PT measurement method is shown in Fig. 1.

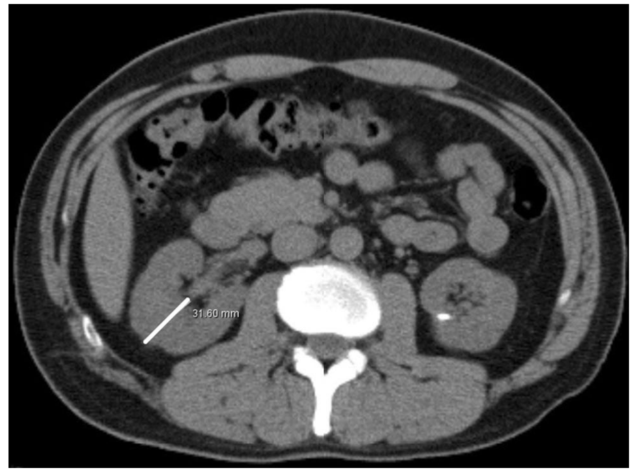

Fig. 1 Application of parenchymal thickness measurement method

A negative urine culture result was sought in all patients preoperatively. Cases with documented urinary tract infections were treated with an appropriate antibiotic prior to the procedure. All patients were given prophylactic antibiotics during the procedure (single dose of 2nd generation cephalosporin). USG, KUB, and NCCT results were evaluated based on the stones' opacity characteristics in determining stone-free status for 3 months after treatment. While in certain stones just KUB or USG with KUB was employed, NCCT was used in all non-opaque stones for this evaluation. For residual pieces that can be clearly seen in KUB, NCCT was not necessary. The absence of any residual fragments or the presence of small stone fragments (< 3 mm) was considered a successful outcome.

All procedures were performed in the lithotomy position and under general anesthesia. A 0.038 Fr guide wire was inserted into the renal pelvis with a 9.5 Fr semi-rigid ureteroscope under fluoroscopic guidance. The pelvicalyceal system was evaluated by retrograde pyelography. A ureteral access sheath (UAS) (9.5/11.5 Fr, Cook Medical, Bloomington, IN) was placed under fluoroscopy. The collecting system was entered with a 7.5 Fr fiber optic flexible ureteroscope (Storz FLEX-X2). Fragmentation of stones was performed with a holmium laser using a 273 μ fiber. Fragments larger than 3 mm were extracted using a nitinol basket (ZeroTip™; Cook Urological Inc.) in patients undergoing fragmentation. Smaller fragments were left for spontaneous passage. According to the assessment that was performed 3 months after surgery, the patients were divided in to two groups based on their stone-free status. The patients observed as stone-free were grouped under Group F, and those with residual fragments were grouped under Group R. Group F included 472 patients, while Group R included 170 patients. The two groups have compared certain preoperative and postoperative laboratory and radiological parameters.

Statistical analysis: Statistical analysis was made using SPSS version 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean ± standard deviation. An independent *T* test or a Mann–Whitney *U* test was used to compare these variables. Numbers and percentages (%) were used to express categorical variables. These variables were compared using the χ^2 test or Fisher's exact test. Predictors of stone-free status were determined using binomial logistic regression analysis. Receiver operating characteristic (ROC) curve analysis was used to assess the parenchymal thickness to predict stone-free status. The odds ratio (OR) and the corresponding 95% confidence interval (CI) were used to express the impact significance. In all statistical analyses, $p < 0.05$ was considered significant.

Results

Evaluation of our results revealed the following findings:

First, no significant difference could be demonstrated in terms of gender and age distribution of all groups. Similarly, the difference in ASA scores between the groups was insignificant. Likewise, a similar distribution regarding the presence of diabetes mellitus and the Charlson Comorbidity Index was present in our groups. Although there was no significant difference in terms of stone lateralization, the mean stone size was found to be smaller in Group F (12.05 ± 5.33 vs. 13.73 ± 5.98, $p = 0.001$). While the two groups did not show any significant difference in the opacity characteristics of the stones, lower calyceal stones were more common in Group R (30.5% vs. 54.1%, $p < 0.001$). The presence of hydronephrosis was not significantly different between the two groups, but patients in Group R tended to have a higher rate of multiple stones than the other groups (39.4% vs. 71.8%, *p* 0.001). Preoperative laboratory findings demonstrated well that mean hemoglobin, creatinine (0.98 ± 0.38 vs. 1.03 ± 0.44, $p = 0.131$), and glomerular filtration (92.19 ± 81.32 vs. 91.11 ± 49.96, $p = 0.871$) values were similar between all groups. Although the use of anticoagulant and/or antiplatelet (12.7% vs. 20.0%, $p = 0.016$) agents was higher in Group R; similar rates were observed in the use of alpha-blockers (6.1% vs. 8.2%, $p = 0.222$). The presence of previous ureteroscopic surgery history was similar among the groups. In addition, no significant difference was observed between the two groups in terms of the methods used in the residual fragment evaluations of the patients 3 months after surgery.

Evaluation of the infundibulopelvic angle (45.63 ± 16.25 vs. 49.28 ± 15.36, $p = 0.011$) showed that it was prominently acute in Group R and patients in Group F tended to have higher values in parenchymal thickness (27.39 ± 8.38 vs. 22.88 ± 5.56, $p < 0.001$). Stone density and body mass index results were similar in groups. Patient demographics and laboratory findings of the two groups are given in Table 1.

In our multivariate logistic regression analysis evaluation, stone size (OR: 1.074, 1.037–1.113; $p < 0.001$), lower calyceal location (OR 0.550, 95% CI 0.364–0.831; $p = 0.005$), multiple numbers of stones (OR 0.254, 95% CI 0.166–0.389; $p = < 0.001$), the value of parenchymal thickness (OR 0.911, 95% CI 0.882–0.941; $p = < 0.001$), and more importantly use of anticoagulants/antiplatelets (OR 0.557, 95% CI 0.333–0.933; $p = 0.026$) appeared to be independent predictors of stone-free status after RIRS. The results are given in Table 2.

Lastly, further evaluation of the data revealed that the cut-off value of the renal parenchymal thickness for an effective stone-free status in a ROC curve analysis was 24.5 with 62.9% sensitivity and 56.8% specificity (area under curve value: 0.654 [95% CI 0.608–0.699, $p < 0.001$]) (Fig. 2).

Discussion

Achieving a completely stone-free status in a single session with RIRS is one of the main goals of current endourologic stone management, and there have been some stone (size, location, hardness) and patient (body habitus, use of anticoagulant agents, anatomy of the kidney) related factors evaluated to predict the final success of this procedure on this aspect. To our knowledge, this is the first study demonstrating the negative effect of anticoagulant/antiplatelet use on the final success rates following RIRS. In their research, Resorlu et al. [6] found that there was no difference between the cases with residual fragments and that of the stone-free ones regarding the anticoagulant use after RIRS. In our study, however, we obtained contradictory findings by demonstrating that anticoagulant/antiplatelet use could be an independent predictor of SFR. Based on the outcomes published so far, it is recommended to discontinue the use of anticoagulants before these procedures to minimize the risk of bleeding [11]. According to our clinical procedure, warfarin is stopped 5 days prior to RIRS while other anticoagulants and antiaggregants should be stopped 1–3 days prior to RIRS, in accordance with the advice of competent cardiologists or neurologists. Again, if not contraindicated as a result of these consultations, all our patients who use an anticoagulant or antiaggregant prior to RIRS are administered low molecular weight heparin

Table 1 Patients' characteristics and clinical findings

	Group F ($n=472$) (stone free)		Group R ($n=170$) (residual fragments)		p
Gender					
Male	302	64.0%	113	66.5%	0.314
Female	170	36.0%	57	33.5%	
Age	50.09	±14.85	51.56	±14.70	0.159
ASA					
ASA 1	137	29.0%	54	31.8%	0.666
ASA 2	296	62.7%	100	58.8%	
ASA 3	39	8.3%	16	9.4%	
Diabetes	67	14.2%	29	17.1%	0.218
Charlson Comorbidity Index	1.59	±1.80	1.78	±1.77	0.243
Lateralization					
Right	218	46.2%	78	45.9%	0.509
Left	254	53.8%	92	54.1%	
Size (mm)	12.05	±5.33	13.73	±5.98	0.001
Opacity					
Opaque	259	54.9%	100	58.8%	0.212
Non-opaque	213	45.1%	70	41.2%	
Hydronephrosis	200	42.4%	71	41.8%	0.482
Localization					
Pelvis + other calyxes	328	69.5%	78	45.9%	<0.001
Lower calyx	144	30.5%	92	54.1%	
Stone number					
Single	288	61%	48	28.2%	<0.001
Multiple	184	39%	122	71.8%	
Preop hemoglobin (g/dL)	14.33	±1.94	14.35	±2.06	0.936
Preop creatinine (mg/dL)	0.98	±0.38	1.03	±0.44	0.131
GFR (ml/min/1.73 m^2)	92.19	±81.32	91.11	±49.96	0.871
Anticoagulant/antiplatelet use	60	12.7%	34	20.0%	0.016
Alfa-blocker use	29	6.1%	14	8.2%	0.222
Previous ureteroscopic surgery	249	52.8%	84	49.4%	0.255
Parenchymal thickness(mm)	27.39	±8.38	22.88	±5.56	<0.001
İnfundibolopelvic angle (°)	45.63	±16.25	49.28	±15.36	0.011
Stone density (HU)	818.86	±342.26	828.81	±395.06	0.487
BMI (kg/m^2)	28.01	±4.72	28.38	±4.52	0.377
Stone-free assessment method					
NCCT	307	65.0%	103	60.6%	0.583
KUB	50	10.6%	20	11.8%	
KUB and USG	115	24.4%	47	27.6%	

BMI body mass index, *IPA* infundibulopelvic angle, *GFR* glomerular filtration rate, *ASA* American Society of Anesthesiologists, *HU* Hounsfield unit, *PT* parenchymal thickness, *PUS* previous ureteroscopic surgery, *CCI* Charlson Comorbidity Index, *Preop* preoperative, *hg* hemoglobin, *cr* creatinine, *USG* ultrasonography, *KUB* kidney–ureter–bladder graphy, *NCCT* non-contrast computed tomography

to avoid the adverse cardiovascular effects of surgery. Interestingly, the stone-free rate was found to be lower in this patient group despite the fact that anticoagulant or antiaggregant medication had been stopped and low molecular weight heparin had been initiated before the surgery. This finding suggests two likely scenarios: Do oral anticoagulants and antiaggregants have a longer lasting effect than we realized, or is this the result of the usage of low molecular-weight heparin? With the information at hand, we simply cannot comment on these matters. However, it is pretty evident that our success is reduced in this patient group. We may speculate that this finding may be due to the capillary hemorrhage in the renal collecting system, which may impair the visualization during RIRS. Despite that,

Table 2 Univariate and multivariate logistic regression analysis of the risk factors for residual fragments after 3 months following surgery

	Univariate			Multivariate		
	p	OR	95% CI	*p*	OR	95% CI
Gender						
Male	0.561	1.116	0.771–1.615			
Female						
Age	0.267	1.007	0.995–1.019			
ASA						
ASA 1						
ASA 2	0.906	0.961	0.496–1.862			
ASA 3	0542	0.823	0.441–1.538			
Diabetes	0.370	0.804	0.500–1.295			
CCI	0.243	1.058	0962–1.164			
Lateralisation						
Right	0.946	0.988	0.695–1.404			
Left						
Size	0.001	1.053	1.021–1.086	< 0.001	1.074	1.037–1.113
Opacity						
Opaque						
Non-opaque	0.374	1.175	0.824–1.676			
Hydronephrosis	0.891	1.025	0.719–1.463			
Localisation						
Other						
Lower calyx	< 0.001	0.372	0.260–0.533	0.005	0.550	0.364–0.831
Stone number						
Single						
Multiple	< 0.001	0.251	0.172–0.368	< 0.001	0.254	0.166–0.389
Preop hg (g/dL)	0.985	1.004	0.918–1.097			
Preop cr (mg/dL)	0.135	1.372	0.906–2.077			
GFR (ml/min/1.73m^2)	0.871	1.000	0.997–1.002			
Anticoa/antiplat use	0.022	0.583	0.367–0.926	0.026	0.557	0.333–0.933
Alpha-blocker use	0.351	0.729	0.376–1.416			
PUS	0.455	1.143	0.805–1.624			
PT (mm)	< 0.001	0.915	0.889–0.942	< 0.001	0.911	0.882–0.941
IPA	0.012	1.014	1.003–1.026	0.576	0.996	0.982–1.010
Stone density (HU)	0.486	1.000	0.999–1.000			
BMI (kg/m^2)	0.367	1.017	0.980–1.056			

BMI body mass index, *IPA* infundibulopelvic angle, *GFR* glomerular filtration rate, *ASA* American Society of Anesthesiologists, *HU* Hounsfield unit, *PT* parenchymal thickness, *PUS* previous ureteroscopic surgery, *CCI* Charlson Comorbidity Index, *Preop* preoperative, *hg* hemoglobin, *cr* creatinine, *Antico* anticoagulant, *Antipla* antiplatelet

some studies are showing that RIRS can be applied safely even if anticoagulant therapy is not discontinued [12, 13].

On the other hand, as a critical parameter studied in various trials for different reasons, very limited information could be derived from the literature about the possible effect of parenchymal thickness on the final success of RIRS. Related to this critical issue, Koc et al. [9] found a significant relationship between PT and SFR with a cutoff value of 19 mm (AUC: 0.708). Similarly, in our multivariate analysis, we identified PT as an independent risk factor in determining SFR after RIRS. Our calculated cutoff value, however, was higher than the value obtained in this study (24.5 mm, AUC: 0.654). However, the parenchymal thickness measurement used in the aforementioned study was applied in the coronal section and from the lower pole, unlike in our study. In another study investigating the effect of PT on the success and hemorrhagic complications of PCNL, the authors found that bleeding rates were low in cases with lower PT (< 14.5 mm) values [14]. According to reports, PT calculated on NCCT is an effective predictor of

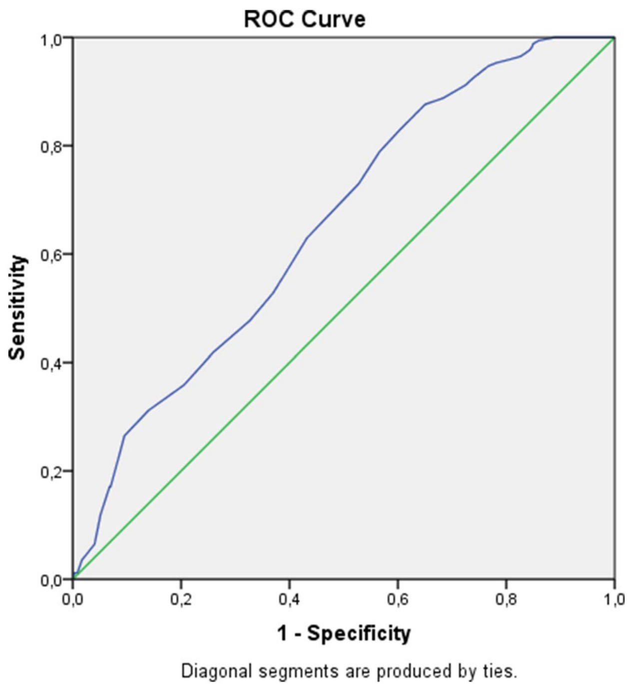

Fig. 2 ROC curve analysis of the parenchymal thickness to predict the stone-free outcomes

relative renal function, and it is useful to distinguish between bilateral renal function based on the variance in renal parenchymal thickness between the two kidneys [15, 16]. These studies allow us to base our conclusion about PT on the following: greater parenchymal thickness may indicate more nephrons and that means more fragment washout in that renal unit. As a result of all this discussion, we cannot go without saying that the cut-off-based evaluation we made with the ROC analysis did not reveal an ideal AUC value. We should also acknowledge that one of the issues limiting the clinical utility of this assessment is the poor sensitivity and specificity values computed. PT by itself may not be clinically meaningful. To facilitate comparison with other publications in the literature, we nonetheless provided our cut-off-based evaluation to the readers. However, with the new studies to be done, it can find a place in prediction models that will be used in the future.

One of the most well-known models used to predict the success of RIRS is the Resorlu-Unsal Stone Score [6]. This study basically states that stone size, stone number, stone composition, infundibulopelvic angle, and renal malformations are significant predictors of RIRS outcome. Contrary to this study, we, unfortunately, did not have stone analysis data. Also, the infundibulopelvic angle did not reach the ability to be an independent marker in our final model. Additionally, patients with renal malformations were excluded because of their small number and the fact that their characteristics made it impossible to classify them under the same heading.

Consistent with the literature, mean stone size was higher in Group R, and stone size was an independent predictive factor for SFR in multivariate analysis. [17] Studies focusing on the predictive factors of the success rates of RIRS have shown that the SFR is lower in cases presenting multiple renal stones. At the same time, the number of stones is a reliable predictive factor for SFR [18, 19]. Consistent with this information, the number of stones in our study was one of the predictive factors in our multivariate model.

Studies have shown that the lower calyx has a disadvantageous structure for the passage of residual stone fragments [20]. In our study, the rate of lower calyceal stones was higher in Group R. Additionally, we found that the presence of stones in this position enabled us to predict SFR, similar to the outcomes of previous studies [17, 21].

An important anatomical marker is the degree of infundibulopelvic angle, which has been demonstrated in the literature to have a significant impact on the success of RIRS [22]. Although it was among the evaluated predictors in our univariate analysis in our IPA study, its effect on SFR was not found to be significant in our multivariate model.

Limitations

The main limitation of this study is that it was conducted retrospectively. In addition, outcomes are obtained from a single center, and the procedures were performed by experienced surgeons, two certain factors which may affect the results. The fact that we do not calculate the current stone load using the stone volume (mm^3) and use the parenchymal thickness instead of the renal parenchyma volume can constitute other limitations. We applied these calculations because of their ease of implementation. However, despite these limitations, we believe that our present findings will be contributive based on the highly limited data published in the literature regarding the predictive role of particularly renal parenchymal thickness and the use of anticoagulant agents enough.

Conclusions

In the light of our findings and the outcomes of limited studies, we may say that evaluation of renal parenchymal thickness and usage of anticoagulant medications along with specific stone and renal anatomy-related factors could enable the endourologist to predict the final stone-free status and let them make more rational decision-making with the help of these predictive factors.

Author contributions ÜY contributed in the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. ME contributed in the conception of the work, conducting the study, revising the draft and agreed for all aspects of the work. MU contributed in the conception of the work, conducting the study, revising the draft and agreed for all aspects of the work. RG conducting the study, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

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Data availability statement The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Declarations

Conflict of interest The authors have no conflicts of interest. The authors have nothing to disclose.

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