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Effects of renal parenchymal volume and total renal volume on success in retrograde intrarenal surgery

Renal parankimal hacim ve total renal hacmin retrograd intrarenal cerrahi başarısına etkisi

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ÖZET

Amaç: Renal parankimal hacim böbrekteki nefron sayısının bir göstergesidir. Renal parankim hacimdeki artışın diürezi artıracağı ve retrograd intrarenal cerrahi (RİRC) sonrası fragmanların atılımını kolaylaştıracağını öngörmekteyiz. Dolayısıyla artan renal parankimal hacim, RİRC başarısına etki eden bir faktör olabilir.

Gereç ve Yöntemler: Kliniğimizde RİRC uygulanan 238 hastadan tek böbrek taşı nedeniyle primer RİRC yapılan ve öncesinde kontrastlı bilgisayarlı tomografi uygulanan 104 hasta çalışmaya dahil edildi. Dahil edilen tüm hastaların demografik, klinik ve radyolojik (renal parankim hacmi ve toplam renal hacim) verileri değerlendirildi. Hastalar RİRC sonrası başarı durumlarına göre başarılı ve başarısız olmak üzere iki gruba ayrıldı.

Bulgular: Toplam renal hacim açısından iki grup arasında anlamlı fark yoktu (başarılı grupta 213.3±54,9 cm3, başarısız grupta 204,4±65,7 cm3, p=0,521). Başarılı grupta ortalama renal parankim hacmi 168,3±46,1 cm3 iken, başarısız grupta ortalama 125,5±29,9 cm3 idi ve aradaki fark istatistiksel olarak anlamlıydı (p<0,001). ROC analizinde RİRC sonrası rezidü taş varlığını ön gören renal parankim hacmi için kestirim değeri ≤141,3 cm3 olarak bulundu. Çok değişkenli lojistik regresyon analizine göre, taş yükünün fazla olması (OR=1,02; 95% CI=1,009-1,03; p<0,001), taşın alt pol yerleşimli olması (OR=31,673; 95% CI=3,315-302,,623; p=0,003) ve RPV≤141,3 cm3 (OR=5,923; 95% CI=2,886-19,263; p=0,008) olması RİRC başarısı için bağımsız risk faktörleri olarak bulundu.

Sonuç: Renal parankim hacmi, böbrek taşı nedeniyle RİRC uygulanan hastalarda başarıyı ön görmek için kullanılabilecek pratik ve uygun maliyetli bir parametredir.

Anahtar Kelimeler: *başarı, renal parankim hacmi, RİRC, taş, toplam renal hacim*

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This study was approved by the Ethics Committee of Ankara State Hospital (Approval Number: E1-20-1200. Date: November 11, 2020). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

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ABSTRACT

Objective: Renal parenchymal volume known as an indicator of the number of nephrons in the kidney. We predict that the increase in renal parenchyma volume will increase diuresis and facilitate the excretion of fragments after RIRS procedure. Therefore, increased renal parenchymal volume might be suggested as a factor affecting the success of RIRS procedure.

Material and Methods: Out of 238 patients who underwent RIRS in our clinic, 104 patients who underwent primary RIRS due to single kidney stone and who underwent contrast-enhanced computed tomoghraphy were included in the study. The demographic, clinical and radiological (renal parenchymal volume and total renal volume) datas of all patients included were evaluated. Patients were divided into 2 groups according to the success status after RIRS, as successful and unsuccessful groups.

Results: There was no significant difference in total renal volume between the two groups (213.3±54.9 cm^3 in the successful group, 204.4±65.7 cm^3 in the unsuccessful group, p=0.521). While the mean renal parenchymal volume in the successful group was 168.3±46.1 cm^3 , it was 125.5±29.9 cm^3 in the unsuccessful group, and the difference was statistically significant (p<0.001). In the ROC analysis, the cut-off value for renal parenchymal volume predicting the presence of residual stones after RIRS was found to be ≤141.3 cm^3. According to multivariate logistic regression analysis, elevated stone burden (OR=1.02; 95% CI=1.009-1.03; p<0.001), localized stones in the lower pole (OR=31.673; 95% CI=3.315-302.623; p=0.003) and RPV≤141.3 cm^3 (OR=5.923; 95% CI=2.886-19.263; p=0.008) were found to be independent risk factors for success of RIRS procedure.

Conclusion: Renal parenchymal volume is a practical and cost-effective parameter that can be used to predict success rates in patients undergoing RIRS for kidney stones.

Keywords: *renal parenchymal volume; RIRS; stone; success; total renal volume*

INTRODUCTION

Significant developments have utilized the treatment of upper urinary tract stones. Minimally invasive treatment procedures have become the most preferred treatment methods with the improvements in endourologic surgery. In particular, retrograde intrarenal surgery (RIRS) has been one of the most important procedures in the treatment of stones <2 cm, due to high stone-free rates, low morbidity, shorter hospitalization time and higher patient comfort. RIRS has become an important treatment alternative in selected patients with adverse factors such as low success of shock wave lithotripsy (SWL) in lower pole stones, hassle in performing SWL and percutaneous nephrolithotomy (PNL) in obese patients, pregnancy and bleeding diathesis (1). Developments in medical devices such as flexible ureterorenoscope (URS) and laser probes have increased the success rates of RIRS procedures. A recent systematic review evaluating the success rates of RIRS in kidney stones larger than 2 cm, showed that a stone-free rate of 91% achieved with 1.45 procedures per patient (2).

In RIRS procedure, the stones are divided into small pieces by laser aiming to take advantage of spontaneous drainage with diuresis that helps stone free state of kidney (3). Various studies in the literature indicate the importance of diuresis for the drainage of fragments after SWL (4,5). According to the study of Koc et al, measurement of renal parenchyma thickness (RPT) is a cost-effective method that can be easily performed on routinely applied non-contrast computerized tomography (CT) and may have predictive value for the surgical success in patients with nephrolithiasis. The main hypothesis of that study was increased RPT, which may be considered as an increased number of nephrons, may provide better diuresis. To the best of our knowledge, this is the only study conducted for this purpose in the literature. However, in this study, only RPT, which is a one-dimensional measurement, was evaluated (6). The aim of our study is to examine the effect of RPV and TRV, that we think to be associated with diuresis, therefore might better indicate the number of nephrons in the kidney, on RIRS success. We believe that our results may reveal a new parameter that can be considered among the factors predicting the RIRS success.

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MATERIAL AND METHODS

This study was prepared in accordance with the principles of the Declaration of Helsinki and was unanimously approved in terms of ethics by the local ethic committee (Ethics committee approval number: E1-20-1200). The informed consent was obtained from each subject or subject's guardian.

In total, 238 patients underwent RIRS procedure applied in our clinic between January 2013 and May 2021 were evaluated retrospectively from the hospital information system. Patients with insufficient data, atrophic or solitary kidney, renal malformation, inaccessible stone and glomerular filtration rate (GFR) < 60 (ml/min/1.73 m2) and secondary cases were excluded from the study. Furthermore, in order to measure the renal parenchymal volume and total renal volume with the customized three-dimensional volumetric software (AW4.7 Ext.13 Software, GE, USA), the images transferred to the workstations should had been performed with contrast. By this way, the structure and borders of the kidney parenchyma were evaluated. Hence, patients who had not undergone contrast-enhanced CT were excluded from the study. Consequently 104 patients were included in the study.

Preoperative and postoperative demographic, clinical and radiological data of all patients included in the study were obtained from the hospital information system. Stone burden (mm2), stone density (Hounsfield Unit [HU]), stone laterality (right-left), stone localization and preoperative GFR (ml/min/1.73m2) were evaluated according to preoperative CT. Stone burden was defined as the two-dimensional area determined by multiplying the longest diameter by the perpendicular diameter of the stone.

Contrast-enhanced CT examinations were performed on CT devices with 128 and 512 detectors (GE Revolution, General Electric, Milwaukee, WI) at the parenchymal phase and at the supine position, covering the distance between the 10th thoracic vertebra and the symphysis pubis, without contrast material and by giving 100 ml of contrast material at a speed of 3 ml/sec, 100 kilovoltage, 110 milliampere-second and 1.25 mm section thickness. Abdomen CT scans were reviewed by a radiologist with 11 years of experience. Abdomen CT examinations were transferred to workstations (AW Volume Share 7, GE, USA) and total renal volumes and renal parenchymal volumes were measured with customized three-dimensional volumetric software (AW4.7 Ext.13 Software, GE, USA). For total kidney volume, the outline of the kidney was traced and where the renal border is discontinuous, the kidney was enclosed by extending a straight line tangential to each hilar lip. For renal parenchymal volume, the tracing excluded renal pelvis, sinus fat, vessels and cysts (Figure 1 and 2).

Patients with positive urine cultures were treated with appropriate antibiotic therapy for at least 7 days. Urine cultures of all preoperative patients were sterilized. Prophylaxis with 4 intravenous 2 g cefazolin was administered to all patients within 1 hour before surgery. RIRS was performed in all patients under general anesthesia in the lithotomy position.

Before RIRS, ureterorenoscopy was performed with a 9.5 F rigid renoscope (Karl Storz, Tuttingen, Germany) for dilatation of the urinary tract. A 9.5-11 F ureteral access sheath (Flexor® Ureteral Access Sheath, Cook Medical, USA) was placed in the ureter to reduce intrarenal pressure and provide optimal view. After the access sheath reached the collector system, the collector system was attended by entering through the access channel with a 7.5 F flexible ureterorenoscope (Karl Storz, Flex X2, GmbH, Tuttlingen, Germany). If the stone was inaccessible, a nitinol basket catheter was used. The stone was fragmented using a holmium-yttrium-aluminum-garnet (Ho: YAG) laser (200-365 µm) sent from the working channel of the flexible ureterorenoscope. At the end of the operation, a double-J (DJ) catheter and urethral catheter were applied to all cases. Urethral catheters were removed 1 day later and DJ catheters were removed after 4 weeks accordingly.

Patients were evaluated with CT in the first postoperative month. Success was defined as the absence of stones in the urinary system or the presence of asymptomatic residual stones below 2 mm. Patients were divided into 2 groups according to the success status after RIRS, as successful and unsuccessful groups. Factors affecting success were evaluated with comparative analysis between each group.

Figure 1. Determination of renal borders in axial (a) and coronal (b) sections in computed tomography and three-dimensional view in customized volumetric software (c) to determine the Total Renal Volume (TRV)

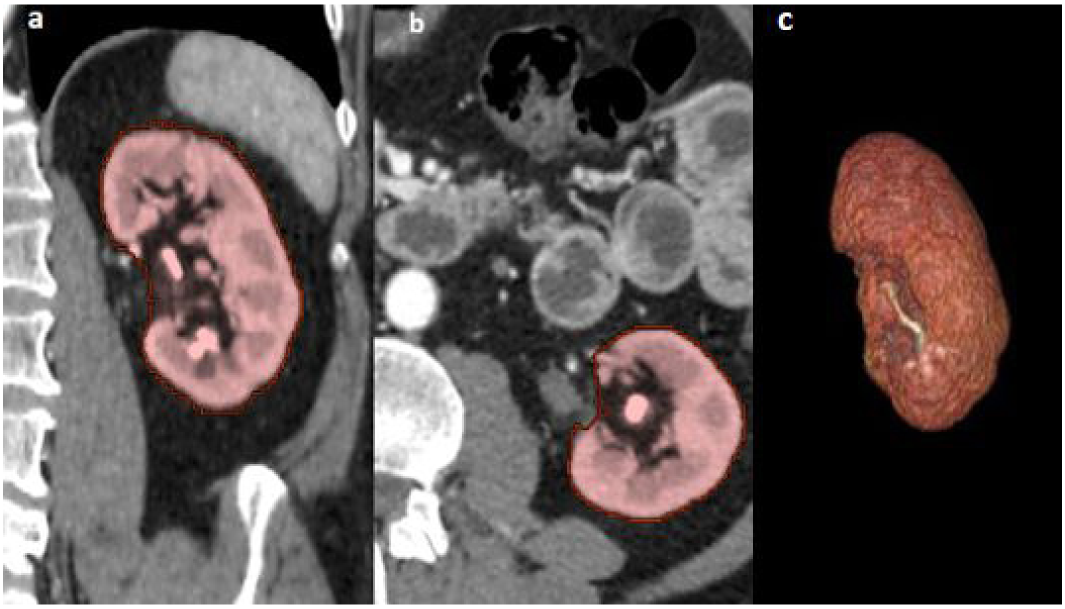
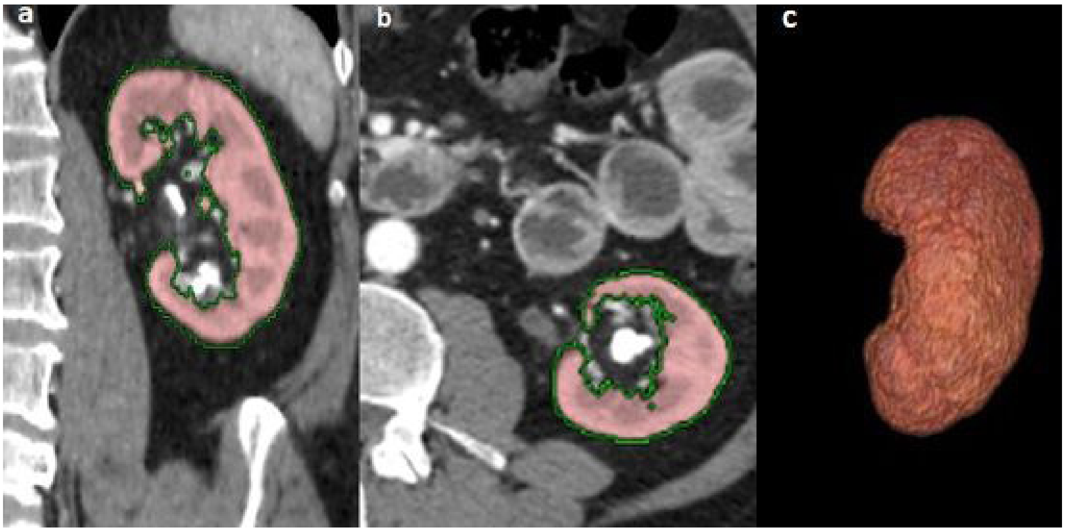


Figure 2. Determination of renal parenchymal borders in axial (a) and coronal (b) sections in computed tomography and three-dimensional view in customized volumetric software (c) to determine Renal Parankimal Volume (RPV)



Statistical Analysis

The coding and statistical analysis of the data were performed on the computer, using the SPSS 22 software (IBM SPSS Statistics, IBM Corporation, Chicago, IL) package program. The compatibility of the variables to normal distribution was examined using Shapiro-Wilk tests. Student's T test and Mann-Whitney U test were used to compare non-categorical parameters between groups. Categorical variables were evaluated with Chi-square or Fisher's exact tests. Decision-making properties of TRV and RPV in predicting RIRS success were analyzed with receiver operating characteristic (ROC) curve at 95% confidence interval. Risk factors for failure in RIRS were determined by univariate logistic regression analysis. The possible factors determined in this analysis were evaluated using the Backward LR method with multivariate analysis to define whether they are independent risk factors or not. The Spearman correlation test was used as the correlation test. The cases with a p value of less than 0.05 were considered statistically significant.

RESULTS

The mean age of 104 patients included in the study was 48.1 ± 14.9. 49 of the patients were male. The success rate was 75.9%. While there was no significant difference between successful and unsuccessful groups in terms of age, gender, laterality, stone density and presence of postoperative complications, the stone burden was higher in the unsuccessful group and this difference was statistically significant (p<0.001). Intraoperative complications were observed in 40 (38.5%) patients, while postoperative complications were observed in 19 (18.3%) patients. While the most common intraoperative complication was hematuria, the most common postoperative complication was high fever. Intraoperative complications were observed higher in the unsuccessful group (64% in the unsuccessful group, 29.4% in the successful group). The demographic and clinical characteristics of patients who underwent RIRS due to a single kidney stone are shown in table 1.

In our study, ROC curves were produced with 95% confidence intervals regarding whether TRV and RPV are determinant factors for success and cut-off points were defined. While TRV was not found to be a predictor of success in RIRS, according to ROC analysis, it was concluded that a RPV>141.3 cm3 is associated with increased success rates (AUC=0.075, p<0.001, 95% CI (0.681-0.872)) (Table 2 and Figure 3).

Moreover, risk factors for the presence of postoperative residual stones in RIRS were revealed with univariate and multivariate logistic regression analyzes using the determined cut-off points. According to logistic regression analysis, elevated stone burden (OR=1.02; 95% CI=1.009-1.03; p<0.001), stone located in the lower pole (OR=31.673; 95% CI=3.315-302.623; p=0.003) and RPV≤141.3 cm3 (OR=5.923; 95% CI=2.886-19.263; p=0.008) were found to be independent risk factors for failure in RIRS (Table 3). Subsequent analysis indicated a positive correlation between RPV and preoperative GFR level (r=0.236, p=0.004).

Figure 3. ROC evaluating the efficiency of total renal volume and renal parenchymal volume in predicting success in retrograde intrarenal surgery

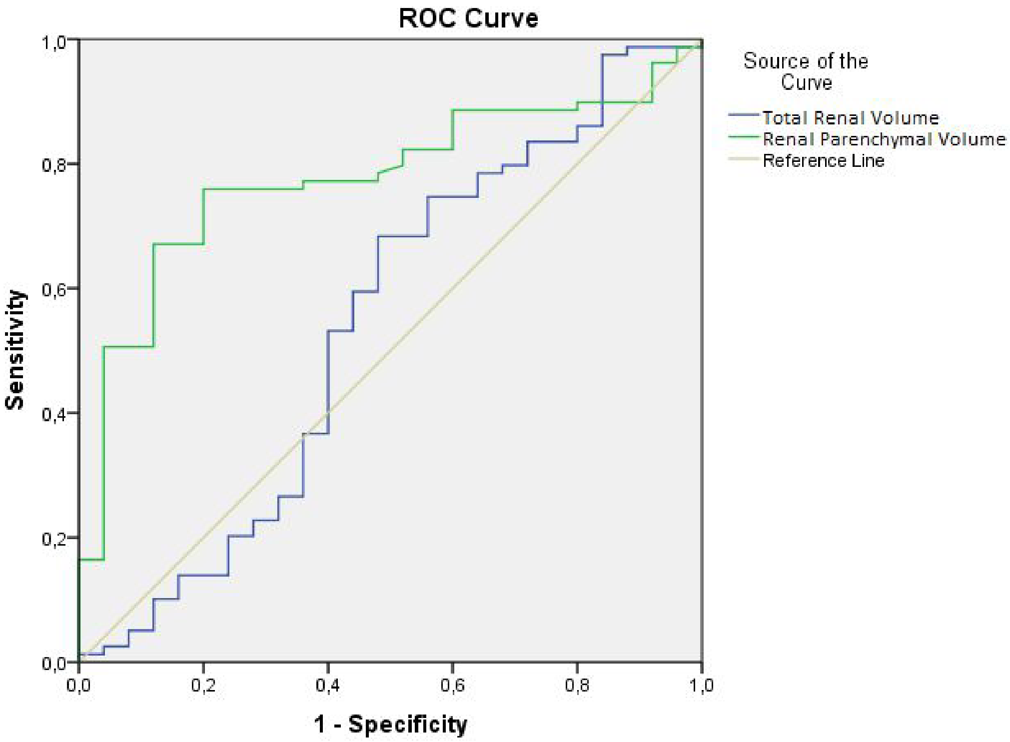


Table 1. The demographic, clinical, and radiological characteristics of patients who underwent retrograde intrarenal surgery

	Total (n=104)	Successful (n=79, % 75.9)	Unsuccessful (n=25, % 24.1)	p
Age (years)	48.1±14.9	47.1±14.8	51.3±14.9	0.829*
Gender				
Male, n (%)	49 (47.1)	39 (49.4)	10 (40)	0.413***
Female, n (%)	55 (52.9)	40 (50.6)	15 (60)	
Laterality				
Right, n (%)	43 (41.3)	35 (44.3)	8 (32)	0.276***
Left, n (%)	61 (58.7)	44 (55.7)	17 (68)	
Stone burden (mm^2) (Mean±SD)	129.7±79.7	124.6±82.6	143.6±76.8	**0.012****
Stone density (HU) (Mean±SD)	921.9±324.5	899.5±320.6	992.6±333	0.819*
Stone localization				
Pelvis, n (%)	45 (43.3)	41 (51.9)	4 (16)	
Upper calyx, n (%)	16 (15.4)	16 (20.3)	1 (4)	**<0.001*******
Medium calyx, n (%)	12 (11.5)	9 (11.4)	2 (8)	
Lower calyx, n (%)	31 (29.8)	13 (16.5)	18 (72)	
Preoperative GFR (ml/min/1.73 m^2)	89±25.8	92.1±26.4	84.7±23.7	0.173**
Intraoperative complications				
None, n (%)	64 (61.5)	55 (69.6)	9 (36)	
Hematuria, n (%)	15 (14.4)	9 (11.4)	6 (24)	
Minimal laceration in mucosa, n (%)	8 (7.7)	6 (7.6)	2 (8)	**0.009*******
Mucosal injury requiring stent, n (%)	11 (10.6)	7 (8.9)	4 (16)	
Need for additional instruments to reach the stone (nitinol basket catheter etc.), n (%)	6 (5.8)	2 (2.5)	4 (16)	
Postoperative complications				
None, n (%)	85 (81.7)	66 (83.5)	19 (76)	
Fever, n (%)	12 (11.5)	9 (11.4)	3 (12)	0.33***
Urinary tract infection, n (%)	4 (3.8)	3 (3.8)	1 (4)	
Sepsis, n (%)	3 (2.9)	1 (1.3)	2 (8)	
TRV (cm^3) (Mean±SD)	222.7±85.3	213.3±54.9	204.4±65.7	0.521**
RPV (cm^3) (Mean±SD)	158±46.4	168.3±46.1	125.5±29.9	**<0.001****

HU: *Hounsfield Unit,* ***GFR****: Glomerular Filtration Rate,* ***TRV:*** *Total Renal Volume,* ***RPV:*** *Renal Parenchymal Volume,* ***SD:*** *Standard Deviation,*
** Student's T Test, ** Mann Whitney U Test, *** Chi-Square Test, **** Fisher's Exact Test*

Table 2. The best cut-off points predicting success for total renal volume and renal parenchymal volume in retrograde intrarenal surgery according to area under the curve ROC at 95% CI.

	TRV (cm^3)	RPV (cm^3)
AUC	0.543	0.775
95% CI	0.398-0.687	0.681-0.872
***p* value**	0.52	<0.001
Cut-off point	195	141.3
Sensitivity	0.624	0.759
Specificity	0.521	0.823

AUC: *Area Under the Curve,* ***CI:*** *Confidence Interval,* ***TRV:*** *Total Renal Volume,* ***RPV:*** *Renal Parenchymal Volume*

Table 3. Evaluation of factors associated with the presence of residual stones in retrograde intrarenal surgery with univariate and multivariate logistic regression analysis

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age (year)	1.019 (0.988-1.051)	0.227		
Gender				
Male	1			
Female	1.462 (0.587-3.647)	0.415		
Laterality				
Right	1			
Left	1.69 (0.653-4.372)	0.279		
Stone burden (mm²)	1.012 (1.007-1.018)	**<0.001**	1.02 (1.009-1.03)	**<0.001**
Stone density (HU)	1.001 (0.999-1.002)	0.212		
Stone localization				
Pelvis	1		1	
Upper calyx	0.641 (0.066-6.177)	0.7	0.13 (0.005-3.293)	0.216
Medium calyx	2.278 (0.36-14.405)	0.382	7.736 (0.585-102.320)	0.12
Lower calyx	14.192 (4.065-49.545)	**<0.001**	31.673 (3.315-302.623)	**0.003**
TRV (cm³)				
>195	1			
≤195	1.388 (0.52-3.704)	0.512		
RPV (cm³)				
>141.3	1		1	
≤141.3	8.632 (2.173-14.233)	**<0.001**	5.923 (2.886-19.263)	**0.008**

HU: *Hounsfield Unit,* ***TRV:*** *Total Renal Volume,* ***RPV:*** *Renal Parenchymal Volume*

DISCUSSION

Our study was designed based on the possible relationship between better kidney function considering better diuresis, and better RIRS success in patients that have larger kidney volumes with nephrolithiasis. It is known that kidney volume as a marker of nephron mass has the highest estimated value compared to other predictors (7). By measuring RPV and TRV, particulars about nephron mass, split kidney function and diuresis can be obtained. In this study, we aimed to evaluate whether RPV and TRV have an effect on success rates in patients who underwent RIRS owing to a single kidney stone. According to our results, there was no relationship between TRV and RIRS success, while RPV≤141.3 cm3 was found to be an independent risk factor for the presence of residual stones after RIRS, and it was concluded that the probability of failure increased 5.9 times.

In RIRS, removing fragmented stones with a nitinol basket is thought to be one of the most important phase that increases the stone-free state rate. However, since this method has complications such as ureteral injury and prolonging the operation time, separating the stones into small fragments and leaving them to spontaneous drainage has become the most preferred method. In this method known as "dusting and fragmentation", the stones are divided into very small fragments and left in place to natural drainage with diuresis at the postoperative period (3). In a study conducted by Lee et al., no difference was found in terms of success between active removal of fragments with a basket and leaving them to natural drainage with diuresis (8). It is known that RPT is associated with renal function (9).

Considering SWL, there are many studies revealing that there is a relationship between better kidney function, including increased diuresis by using diuretics as well, and stone-free rates. (4,5). However, according to our literature review, there is only one study assessing the relationship between renal parenchyma and success rates in RIRS. In a study conducted by Koc et al., it was shown that the probability of failure increased 5.6 times in RIRS cases with RPT≤ 19 mm (6). However, we think that RPT may be limited in evaluating the renal parenchyma. As a matter of fact, in this study, the authors argued that kidney function can be predicted more accurately with RPV. In addition, TRV was also evaluated in our study. The results of our study showed that RPV is a factor affecting the success rate of RIRS. We believe that the insufficiency of TRV in predicting success is because of the collecting system dilatation caused by obstruction of the kidney stone. When the collecting system, which does not have a functional part in urine production, is taken into consideration, it is obvious that the renal volume unfit to predict the drainage and clearance of stone fragments by diuresis.

Patients that have an ineffective RIRS procedure, may face with urinary tract infection, renal colic and steinstrasse due to residual stones; thus, re-intervention may be required. Recurrence occurs in about half of these patients within 5 years and in 80% within 10 years. The presence of residual stone fragments is associated with a higher rate of recurrence, and this situation brings a large economical burden (10). Our study is the first study to indicate that RPV is associated with RIRS success. Patients that may have an ineffective RIRS procedure can be predicted before the operation. Thus, re-intervention and economic burden might be reduced.

There are many studies in the literature about the factors affecting the success of RIRS, and the success rate has been reported to be 50-94.2% (11). It has been stated that stone burden is the most important factor in predicting RIRS results, and the possibility of residual stone and the need for additional sessions increase as the stone size increases (12,13). In one study, 279 patients who underwent RIRS were evaluated and the success rate was found to be 84.4% for kidney stones 2 cm (14). In the study of Resorlu et al. it was stated that 63% of stone-free patients had stone size <15 mm, whereas in the unsuccessful group, the stone size was ≥15 mm in all patients (15).In our study, the success rate was found to be 75.9%, in accordance with the literature. Stone burden was defined as the area in two-dimensional mm2 determined by multiplying the longest diameter and the vertical diameter of the stone, with an average stone burden of 129.7±79.7 mm^2 . It has been indicated that the increase in stone burden reduces the success of RIRS.

In a study of 219 patients in which the effect of stone density on stone-free rates was examined, no relationship was found, but it was found that the stone density was inversely related to the operation time and fragmentation efficiency (16). In a study by Gucuk et al., stone density had no effect on the stone-free rate in RIRS procedure (17). In our study, the mean stone density was 921.9 ± 324.5 HU and no relationship was found between stone density and stone-free rate.

The localization of the stone in the kidney has also been evaluated in terms of being a factor affecting the success. In one study, while the success rate of the RIRS was found to be 74.1% for lower pole stones, it was shown that this rate was 78% in other localizations and there was no significant difference between them (p=0.224) (18). On the contrary, Lim et al. stated that the success rate of RIRS for lower pole stones (73.3%) was lower than for upper pole, middle calyx and pelvic stones (94.4%) (19). In our study, we found that the possibility of residual stones in lower pole stones was 14.2 times higher than in pelvic stones.

Our study has some limitations. First of all, it has been designed retrospectively. Secondly, there is no postoperative data of the amount of urine to demonstrate the postoperative diuresis status of the patients. Nonetheless, our study will contribute to the literature as it is the first study evaluating the effect of RPV on RIRS success.

CONCLUSION

Consequently, RPV≤141.3 cm3 might be considered as a parameter that increases the success of RIRS. However, a similar relationship was not found between total renal volume (TRV) and RIRS success. This inconvenience could be explained by the fact that the parenchyma is the part of the kidney that is responsible for diuresis. RPV measurement may be applied as a new parameter and could be included in the factors predicting the RIRS success. It may be appropriate to evaluate it preoperatively in order to choose the proper surgical treatment procedure or lithotripsy method for patients that have kidney stones.

Conflict of Interest: The authors declare to have no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

Ethical Approval: The study was approved by the Ethics Committe of Ankara State Hospital (No: E1-20-1200, Date: November 11, 2020). The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

Author Contributions: Conception and design; Taştemur S; Ölçücüoğlu E; Uzun E, Data acquisition; Şenel S, Data analysis and interpretation; Taştemur S; Ölçücüoğlu E; Uzun E, Drafting the manuscript; Şenel S; Kasap Y, Critical revision of the manuscript for scientific and factual content; Taştemur S; Uzun Y, Statistical analysis; Şenel S, Supervision; Kasap Y; Uzun E.

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