











## PREDICTION OF POSSIBLE FACTORS THAT AFFECT STONE-FREE RATE OF RETROGRADE INTRARENAL SURGERY; A MULTICENTER STUDY

### Retrograd İntrenal Cerrahi'de Taşsızlığı Öngören Faktörler; Çok Merkezli Bir Çalışma

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#### Abstract

**Aim:** The aim of the study was to evaluate possible factors predicting stone-free status at retrograde intrarenal surgery for renal stones.

**Materials and Methods:** A retrospective multicenter study was performed using data from 513 patients treated between February 2016 and January 2020 at four referral centers in Turkey. The patients were divided into two groups whether they had no residual stone over 3 mm (Group 1) or had residual stones (Group 2). Pre and peroperative parameters were compared in both groups (Table 1). Univariate and multivariate analyzes were performed to identify any factors affecting the stone-free rate (Table 2).

**Results:** Overall stone-free rate was 88.5% (454/513). Lower calyx stones and multipl stones were significantly higher in Group 2 (p=0.006, p=0.02, respectively). Also access sheathless procedure rate was significantly higher and the basket catheter useage rate was significantly lower in Group 2 (p=0.04, p<0.001, respectively) (Table 1). Multiple stone presence and basket catheter usage during the procedure were found as independent factors to predict the stone-free status of Retrograde Intrarenal Surgery according to the results of logistic regression analysis (95%CI 3.3577-0.9999; H-L p= 0.05 and 95%CI 0.4442-0.1290; H-L p< 0.001, respectively) (Table 2).

**Conclusion:** The presence of multiple stones in preoperative imaging and the use of basket catheters peroperatively are independent factors predicting stone-free status in Retrograde Intrarenal Surgery. The presence of multiple stones increases the probability of residual stones after the procedure, while the use of basket catheters is to reduce this possibility.

**Keywords:** Kidney stone, retrograde intrarenal surgery, stone-free.

#### Öz

**Amaç:** Bu çalışmanın amacı Retrograd İntrenal Cerrahi'de taşsızlığı öngören olası faktörleri araştırmaktır.

**Materyal ve Metot:** Şubat 2016-Ocak 2020 tarihleri arasında Türkiye'deki dört ayrı merkezde tedavi edilen 513 hastanın verileri kullanılarak retrospektif çok merkezli bir çalışma gerçekleştirildi. Hastalar 3 mm'nin üzerinde rezidü taş saptananlar (Grup 1) ve rezidü taş saptanmayanlar (Grup 2) olmak üzere iki gruba ayrıldı. Pre ve peroperatif parametreler her iki grupta karşılaştırıldı (Tablo 1). Taşsızlık oranını etkileyen faktörleri araştırmak için univariate ve multivariate analizler yapıldı (Tablo 2).

**Bulgular:** Toplam taşsızlık oranı % 88.5 idi (454/513). Alt kaliks taşları ve multipl taşlar Grup 2'de anlamlı olarak daha yüksekti (sırasıyla p = 0.006, p = 0.02). Ayrıca erişim kılıfsız prosedür oranı Grup 2'de anlamlı olarak yüksek ve basket kateter kullanım oranı anlamlı olarak düşüktü (sırasıyla p = 0.04, p <0.001) (Tablo 1). İşlem sırasında çoklu taş varlığı ve basket kateter kullanımı lojistik regresyon analizi sonuçlarına göre Retrograd İntrenal Cerrahi'de taşsızlığı öngörmeye bağımsız faktörler olarak bulundu (% 95 CI 3.3577-0.9999; HL p = 0.05 ve % 95 CI 0.4442-0.1290; HL p < 0.001) (Tablo 2).

**Sonuç:** Ameliyat öncesi görüntülemeye çoklu taş varlığı ve basket kateterlerin peroperatif olarak kullanılması Retrograd İntrenal Cerrahi'de taşsızlık durumunu öngören bağımsız faktörlerdir. Multipl taş varlığı işlemde rezidü taş olasılığını artırırken, basket kateterlerinin kullanımı bu olasılığı azaltmaktadır.

**Anahtar Kelimeler:** Böbrek taşı, retrograd intrarenal cerrahi, taşsızlık.

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## INTRODUCTION

Retrograde Intrarenal Surgery (RIRS) has emerged as a minimally invasive alternative to other traditional treatment options such as open and percutaneous nephrolithotomy in the treatment of renal and upper ureteral stones<sup>1</sup>. It is a very sophisticated method, requires both a high surgeon experience and a wide instrument park (scopes and disposables such as guide wires, access sheaths, baskets). When compared with the other methods, the most important priority of the RIRS is not only higher stone-free rates but also its minimally invasive nature.

The effects of stone and patient related factors on the results of the operation are well known. The surgical success of this operation is directly based on the stone-free status and it is well known that stone related factors such as location, density, and larger stone burden might directly affect the stone-free rates of RIRS. Many scoring systems have been developed based on stone parameters<sup>2</sup>. One of the most important stone related parameter that predicts the results of RIRS is stone burden. However, this limitation was accepted by surgeons as a challenge. The series that force the stone diameters of 2 cm and then 3 cm are reported with the increasing surgical and institution experience following the gradual widespread of the procedure<sup>3,4</sup>. Another trend is to perform RIRS with fewer additional instruments and tools. Increasing data in this area will show the effects of new approaches (radiation-free, sheathless or without basket catheter) on RIRS results. But, studies evaluating surgeon's attitude to using instruments and the stone related parameters together are insufficient in the literature.

The aim of the study was to evaluate possible factors (not only patient or stone related factors but also surgeon's attitude to using instruments) predicting stone-free status after RIRS for renal stones from a multi-center perspective.

## MATERIAL AND METHODS

The data of four different referral centers were analyzed retrospectively. Following the approval of the ethics committee, a multicenter study was planned. Demographic data (age, gender, side), stone properties (stone burden, Hounsfield Unit (HU), localization, multiple stone presence), operation data (preoperative double J stent presence, access sheath, and basket catheter usage), postoperative residual stone status were recorded.

All patients underwent computed tomography in the primary evaluation before the operation. The largest stone diameters were measured for stone burden. The highest HU value in computed tomography (CT) bone window value was used for stone density. Preoperative urine cultures of all patients were sterile. All patients received antibiotic prophylaxis with second or third-generation cephalosporin. Stone-free status was evaluated by fluoroscopy early perioperatively and postoperatively by kidneys, ureters, and bladder (KUB) imaging, ultrasonography (US), CT or direct examination with second-look flexible ureterorenoscopy during stent removal. Fragments larger than 3 millimeters were considered as residual stones.

## Study Population

The study was performed using data from 513 patients treated between February 2016 and January 2020 at four referral centers in Turkey (Tekirdağ, İstanbul, Çanakkale, Zonguldak). The patients were divided into two groups whether they had no residual stone over 3 mm (Group 1) or had (Group 2). Preoperative and peroperative parameters were compared in both groups. Univariate and multivariate analyzes were performed to identify any factors affecting the stone-free rate.

## Objectives

The primary objective of the study was to investigate the presence of independent patient, stone or surgery-related factors predicting stone-free status in RIRS.

## Statistical Analysis

Normality of the variables were checked by Kolmogorov-Smirnov test. The Chi-Square and Fisher exact tests were used for the difference between the categorical parameters and Mann-Whitney U test was used for the difference between the continuous variables. Multivariate analysis was performed using the logistic regression test. Also, relative risk (RR) and odds ratio (OR) calculations were made regarding the statistically significant factors. All statistical analyses were performed using the SPSS Statistics version 24 (IBM, Armonk, NY, USA) software. P value lower than 0.05 was considered as statistically significant.

## RESULTS

The overall stone-free rate was 88.5% (454/513). Two groups were similar in terms of age ( $48.7 \pm 14.2$  vs  $47.8 \pm 13.9$  years) and gender (57.5%/42.5% vs 59.3%/40.7% male/female ratio) distributions. In addition, some stone parameters (stone burden, side, density) were similar ( $13.6 \pm 5.9$  vs  $14.7 \pm 7.1$  mm, 48.8%/51.2% vs 52.5%/47.5% right/left ratio and  $1013 \pm 326$  vs  $1007 \pm 303$  HU, respectively). There was no statistically significant difference between the two groups in terms of age, gender, side, stone burden, mean HU, and preoperative double j stent presence ( $p=0.67$ ,  $p=0.79$ ,  $p=0.58$ ,  $p=0.33$ ,  $p=0.63$  and  $p=0.54$ , respectively). Lower calyx stones and multiple stones were significantly higher in Group 2 ( $p=0.006$ ,  $p=0.02$ , respectively). Also access sheathless procedure rate was significantly higher and the basket catheter usage rate was significantly lower in Group 2 ( $p=0.04$ ,  $p<0.00001$ , respectively) (Table 1). Multiple stone presence and basket catheter usage during the procedure were found as independent factors to predict the stone-free status of Retrograde Intrarenal Surgery according to the results of logistic regression analysis (95%CI 3.3577-0.9999; H-L  $p=0.05$  and 95%CI 0.4442-0.1290; H-L  $p=0.00001$ , respectively) (Table 2).

The residual stone risk in the interventions without basket catheter increased more than 3 times compared to the other group ( $p<0.00001$ , RR=3.19, OR=3.84). The residual stone risk after access sheathless RIRS was more than doubled compared to the other group ( $p=0.036$ , RR=2.17, OR=2.52). In addition, the relative risks of stone-related factors in which statistically significant differences were obtained (multiple stone presence and lower calyx localization), were lower than those mentioned above (RR =1.75,  $p=0.02$ , and RR=1.94,  $p=0.006$ , respectively).

**Table 1.** Change in patient pre/per-operative characteristics according to results

Characteristic	Stone-Free	Residual Stone	p value
Number	454	59	
Age (year, mean)	48.7±14.2	47.8±13.9	0.67*
(median, range)	50 (14-86)	49 (17-80)	
Gender			
Male	261/454 (57.5%)	35/59 (59.3%)	0.79
Female	193/454 (42.5%)	24/59 (40.7%)	
Side			
Right	221/454 (48.8%)	31/59 (52.5%)	0.58
Left	233/454 (51.2%)	28/59 (47.5%)	
Stone Burden (mm, mean)	13.6±5.9	14.7±7.1	0.33*
Hunsfield Unit (mean)	1013±326	1007±303	0.63*
Localisation			
Lower Calyx	135/454 (29.8%)	28/59 (47.5%)	0.006
Other	319/454 (70.2%)	31/59 (52.5%)	
Multiple Stone Rate	183/454 (40.3%)	33/59 (55.9%)	0.02
Preoperative Double J Stent	136/454 (29.9%)	20/59 (33.9%)	0.54
Access Sheathless Pro. Rate	23/454 (5%)	7/59 (11.9%)	0.04
Basket Cath. Usage Rate	347/454 (76.4%)	27/59 (45.8%)	<0.00001

\* Mann-Whitney U test, other p values calculated by Chi-square test.

**Table 2.** Results of logistic regression analysis

Characteristic	Coeff.	Standard Errors	p value	Odds Ratios	95% Confidence Limits	
					Low	High
Age	-0.0004	0.0108	0.97	0.9996	0.9786	1.0210
Gender	0.1332	0.3036	0.67	1.1424	0.6302	2.0712
Side	-0.2082	0.2955	0.48	0.8120	0.4550	1.4491
Stone Burden	0.0423	0.0222	0.06	1.0432	0.9987	1.0897
Hunsfield Unit	-0.0000	0.0005	0.99	1.0000	0.9991	1.0009
Localisation	0.4721	0.3076	0.12	1.6033	0.8774	2.9297
Multiple Stone Rate	0.6056	0.3090	0.05	1.8323	0.9999	3.3577
Preoperative Double J Stent	0.1046	0.3205	0.74	1.1103	0.5925	2.0807
Access Sheathless Pro. Rate	-0.4916	0.5142	0.34	0.6116	0.2233	1.6755
Basket Cath. Usage Rate	-1.4298	0.3155	0.00001	0.2393	0.1290	0.4442

## DISCUSSION

Our primary findings are that the presence of multiple stones in preoperative imaging and usage of basket catheters peroperatively are independent factors predicting stone-free status in RIRS. Despite strong statistical differences, a higher clinical significance has been attributed to the use of basket catheters from these two independent predictive factors. Because multiple stone presence is a factor that we cannot change, but the use of a basket catheter is a habit that can be achieved by changing our attitude towards the RIRS. Using a basket catheter may increase the cost of the operation, but it reduces the financial burden on the general health system (by reducing the need for additional hospital visits, treatment or intervention)<sup>5,6</sup>.

There is strong evidence in the literature in favor of basket catheter usage. The results of 67 procedures using basket catheters and 50 procedures without basket catheters during endoscopic stone surgery were compared in a study conducted in Japan in 2013. Stone-free rates of the group using basket catheter were reported to be significantly higher than the other group (88% vs 76%, p = 0.04). Early (intraoperative) stone-free rates of the group without basket catheter were much lower (43% vs 71%, p=0.002)<sup>7</sup>. Even though some of the fragments that are thought to small enough to the spontaneous passage, it is possible to say that the stone-free rates do not reach the rates provided by the basket catheter usage.

Surgeons with increasing RIRS experience tend to perform the procedure without using instruments such as fluoroscopy, access sheath, and basket<sup>8,9</sup>. Especially developing LASER technologies force

urologist to use fewer additional instruments such as fluoroscopy, access sheath or basket catheter during RIRS. With the new 120 Watt LASERs, the stones can be completely powdered<sup>10</sup>.

On the other hand, stone sampling with a basket catheter is important in planning preventive metabolic treatments, especially for patients who are recurrent stone-formers or children. As the stones get smaller, they move more and it becomes difficult to completely dusting. Meanwhile, LASER-induced mucosal injuries may occur. We advocate using basket catheters for all these medical, financial, and perhaps ethical reasons.

Another remarkable result we obtained in our study was related to the use of an access sheath. Access sheath usage was significantly higher in stone-free patients than patients had residual stones (95% vs 88.1%,  $p = 0.04$ ). However, this difference obtained with univariate analyzes could not be confirmed by multivariate analysis ( $p = 0.34$ ). This suggests that the difference is dependent on other factors. A large meta-analysis in 2018 did not show the advantage of using ureteral access sheath<sup>11</sup>. It was even emphasized that the use of access sheath increases the risk of postoperative complications (OR=1.46). Although previous studies reported high complication rates related to access sheath, it has been shown in a recent prospective study that endoscopically visible injuries associated with ureteral access sheath placement do not correlate with increased risk of stricture on intermediate-term follow-up<sup>12</sup>.

When we put the statistically significant factors to risk analysis, we found that the factors that arise from the surgeon's attitude about using instruments (access sheath or basket catheter usage) have higher relative residual stone risks than the stone related factors (multiple stone presence and lower calyx localization)(RR=2.17, RR=3.19 vs RR=1.75, RR=1.94, respectively). The residual stone risks after RIRS that occurred when the access sheath or basket catheter were not used were higher than the risks caused by the patient having multiple or lower calyx stones. These results show that the use of basket catheter and ureteral access sheath is one of the indispensable principles of Retrograde Intrarenal Surgery.

The study has some limitations that need to be considered. First, this is a retrospective study causing missed data which can affect the results by reducing the size and power of the study. Second, though all surgeons had a minimum of 5 years of experience, the variation of surgeons and hospitals might affect surgical outcomes. However, we think that this high-volume multicenter study is very important to show the importance of proper surgical equipment utilization and the impact of the stone related parameters whether these parameters decrease stone-free status or not.

## CONCLUSIONS

The presence of multiple stones in preoperative imaging and the use of basket catheters preoperatively are independent factors predicting stone-free status in RIRS. The presence of multiple stones increases the probability of residual stones after the procedure, while the use of basket catheters reduces this possibility. Also, the rate of lower calyx stone and access sheathless procedure is higher in patients with residual stones than stone-free patients.

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**Conflict of Interest**

The authors declare no conflicts of interest.

**Kaynaklar**

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