## Safety and Efficacy of RIRS in Geriatric Patients: A Comparative Evaluation on an Age Based Manner

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Purpose: In this retrospective study, we aimed to comparatively evaluate the efficacy and safety of RIRS procedure on an age-based manner in patients younger and above 65 years.

Materials and Methods: A total of 165 patients undergoing RIRS procedure for renal stones were divided into two groups on an age-based manner namely; Group 1 (n=122) patients aging < 65 years and Group 2 (n=43) patients aging above 65 years. Demographic and clinical data regarding the stone free rates, complication rates and need for secondary procedures were retrospectively evaluated.

Results: Of all the patients undergoing RIRS for kidney stones, 122 were below the age of 65 (73.9%) and 43 were above the age of 65 (26.1%). Mean age value for the patients aging more than 65 years was  $74.16 \pm 5.03$  years and in addition to higher percentage of comorbidities, serum creatinine levels as well as ASA scores were also higher in this group when compared with younger counterparts. Although there was no statistically significant difference with respect to the operative duration, stone-free rates (SFR) and hospitalization period between the two groups, both complication rates and the need for additional interventions were higher in the older patient group (p = 0.038; p = 0.032). All complications noted in the both groups were minor (Grade I) complications according to the Clavien classification system.

**Conclusion:** RIRS procedure can be applied as an effective and safe treatment alternative for the minimal invasive management of renal stones in relatively older patients (> 65 years) with similar hospitalization as well as stone free rates noted in the younger patients. No procedure related severe complication was noted in these cases.

Keywords: geriatric patients; renal stones; RIRS

## **INTRODUCTION**

ublished data clearly point out that the population above the age of 60 years will have surpassed 2 billion by the year  $2050^{(1)}$ . As a result of the increase in this age group the prevalence of urolithiasis is also expected to increase to the levels of 10-12% in the near future<sup>(2)</sup>. Aging population will suffer from decreased functional reserves in different organ systems and associated comorbidities with aging will cause certain problems that could be encountered either in the perioperative and/or postoperative follow-up periods after certain treatment approaches<sup>(3)</sup>. Additionally, decreased cardiopulmonary and renal functional status in geriatric patients may also lead higher rate of complications associated with major surgeries making it difficult to cope with the perioperative problems when compared with the younger cases<sup>(4)</sup>. As the least invasive method available so far, extracorporeal shock wave lithotripsy (SWL) is a commonly performed treatment alternative for kidney stones compared to other endourological approaches. Despite its well-known advantages, this technique requires repeated treatments which may commonly be associated with colic pain during the passing of fragmented stones causing discomfort to the patients. In light of these disadvantages and the advances in endoscopic technology, other minimally invasive endourologic methods with high stone-free and acceptable complication rates have been introduced into the clinical practice in the last two decades<sup>(5)</sup>. Of these procedures, despite its markedly higher stone-free rates particularly for stone sizing smaller than 2 cm, percutaneous nephrolithotomy (PCNL) procedure may be associated with certain severe complications such as bleeding requiring transfusion, visceral organ damage and hydrothorax in the perioperative/postoperative period<sup>(6)</sup>. Such complica-tions may be associated PCNL method with a higher percentage particularly in geriatric patients presenting with higher comorbidities

Retrograde intrarenal surgery (RIRS) has become popular in the minimal invasive management of renal calculi in the last two decades due to its higher stonefree rates than SWL, particularly for lower pole stones, and significantly lower morbidity than PCNL<sup>(8)</sup>. Due to the certain advantages of this approach such as similar success as well as lower complication rates along with the shorter hospitalization period currently RIRS

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	Group 1 (age<65)	Group 2 (age≥65)	р
Age, Mean ± Std (minmax.)	41.4 ± 15.97 (19-65)	74.16 ± 5.03 (65-86)	< 0,001*
Sex, (Male/Female)	70/52	20/23	0.482
Stone Burden, (mm <sup>2</sup> ) Mean±Std (minmax.)	222.16 ± 101.9 (74-460)	227.88 ± 57.24 (132-378)	0.653
Side, (right/left)	63/59	15/28	0.036*
Localization,	45 (36)	17(39.5)	0.673
<ul> <li>Renal pelvis, n (%)</li> </ul>	22 (18)	6 (13.9)	
<ul> <li>Upper calyx, n (%)</li> </ul>	29 (24)	6 (13.9)	
<ul> <li>Middle calyx, n (%)</li> </ul>	26 (22)	14(32.5)	
<ul> <li>Lower calyx, n (%)</li> </ul>			
Number and rate of cases with multiple stones, n (%)	51/122 (41.8)	21/43 (55.8)	0.27
Stones' Hounsfield Units (HU), Mean±Std (minmax.)	896,83±323,25 (260-2010)	834.35±292.16 (307-1530)	0.334
≥3 ASA score, n (%)	7 (5.7)	15 (34.8)	< 0.001*
Presence of hyperlipidemia, n (%)	18 (14.7)	15 (34.8)	0.005*
Presence of coronary artery disease, n (%)	9(7.3)	14 (32.5)	< 0.001*
Presence of diabetes, n (%)	27 (22.1)	19 (44.1)	0.038*
Presence of hypertension, n (%)	34 (27.8)	31 (72.1)	< 0.001*
Presence of chronic kidney disease, n (%)	0 (0)	7 (16.2)	0.003*
Presence of anticoagulant use, n (%)	9 (10.6)	14 (32.5)	0.004*
Presence of hydronephrosis, n (%)	39 (31.9)	16 (37.2)	0.598

Table 1. Demographic as well as stone related	l characteristics of patients undergoing RIRS.
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\* p < 0.05: statistically significant

is being recommended as the primary treatment modality particularly for kidney stones smaller than 20 mm<sup>(9)</sup>. In the light these advantages and the accumulated experience so far, endourologists began to perform RIRS procedure more commonly also in the older population as a minimal invasive method to limit the likelihood of complications associated with SWL as well as PCNL approaches. Although limited, RIRS has been used in older cases with varying success rates as reported in the literature, there is really very limited data in the published literature comparing the safety and efficacy of this approach in older population on an age based manner. In this present retrospective study we aimed to evaluate the effectiveness and safety of the RIRS technique in the minimal invasive management of renal stones in older patients (> 65 years) compared to their relatively younger counterparts.

# MATERIALS AND METHODS

A total of 165 cases with kidneys stones have been managed with RIRS method between 2017 January-2018 May and the data obtained from departmental files at the Department of Urology at Cumhuriyet University Health Sciences Practice and Research Hospital were evaluated in a retrospective manner. Depending on the age interval, patients undergoing this procedure were divided into two groups as follows; Group 1 (n = 122) including the patients below the age of 65 years and Group 2 (n = 43) patients above the age of 65 years. All patients were well evaluated well with respect to their demographic characteristic, medical comorbidities, American Society of Anesthesiologists (ASA) scores, anticoagulant therapy use, number and stone size, presence of hydronephrosis, preoperative serum creatinine and hemoglobin levels, use of ureteral access sheath (UAS), operative time, complication as well as stone-free rates (SFR) and lastly need for additional interventions. In our study, patients who underwent a stone surgery previously were excluded from the study. Preoperative evaluation of the cases included urinalysis, full blood count, serum biochemical evaluation, coagulation tests, and urine culture antibiogram tests. In cases with culture proven urinary tract infections, antimicrobial therapy matching with the antibiogram sensitivity tests was initiated to eradicate the infection and bring the urine sterile prior to the procedure to limit the possible risk of infective complications. A non-contrast computed tomography (NCCT) was performed in all patients to evaluate the stone characteristics and surface area (mm<sup>2</sup>) was calculated by the multiplication of the longest diameters in axial and coronal sections in millimeters. In patients with multiple stones however, data for each stone was calculated individually and the total value was recorded. Last but not least an informed consent form explaining all details related with the application as well as possible complications of RIRS was obtained from all patients and they were informed about the possible need for a multi-stage procedure to obtain satisfactory stone clearance if needed.

Prior to procedure, 1 gr cefazolin via intravenous route was applied for infection prophylaxis. All patients were operated in the lithotomy position under general anesthesia. Based on the surgeon's preference and experience, UAS (11.5/9.5 Fr 45/55 cm) was passed over the guidewire into the ureter before lithotripsy by using 200-µm Holmium: YAG Laser (StoneLight® Holmium Laser System; AMS Inc., Minnetonka, MN, USA) accompanied by a 7.5 Fr flexible ureterorenoscope (Storz Flex-X2, Tuttlingen, Germany). Laser lithotripsy was applied using values between 1.0 - 1.5 Joule and 8 -10 Hz. In the end of laser lithotripsy, stone fragments < 2 mm that could be passed spontaneously were left to remain in the collecting system while fragments > 2mm were extracted using a basket in the presence of a UAS. In the end of the operation, 4.8 F Double-J (DJ) stents were routinely inserted to all patients which was planned to be removed after 3 weeks postoperatively. In both groups: patients DJ stents' were removed under local anesthesia.

The operative time was calculated as the time between the introduction of the cystoscope into the urethra and the insertion of the DJ stent into the ureter after the procedure. Intraoperative and postoperative complications were evaluated and noted based on the modified Clavien classification system<sup>(10)</sup>.

Although patients were evaluated and followed by plain abdominal film as well as urinary sonography at regular

Table 2. Procedure related (su	access and complication rates	s) findings and need for add	itional interventions in r	patiens underoing RIRS.

	Group 1 (age<65)	Group 2 (age $\geq$ 65)	р
Preoperative hemoglobin value (mg/dL) Mean ± Std (minmax.)	14.42 ± 1,62 (10.7-18.2)	13.76 ± 1,85 (8.8-17.5)	0.057
Postoperative hemoglobin value (mg/dL) Mean ± Std (minmax.)	13.98 ± 1.57 (10.9-17.4)	13.49 ± 1.73 (9.8-17.8)	0.082
Percent change of hemoglobin value (mg/dL) Mean ± Std (minmax.)	$-0.03 \pm 0.03$ (-0.13-0.4)	$-0.02 \pm 0.05$ (-0.10-0.23)	0.175
Preoperative serum creatinine value (mg/dL) Mean ± Std (minmax.)	$0.98 \pm 0.29 \ (0.23 - 1.82)$	$1.23 \pm 0.64 \ (0.7-3.72)$	< 0.001*
Postoperative serum creatinine value (mg/dL) Mean ± Std (minmax.)	$0.86 \pm 0.26 \ (0.22 - 1.65)$	$1.09 \pm 0.46 \ (0.59-2.7)$	< 0.001*
Percent change of serum creatinine value (mg/dL) Mean ± Std (minmax.)	-0.10±0.19 (-0.56-0.76)	-0.09±0.15 (-0.58-0.14)	0.197
Operative time (min) Mean±Std (minmax.)	64.8±15.6 (30-90)	67.3±16.2 (50-100)	0.248
Complication rate	4 (3.2%)	5 (11.6%)	
	Fever: 4	Fever: 2	
		Hematuria: 3	0.038*
UAS use, n/total (%)	98/122 (%80.3)	34/43(%79.1)	0.487
Hospitalization time (days), Mean ± Std (minmax.)	$1.4 \pm 0.6 (1-3)$	$1.7 \pm 0.8 (1-4)$	0.162
SFR, n/total (%)	112/122 (91.8)	35/43 (81.4)	0.060
Number and rate of repeated RIRS, n (%)	8 (6.6)	8 (18.6)	0.022*

\* p < 0.05: statistically significant

follow-evaluations, final stone-free status was evaluated by performing a NCCT for during post-operative 3-months follow-up evaluation in all cases. A stonefree state was considered as no remaining residual fragment or the presence of fragments sizing  $\leq$ 3 mm. Patients demonstrating residual fragments were planned to remove these fragments with a second RIRS session. Statistical Methods

Statistical analysis was performed with IBM SPSS Statistics for Windows (Version 22.0). Data was given as mean±standard deviation (Std), minimum and maximum values for continuous variables. The Mann–Whitney U test was used to evaluate numerical variables with a skewed distribution. Categorical variables were compared using chi-square test, while continuous variables were compared using independent sample t-test. For the comparison of hemoglobin and serum creatinine perioperative values, percent changes were calculated according to perioperative measurement as: Percent Change=(Postoperative-preoperative)/preoperative.

Statistical significance was considered at  $P \le 0.05$  level.

#### RESULTS

While the mean age in Group 1 was  $41.4 \pm 15.97$  years (19-64), this value was  $74.16 \pm 5.03$  (65-86) years in Group 2 cases (p < 0.001). Male ratio was 70/122 in Group 1 and 20/43 in Group 2. Stone burden was 222.16  $\pm$  101.9 (74-460) mm2 for Group 1 and 227.88 $\pm$ 57.24 (132-378) mm2 for Group 2; with no statistically significant difference between the two groups (p = 0.653). Patients demographics, stone characteristics as well as the presence and degree of hydronephrosis are summarized in **Table 1**. As demonstrated in **Table 1** again comorbidity rates as well as the use anticoagulant medication were statistically higher in Group 1 when compared with the younger group.

Regarding the procedure related parameters, while the mean operative time was  $64.8 \pm 15.6$  (30-90) minutes in Group 1, this value was  $67.3 \pm 16.2$  (50-100) minutes in Group 2. Additionally, UAS was used in 98 patients (80.3%) in Group 1 and 34 patients (79.1%) in Group 2 with no statistically significant difference on this aspect. There was also no significant difference with respect to the post-operative hospitalization period as demonstrated in **Table 2**. Comparative evaluation of preoperative and postoperative (day 1) serum creatinine levels with significantly higher mean values were found in Group 2 and the type as well as percentage of complications

are given in **Table 2**. Although being minor in nature, complications were observed more common in older patients when compared with the younger counterparts. Evaluation of the final stone-free rates after 3 months did show that although not statistically significant lower success rates observed in Group 1 cases compared to Group 2 (91.8% vs 81.4%; p = 0.060). Last but not least as demonstrated in Table 2 again need for additional RIRS procedures for remaining residual fragments was slightly higher in Group 1 cases (p = 0.022).

#### DISCUSSION

The incidence of urolithiasis is gradually increasing with a prevalence rate of varying between 4-20%<sup>(11)</sup>. Parallel to this fact, the incidence of kidney stones in older patients is expected to rise as result of the increasing elderly population in developed countries among which struvite and uric acid stones are being the more common ones<sup>(12)</sup>. Taking the reported severe complications of PCNL and to a certain extent for SWL approach, as a minimally invasive endourologic approach, RIRS has become a preferred option in the treatment of kidney stones with its acceptable success and limited complication rates particularly in complex situations such as pregnancy, obesity, coagulopathy, skeletal deformities, large kidney stones, calyceal diverticula and kidney anomalies<sup>(13)</sup>. In this present retrospective study we aimed to evaluate the efficacy of RIRS in the older populations namely patients older than 65 years presenting with possible associated problems like ASA scores ≥3, hyperlipidemia, coronary artery disease, diabetes, hypertension, chronic kidney disease, and common anticoagulant use as expected. Our findings did clearly demonstrate that despite relatively lower stone free rates and higher incidence of minor (Clavien grading I) complication rates encountered, RIRS procedure can be applied in patients older than 65 years in a safe and effective manner when compared with younger counterparts. When compared with the other available endourologic stone management techniques (PCNL and SWL) RIRS with its minimal invasive nature enables us to remove the majority of moderate sized stones in one session in the majority of such cases.

Related with this issue, in a study comparing management of moderate sized stones with PCNL and RIRS procedures in geriatric patients, overall SFR following a single-stage procedure were 82.1% and 92.8% respectively for the RIRS and PCNL groups, indicating that

RIRS could be performed in a safe and effective manner in the older patient group as well. In the same study 17.8% of the older patients treated required a second RIRS procedure<sup>(7)</sup>. In our study, the need for a second procedure was determined as 18.6% in the older group. Related with this issue again data reported from experienced centers on flexible URS (fURS) demonstrated similar final SFRs compared with PCNL and lower complication rates associated with shorter postoperative hospitalization period<sup>(3,8,14,15)</sup>. Although studies focusing on the success and safety of RIRS in older patients compared to relatively younger populations are limited, Beradinelli et al. showed that SFR, operative time, UAS use, hospitalization period, and the need for additional procedures were not affected by the patient's  $age^{(16)}$ . Similarly our findings also did not show significant differences with regard to SFR and UAS use where the SFRs were determined as 91.8% and 81.4% for Group 1 and Group 2, respectively. In the light of the data reported in meta-analysis studies including patients undergoing additional interventions; SFRs of 71.5-100% in moderate sized stones and the 91.5 % SFR after a mean of 1.4 RIRS sessions in cases with large stones  $(> 2 \text{ cm})^{(17,18)}$ , despite the need for additional sessions, RIRS can be preferred as a primary treatment for larger stones with higher SFRs than SWL<sup>(19-21)</sup>.

Despite the similar operative duration values in two groups, a higher prevalence of minor (Grade 1 according to Clavien classification) complications such as fever managed with antipyretic agents and postoperative hematuria requiring no erythrocyte replacement have been observed in our cases as demonstrated also in other trials(22. The higher complication rates observed in Group 2 in our study was thought to originate from the hemorrhagic diathesis and associated other comorbidities of the older patients treated. While the overall complication rate for fURS was 3.2 % in younger (< 65 years) cases and this rate was determined as 11.6% for the older group in our study which were certainly were in accordance to the reported percentages in the literature<sup>(3,16,18)</sup>. As mentioned above the number of studies focusing on the safety as well as efficacy of RIRS in older patients is limited and demonstration of no severe complication in both groups is the difference of our data from the other reported ones with notable complications. Regarding the PCNL procedure again, an age value of above 70 was stated to be an independent risk factor for the presence and severity of complications as well as prolonged hospitalization in the CROES Global Study<sup>(23)</sup>. Published data show that while the overall rate of PCNL related complications is 12.5% in the general population and 8.3% of these are higher than Grade 1 requiring intervention, the complication rate was reported to be 17.5% in older patients which is significantly higher than noted in our older patients<sup>(22,2)</sup>

In our study, additional RIRS was performed 18.6% in older patients for the residual fragments and the possible causes could be restricted fluid intake and immobilization and low renal function in this age group of cases compared to the relatively younger ones. A review of the literature in this regard reveals that, similar to our results, the need for additional interventions in older patients treated with fURS was connected to prolonged operative times in the first session, large stones, and the decisions of the physician or the patient<sup>(7)</sup>.

Our study has certain limitations where the retrospec-

tive design is the major one. Additionally, the limited number of cases included, inability to evaluate the need for postoperative analgesia and pain scores and the lack of stone analysis are the additional limitations. However, taking the limited number of studies focusing on the safety and efficacy of RIRS in older cases (particularly in a age based comparative manner as performed in our study) our results will be contributive enough to the existing limited data in the literature. We certainly think that further confirmed by prospective and multicenter studies with larger series of cases on this topic are certainly needed.

## CONCLUSIONS

The increased prevalence of stone disease in advanced age and the higher number of comorbidities encountered in these patients complicate the decision making of the urologist for the most appropriate procedure to achieve a successful outcome with limited complications. Our results clearly demonstrated that RIRS could be performed as a safe and effective treatment alternative in the minimal invasive management of moderate sized stones in older patients. Despite the higher percentage of minor complications as well as relatively higher need for additional interventions RIRS in older patients may offer shorter hospitalization duration comparable and acceptable SFRs in elderly patients when compared with other available modalities in this specific population particularly in experienced centers.

### **CONFLICT OF INTEREST**

The authors declare that they have no conflict of interest.

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