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Acute kidney injury following supine mini-PNL versus retrograde intrarenal surgery in patients with renal stones < 3 cm: a prospective comparative study

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Abstract

Background: The purpose of the current study was to prospectively compare mini-PNL and RIRS for development of acute kidney injury (AKI), success, and complication rates in a cohort of patients with kidney stones less than 3 cm.

Methods: In this prospective study, data of 60 consecutive patients underwent mini-PNL ($n = 31$) or RIRS ($n = 29$) was investigated. Urinary NGAL levels were measured preoperatively and at postoperative 6th hour to evaluate AKI. Success and complication rates were also compared.

Results: The mean stone size was significantly higher in the mini-PNL group (24.6 mm vs. 18.2 mm, $p = 0.02$). The mean postoperative NGAL levels were 45.6 ± 12.4 and 48.1 ± 13.6 for the mini-PNL and RIRS groups, respectively. The increase was statistically significant for both groups (p: 0.01). The difference between the two groups for mean postoperative NGAL measurements was not statistically significant ($p = 0.47$). The SFR was significantly higher in the mini-PNL group (96.7% vs. 79.3%, $p = 0.04$). The complication rates were similar for the two groups ($p = 0.99$). The mean duration of operation was 48.2 ± 22.5 min in the mini-PNL group and 62.6 ± 18.1 min in the RIRS group ($p = 0.03$). The median duration of hospitalization was 1 day for both groups.

Conclusions: In patients with renal stones < 3 cm in diameter, mini-PNL in supine position provides higher SFR and shorter operative times with similar rates of complications and AKI when compared with RIRS. Mini-PNL should be considered as the primary treatment option together with RIRS for renal stones and should not be ruled out for being a more invasive option.

Keywords: Percutaneous nephrolithotomy, Retrograde intrarenal surgery, NGAL, Acute kidney injury

1 Background

Retrograde intrarenal surgery (RIRS) and percutaneous nephrolithotomy are recommended as the main surgical treatment options for management of renal stones by the recent EAU and AUA guidelines [1, 2]. These two options have unique advantages over each other and were compared in a recent meta-analysis [3]. In this meta-analysis, the authors concluded that large bore percutaneous nephrolithotripsy (PNL) provides higher stone free rates (SFR) over RIRS at the expense of increased morbidity and SFR of the RIRS was higher than minimally invasive PNL (mini-PNL) [3].

The main objective of stone surgery is to provide a stone free status with maximal safety and least amount of kidney injury. Determination of the possible amount of kidney injury is important and biomarkers such as Neutrophil gelatinase-associated lipocalin (NGAL), Kidney injury molecule-1 (KIM-1), liver fatty acid binding

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protein (L-FABP) have been reported to be used for this purpose. NGAL has been studied as a biomarker of acute kidney injury (AKI) related to urinary stones [4] and NGAL levels were shown to increase after both PNL and ureterorenoscopy [5, 6]. PNL has the potential to cause AKI by renal parenchymal penetration [6] and RIRS results in elevated intrarenal pressures and therefore AKI [5].

Although mini-PNL and RIRS have established their role in the management of kidney stones with well-documented outcomes, the current existing literature lacks studies comparing RIRS and PNL in terms of AKI with biomarkers in addition to complication and success rates. The purpose of the current study was to prospectively compare mini-PNL and RIRS for development of AKI, success and, complication rates in a cohort of patients with kidney stones less than 3 cm.

2 Methods

In this prospective study, data of 60 consecutive patients that underwent mini-PNL ($n=31$) or RIRS ($n=29$) and consented for the study between March 2019 and June 2019 was investigated. All of the procedures were performed by a single experienced surgeon with expertise of > 150 PNL and RIRS cases annually.

2.1 Inclusion and exclusion criteria

All of the patients were scheduled for active stone removal for stones < 3 cm in greatest diameter by mini-PNL or RIRS. The cut-off value of 3 cm was determined with respect to the institutional policy of performing RIRS for stones < 3 cm in diameter. All patients were evaluated with a non-contrast computerized tomography (NCCT) prior to surgery. The choice of the surgical method was decided by the surgical team with collaboration of the patients for their expectations without randomization. All of the patients were free of urinary tract infection verified by sterile urine cultures and all patients had normal preoperative serum creatinine levels. Patients with active UTI or elevated creatinine levels were excluded from the study for standardization. All patients underwent surgery for only kidney stones and none of the patients had concomitant ureteral stones. All patients included in the RIRS group were operated with proper placement of a ureteral access sheath. We excluded patients in whom access sheath could not be placed for the sake of standardization as the intrarenal pressure is the hypothesized surrogate for AKI in RIRS cases.

2.2 Surgical procedures

Mini-PNL cases were performed in Galdakao-Modified Supine Valdivia position. Initially cystoscopy was performed and a ureteral catheter was placed in the ureter and retrograde pyelogram was performed by injection of the radiopaque contrast material. Renal puncture was performed with aid of fluoroscopy and a hydrophilic guidewire was placed in the collecting system. The MIP-M kit (Karl Storz, Tuttlingen, Germany) was used for mini-PNL cases. One shot dilation with 15 Fr metallic dilator was performed and 16 Fr metallic sheath was placed. 12 Fr nephroscope was introduced and laser lithotripsy was performed in all cases. For active stone clearance vacuum cleaner effect was applied [7]. Nephrostomy tube was not placed in any of the cases and a 6 Fr JJ stent was placed in all of the cases.

RIRS case were performed in lithotomy position. A hydrophilic guidewire was placed in the ureter and a 9.5/11.5 Fr ureteral access sheath (Cook, Flexor®, Bloomington, IN, USA) was introduced over the guidewire under fluoroscopic guidance. A fiberoptic flexible ureterorenoscope (FLEX-X2, Karl Storz, Tuttlingen, Germany) was used and stones were fragmented by holmium laser. The main strategy was to dust the stone to tiny particles that can pass spontaneously and in case of small fragments active stone retrieval was also performed by a nitinol basket. A JJ stent was placed in all of the cases following the procedure. Irrigation during both PNL and RIRS procedures was performed with gravity and no active manual or automized pumping system was applied. The height of the saline bag was fixed in less than 50 cm.

At the beginning of the procedure cystoscopy was performed in all patients for ureteral catheterization and the baseline urine samples (0 h) for measurement of NGAL levels were collected through the cystoscope. The second urine samples were collected at the postoperative 6th hour. The urine samples were stored at—80 °C until analysis. NGAL levels were measured by the chemiluminescence microparticle immune assay using the Abbot Architect i1000 immunology analyzer with a commercially available kit (Abbott Ireland Diagnostic Division, Sligo, Ireland).

The other parameters collected were age, gender, stone diameter, duration of operation, duration of hospitalization, perioperative complications, SFR, and auxiliary procedures. Residual fragments were evaluated with ultrasonography or KUB prior to JJ stent extraction and in cases of suspicious residual fragments an NCCT was also performed. Stone free was defined as the absence of residual fragments of any size in the postoperative imaging. Complications were recorded according to Clavien Classification.

2.3 Sample size calculation

The primary end point of the study was to compare the changes of NGAL levels and sample size calculation was performed according to this parameter. In the previous

studies NGAL levels showed an increase of 50% for PNL cases[6] and 30% for ureterorenoscopy [5] postoperatively. Sample size calculation revealed that 28 patients were needed for each group to determine a difference of 20% increase in NGAL levels with an alpha value of 0.05 and power level of 80%.

2.4 Statistical analysis

Statistical analysis was performed with SPSS for Windows, ver. 22.0 (SPSS Inc., Chicago, Illinois, USA). The normality of the data was evaluated with Kolmogorov–Smirnov test. The Student's *t* test or Mann–Whitney *U* test was used to compare the continuous variables according to the normality of the data. Categorical variables were compared with the Chi-square test. Paired sample t test was used to compare preoperative and postoperative NGAL levels in each group. For statistical significance *p* value of 0.05 was accepted.

3 Results

The mean age of the population was 44.5 ± 5.5 years and 37 (61.7%) of the patients were males. The mini-PNL and the RIRS groups were similar for mean age, gender distribution, stone location and mean baseline NGAL levels. The mean stone size was significantly higher in the mini-PNL group (24.6 mm vs. 18.2 mm, $p=0.02$) and mean stone density was significantly higher in the mini-PNL group as well (998 ± 128.6 HU vs. 880 ± 120.1 HU, $p=0.04$). The results are summarized in Table 1.

The mean postoperative NGAL levels were 45.6 ± 12.4 and 48.1 ± 13.6 for the mini-PNL and RIRS groups, respectively. The increase was statistically significant for both groups (*p* value: 0.01 for both groups). However, the difference between the two groups for mean postoperative NGAL measurements was not statistically significant ($p=0.47$).

The SFR was significantly higher in the mini-PNL group compared to the RIRS group (96.7% vs. 79.3%, $p=0.04$). The complication rates were similar for the two groups ($p=0.99$). Clavien grade I and II complications were observed in 3 patients in each group and grade 3 or higher complications were not observed in any of the cases. The mean hemoglobin drop was 0.5 g/dl in the mini-PNL group and blood transfusion was performed in only one patient. The mean duration of operation was 48.2 ± 22.5 min in the mini-PNL group and 62.6 ± 18.1 min in the RIRS group and the difference was statistically significant ($p=0.03$). The median duration of hospitalization was 1 day for both groups. The results are summarized in Table 2.

4 Discussion

Surgical management of renal stones aims to provide stone free status with the lowest morbidity and both PNL and RIRS are worldwide successfully applied options. PNL provides higher stone free rates but the penetration of the renal parenchyma to reach the collecting system increases its morbidity over RIRS which is performed through the natural orifice [3]. Miniaturization of the PNL instruments aims to decrease the morbidity rates and with recent advances in this manner mini-PNL was shown to be a good alternative to RIRS with increased SFR and decreased morbidity [8]. Our results compares the two techniques for both SFR and safety and mini-PNL is shown to provide better SFR without increasing the risk of neither AKI nor complications.

AKI develops following stone surgery and NGAL has been shown to be a good marker for detection of the level of AKI [5, 6, 9]. Renal parenchymal injury mainly causes the elevation of NGAL in the PNL cases and increased intrarenal pressure is blamed for AKI in RIRS cases [5, 6]. In a recent study, Daggulli et al. evaluated the changes

Table 1 Comparison of the two groups for the demographic and baseline characteristics

Parameters	Mini-PNL group ($n=31$)	RIRS group ($n=29$)	*p* value
Age, mean ± SD	44.2 ± 5.4	44.8 ± 5.6	0.87
Gender, *n* (%)			0.63
Male	20 (64.5)	17 (58.6)	
Female	11 (35.5)	12 (41.4)	
Stone location *n* (%)			0.41
Upper	2 (6.4)	2 (6.9)	
Middle	8 (25.8)	12 (41.4)	
Lower	21 (67.8)	15 (51.7)	
Stone size, (mm) mean ± SD	24.6 ± 5.4	18.2 ± 4.4	0.02
Stone density (Hounsfield Unit), mean ± SD	998 ± 128.6	880 ± 120.1	0.04
Preoperative uNGAL (ng/ml) mean ± SD	21.8 ± 9.4	24.2 ± 8.8	0.76

Table 2 Comparison of the two groups for the demographic and operative characteristics

Parameters	Mini-PNL group ($n=31$)	RIRS group ($n=29$)	p value
Postoperative uNGAL (ng/ml) mean ± SD	45.6 ± 12.4	48.1 ± 13.6	0.47
Stone free rate, *n* (%)	30 (96.7)	23 (79.3)	0.04
Complication rate, *n* (%)			0.99
Grade I	2 (6.4)	3 (10.3)	
Grade II	1 (3.3)	–	
Grade III or higher	–	–	
Duration of operation (min) mean ± SD	48.2 ± 22.5	62.6 ± 18.1	0.03
Duration of hospitalization (days), median (range)	1 (1–2)	1 (1–3)	0.99

in NGAL levels in PNL cases and reported a doubled NGAL/creatinine ratio in the postoperative measurement. Different from our study, the authors used NGAL/creatinine ratio for standardization and performed PNL cases in prone position with 30 Fr dilation [6]. We included only patients with preoperative creatinine levels in normal ranges for standardization and therefore, did not use the NGAL/creatinine ratio. To compare our results, we used the increase in percentage of NGAL levels and detected a lower percentage of increase. We believe that this difference is mainly due to the diminished tract size (16 Fr vs. 30Fr) in our study. Additionally, we performed our cases in supine position in which the trajectory of the sheath is downwards and this provides spontaneous flow of the irrigation fluid out of the collecting system, resulting in lower intrarenal pressures.

Dede et al. evaluated the changes in AKI markers in patients underwent RIRS in comparison with a control group. The authors also used NGAL/creatinine ratio and reported a 60% increase in the postoperative measurement at 2 h. They also performed a correlation analysis and found that NGAL levels were correlated with duration of operation and irrigation fluid used [9]. We found out an increase of about 100% (24.2–48.1 ng/ml) at postoperative 6th hour. Our results prove that NGAL levels increase following RIRS and a more prominent increase may be related to the time of measurement in the postoperative period, difference in stone size, and also amount and height of irrigation fluid used.

Sabnis et al. compared mini-PNL and RIRS in a prospective non-randomized study and reported SFR of 100% and 96.8% for the mini-PNL and RIRS, respectively [10]. The authors reported higher SFR compared to our study especially for the RIRS cases. This is possibly related to smaller mean stone size in this study which was 1.4 cm for the RIRS group. The authors also reported longer operative times for RIRS compared to mini-PNL parallel to our findings. The operative times in this study are about 10 min shorter compared to our study which is again probably associated with the difference mean stone size. The authors concluded that both RIRS and min-PNL are effective and safe options for management of renal stones 1–2 cm [10]. In another study, Kirac et al. retrospectively compared mini-PNL and RIRS for lower pole stones < 15 mm in diameter and reported SFR of 89.1 and 88.8%. The authors concluded that RIRS is a safe and effective alternative to mini-PNL with shorter hospitalization time and lower morbidity [11].

Pan et al. compared RIRS and mini-PNL in patients with stone diameter of 2–3 cm. The reported SFRs were similar to our results (96.6% for mini-PNL and 71.4% for RIRS) as the mean stone size was similar as well. The authors reported a shorter operative time but a longer hospital stay for the mini-PNL group [12]. In another study, Kruck et al. compared the mini-PNL and RIRS with shock wave lithotripsy and reported SFR of 80.4% for mini-PNL and 69.2% for RIRS in patients with stones > 1 cm in diameter. The authors also reported higher morbidity for both of these surgical options compared to shock wave lithotripsy [13].

In a recent meta-analysis comparing PNL and RIRS for renal stones, a separate analysis was performed for mini-PNL subgroup. The authors concluded that PNL overall provides higher SFR at the expense of higher complication rates, operative times, hospitalization duration, and blood loss. On the other hand, they also concluded that mini-PNL provides lower SFR with increased morbidity and therefore, RIRS should be the standard option for stones < 2 cm [3]. However, our study revealed higher SFR for mini-PNL with similar complication rates, shorter operative times and equal hospitalization duration despite a higher mean stone diameter compared to RIRS. Furthermore, the comparison of AKI for the two groups also resulted in similar increases in NGAL levels which also proves the safety of the mini-PNL. It should be noted that all the cases in our series were performed by a single experienced surgeon and this should be associated with low morbidity high success rates especially in the

mini-PNL group. We believe that mini-PNL is the primary treatment option for renal stones < 3 cm as it provides highest immediate SFR with acceptable morbidity.

5 Study limitations

The main limitation of the current study is the lack of randomization. The mean stone size was significantly higher in the mini-PNL group but still higher SFR was established. Additionally, the current series reflects the outcomes of an experienced surgeon and therefore, the results may not be generalizable to general population. Especially the complication rates of the mini-PNL procedure may be higher depending on the experience of the surgeon and operative times may vary depending on the patient position as well.

6 Conclusions

In patients with renal stones < 3 cm in diameter, mini-PNL in supine position provides higher SFR and shorter operative times with similar rates of complications and AKI when compared with RIRS in experienced hands. Mini-PNL should be considered as the primary treatment option together with RIRS for renal stones and should not be ruled out for being a more invasive option.

Abbreviations

AKI: acute kidney injury; RIRS: retrograde intrarenal surgery; PNL: percutaneous nephrolithotripsy; SFR: stone free rates; NGAL: neutrophil gelatinase-associated lipocalin; NCCT: non-contrast computerized tomograph.

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Authors' contributions

MY performed the literature search, conducted the statistical analysis and the quality assessment. ST conceived the idea and wrote the manuscript. TC tabulated the data and wrote the manuscript. MIG contributed to the quality assessment and critically revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

All data and materials belonging to the manuscript are available.

Ethics approval and consent to participate

Our study is a prospective study, and all procedures performed in our study participants were in accordance with the ethical standards of the National Research Committee and Faculty of Medicine Research Ethics Committee at Ufuk University, Ankara, Turkey (20190328/6). A written informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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