Are Stone Density and Location Useful Parameters That Can Determine the Endourological Surgical Technique for Kidney Stones That Are Smaller than 2 cm? A Prospective Randomized Controlled Trial

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ABSTRACT

Purpose: We aimed to evaluate whether these parameters could be guiding for us in selection between retrograde intrarenal surgery (RIRS) and mini-percutaneous nephrolithotomy (PNL) procedures in kidney stones that are smaller than 2 cm.

Materials and Methods: The patients who had kidney stones smaller than two cm and were planned to undergo surgery were randomly distributed into 2 groups prospectively. RIRS was performed in the RIRS group using a 7.5-F fiberoptic flexible ureterorenoscope while mini-PNL group was dilated up to 16.5F and mini-PNL was performed with 12F nephroscopy. Preoperative characteristics, operative and postoperative results were compared in two groups. Thereafter, intra and intergroup comparisons were made to determine the effects of Hounsfield unit (HU) value indicating the stone density being higher or lower than 677 and stone location on stone-free rates.

Results: The study involved 60 patients including 30 in each group. The groups' preoperative values were similar. The hospitalization time and the total duration of scopy were longer in mini-PNL when the postoperative values were compared ($p < .0001$). In terms of stone densities, HU values that were lower than 677 in the mini-PNL group affected the stone-free rate and reduced it from 100% (> 677HU) to 55.6% (< 677HU), whereas the change was significant ($p=.005$). Lower calyx stones affected the RIRS results negatively, whereas multiple calyceal stones affected the mini-PNL group negatively.

Conclusion: Both methods had a similar success rate, but lower pole stones, multiple calyceal stones and stone density parameters affected the stone-free rates significantly, and these may be effective in treatment selection.

Keywords: density; kidney stones; location; percutaneous nephrolithotomy; retrograde intrarenal surgery

INTRODUCTION

Percutaneous nephrolithotomy (PNL) and retrograde intrarenal surgery (RIRS) have taken the place of shock wave lithotripsy (SWL) for treatment of kidney stones as a result of development of minimally invasive techniques and instruments in the last 10-15 years. Each procedure has its own advantages and disadvantage [1,2]. Mini-PNL and RIRS are procedures that are preferred for minimally invasive treatment due to their negligible stone-free and complication rates[3,4]). RIRS has increasingly been used for moderately sized kidney stones in recent years [5,6]. However, this technique has limitations such as low success rate in the lower calyx, necessity of using ureteral access sheath, necessity of placing JJ stent in case of failure due to inability to gain access in the first session and requirement of a second session, and longer duration of the surgical period as the stone size increases [7,8]. It is known that parameters such as stone density, opacity, disorganized settlement and location of the stone generally affect stone-free rates[7,9]. The efficacy and safety of using minimally invasive techniques such as RIRS or mini-PNL in moderately sized kidney stones is still a debated matter [10,11]. The European Association of Urology guidelines recommend endourology (all PNL and URS interventions) as the standard treatment option for small to medium (≤ 2cm) renal stones. However, it is not yet clear which endourology option would be more appropriate for this group of stones.

In this study, we aimed to compare patients with kidney stones smaller than 2 cm who underwent mini-PNL and RIRS and tried to determine if preoperative stone properties affecting the choice of treatment, if any, could be parameters that could lead us to make a choice about these procedures.

MATERIALSS AND METHODS

Study population

Patients with kidney stones who visited our clinic between April 2016 and May 2017 were evaluated following the approval of the ethics committee. The patients were evaluated with non-contrast abdominopelvic CT after detailed anamnesis and physical examination. Patients who had a kidney stone with a maximum diameter of less than 2 cm and did not prefer to undergo SWL were included in the study. Patients with anomalous kidneys, skeletal deformities, severe obesity (BMI > 35) and those who previously underwent SWL treatment for the same stone were excluded from the study. The study was explained to each patient and informed consent was obtained. Patients' enrollment algorithm is illustrated in Figure 1.

In all patients**,** hemoglobin, platelet, coagulation tests, serum creatinine levels and urine culture tests were performed preoperatively, and treatment was provided according to the findings if necessary. Information was recorded on the patients' age, sex, body mass index (BMI), stone density, stone size and stone location. Stone densities and surface areas were obtained as previously described (12). Stone location is classified under three categories, lower calyx, upper calyx or multiple.

Study design

This study was a prospective single-center, parallel-group randomized clinical trial with balanced randomization [1:1] which was performed in a referral hospital in Bolu, Turkey. The patients were randomly divided into 2 groups (mini-PNL and RIRS) by a computer software as described in the literature (13). The allocated treatment for each patient was recorded in concealed envelopes. After achieving eligibility criteria and the patient's agreement on participation, the concealed envelopes were opened by one of the researchers and the allocated treatment was performed as explained below (13). The surgeon learned of the randomization group in the operating room before surgery and had no opportunity to schedule patients according to the randomization list. In this study, it was aimed to study a total of 52 subjects with 95% confidence level, 0.80 effect size and 80% power provided that there are at least 26 subjects in each group, and the study was completed with 60 patients.

Surgical technique

All operations were performed or supervised by the same surgeon. Right after the patients in mini-PNL group were placed a 5F ureteral catheter with general anesthesia, they were given a prone position and access was performed by choosing the optimal calyx to reach the stone after the contrast agent was given. The guide wire was then placed, and the stones were broken with a laser lithotripter using a 12F nephroscope (Modular minimally invasive PNL system, Karl Storz, Tuttlingen, Germany) following the dilatation using a one step dilator with a 16.5F access sheath. When necessary, the stones were removed using stone removal forceps. Right after a 14F nephrostomy tube was inserted and an antegrade pyelography was taken, the operation was completed.

Following the general anesthesia performed in the RIRS group, a safety guide wire was placed and semirigid ureteroscopy (9.5 / 11.5F) was performed to see the ureter and possible pathologies as well as facilitate the placement of the ureteral access sheath. The stones were fragmented using a 270 micrometer laser fiber with the help of a 7.5-F fiber optic flexible ureterorenoscope (Storz FLEX-X2, Tuttlingen, Germany) after the placement of ureteral access sheaths (9.5 / 11.5 F) (Elit Flex, Ankara, Turkey). Stone fragmentation was accomplished using a laser energy of 0.5-1.5 J and a rate of 5-15 Hz (Sphinx Jr 30 watt), and this range was adjusted based on stone hardness. Stones smaller than 2 mm were left to pass on their own while the larger ones were removed with a basket catheter. A 4.7F JJ stent was routinely placed at the end of the operation because of concerns about possible edema and other problems that might be caused by the access sheath. In this group, access sheaths could not be placed in 2 patients due to the small diameter of their ureters, and a JJ stent was placed. 2 weeks later, the procedure was performed as it was in the others. The durations of the operation were recorded by adding the durations of 2 procedures.

Outcome assessment

The primary outcome of interest was stone-free rate after RIRS and Mini-PNL. The stone-free conditions were determined by low-dose spiral CT taken in the third postoperative month. The procedure was considered successful if there were no residual stones. Secondary outcomes included the relationship between stone-free rates and parameters of stone density and location, pain after procedures, hospitalization time, operative time, fluoroscopy time and complications.

The visual analogue scale (VAS; range= 1-10) that was applied in the first hour was used as the pain scale. Surgical times were calculated from the beginning of cystoscopy to the end of the procedure carried out by placing a urinary catheter. Clavien classifications were used for the complications.

Firstly, the preoperative and postoperative results of both groups were compared. Then the effects of "stone density and location" that could influence the stone-free condition within the groups were evaluated. We used a cutoff value of 677.5 HU that was determined in our previous study to assess the effects of stone density(12). According to this value, we divided the groups into 2 subgroups and looked into the effects of stone density. These subgroups were compared within themselves, and cross comparisons were also made. The effect of stone location on stone-free rates was also assessed.

Data obtained from this study were analyzed using the SPSS 20 statistics software. While investigating whether the variables were normally distributed, Shapiro Wilk's was used due to the number of units.. The Mann-Whitney U test was used for analyzing the differences between the groups due to the non-normal distribution of the variables. The relationship between the categorical variables was analyzed by Chi-square test. The results were interpreted using a significance level of .05.

RESULTS

The study was completed with a total of 60 patients including 30 in each group. The preoperative characteristics of the patients and the stones are shown in Table 1. There was no difference between the groups with regards to this aspect ($p > .05$). The groups were similar in terms of patient and stone characteristics.

The whole mini-PNL procedure was completed with a single tract in a single session. Intercostal intervention was performed in 2 patients with upper calyx stones. The others underwent a subcostal approach. 9 patients in the mini-PNL group and 6 patients in the other group showed temporary fever that was overcome by antipyretics, and this was recorded as Clavien grade 1 complication. Bleeding that required blood transfusion was observed in 1 patient in the PNL group. 2 patients in the PNL group and 1 patient in the other group showed fever that was overcome in the 2nd day by alternating antibiotics, and this was recorded as Clavien grade 2 complicaiton. Because of the small ureteral diameter in the 2 patients in the RIRS group, the access sheath could not be placed in the 1st session. The procedure was repeated two weeks after the JJ stent was inserted. The stent requirement for these 2 patients was stated as Clavien 3 complication. The operative and postoperative data of the patients are shown in Table 2. The mean duration of fluoroscopy and hospitalization were significantly higher in the mini-PNL group in the intergroup comparison (p=.0001).

After the evaluations mentioned above, the effects of stone location and stone density on stone-free rates were evaluated within the groups. In the mini-PNL group, the stone-free rate was found to be 62.5% in the cases of multiple calyceal stones, while it was 87.5% in the cases of upper calyx stones and 100% in the cases of lower calyx stones. Multiple caliceal stones decreased the stone-free rate significantly in comparison to the other locations (p=.037). In terms of stone densities, HU values that were lower than 677 in the mini-PNL group affected the stone-free rate and reduced it from 100% (> 677HU) to 55.6% (< 677HU), whereas the difference was significant (p = .005). There was no significant difference in the RIRS group in terms of the same parameters (p > .05).

After the effects of stone density and location were analyzed within the groups, the results of the intergroup comparisons in terms of the effects of these values are shown in Table 3. In this evaluation, it was determined that stone densities of lower than 677 and multiple caliceal stones had significant and negative effects on stone-free rates. Although the effect was not statistically significant, it was observed that presence of lower calyx stones affected stone-free status negatively.

DISCUSSION

The European Association of Urology Guidelines recommend using SWL or Endourology procedures for stones smaller than 2 cm as the first-line treatment [14]. The term endourology refers to all PNL and ureterorenoscopic interventions, but no suggestion has been made about which of these might be more appropriate. It was stated that both methods have similar success rates and reliability in studies with this size of stones [1,15]. Some publications pointed out that mini-PNL methods used for lower pole stones are more advantageous in terms of stone-free rates [1]. We prospectively compared these two groups in this study. We predicted that we could partially determine which of these procedures is more appropriate for these groups of stones considering both stone location and stone density.

The power analysis for the targeted values mentioned above suggested that each group should include at least 26 subjects. The fact that both groups had 30 patients can tell us that our results are statistically reliable to a certain extent. When we compared our groups with regard to patient and stone characteristics, it was determined that they were similar ($p<.05$). In this respect, our groups were homogeneous.

When we compared the operative and postoperative data of our groups, we found that the mean duration of fluoroscopy and hospitalization time were significantly greater in the mini-PNL group ($p < .0001$). Demirbaş et al. compared ultra mini PNL and RIRS in their study and found a duration of fluoroscopy of 57 sec corresponding to 185 sec respectively[1]. When the total average values were taken into consideration, the duration of fluoroscopy was shorter than those in other studies[1, 15]. We think this depended on our experience and praxis of using fluoroscopy. The hospitalization time was also higher in mini-PNL and this agreed with the literature. These data can be considered as a disadvantage of mini-PNL.

When the other parameters are considered, similar stone-free rates, hospitalization times and durations of operation were found in the study by Schoenthaler et al. While there was no significant difference in pain scores, Clavien grade 3 complications were observed in 2 patients in the RIRS group. In 2 patients, these complications depended on failure of the placement of the access sheath due to small ureteral diameter in the first session, and the placement of a JJ stent to provide passive dilation. An additional surgery was required for the patient about 2 weeks later, and this was a discomfort for both the patient and the surgeon. In fact, in these patients whose RIRS operations have begun, if there is no condition that prevents the patient from undergoing mini PNL, it may be a reasonable option to switch to mini-PNL in the same session, and rid the patient of the stone in a single session. The Clavien 1 and 2 complications were usually fever-related. While most of these were overcome by antipyretics, some required alternating antibiotics. There was no difference between the groups in terms of these complications, but these were seen more frequently than the minor complications reported in the literature to reach up to 10%[16,13]. We believe that this difference in results might have been related to our inability to achieve the same conditions in our operating room every time.

In this study, we evaluated the effects of stone density and location that could influence the stone-free status after these comparisons. We classified stone locations under three categories as lower pole, upper pole and multiple. However, at the beginning, we thought of using one of "Guy's stone score", "S.T.O.N.E score" or "resorlu-unsal stone score" systems for scoring the stone classifications. However, we have seen that these scoring systems are used to predict the outcomes of either PNL or RIRS, and they do not consider the factors that are effective in choosing between them. When we considered the effects of stone location on the stone-free rates, in the comparison within the mini-PNL group, we found that stones in multiple calyces and stone densities of lower than 677 affected stone-free rates in a negative way ($p<.05$). It was found that RIRS was affected negatively by lower caliceal stones when the 2 groups were compared in terms of stone location ($p<.05$). We also found that multiple caliceal stones reduced the success of mini-PNL but had no effect on RIRS. In another study comparing Ultra mini-PNL and RIRS, it was stated that lower pole stones negatively affected the RIRS results, and the stone-free rate of this group decreased to 42%, and thus ultra mini-PNL might be more effective in such groups [1]. There are studies which showed that RIRS has similar effectiveness, but ultra-mini PNL seems to make a greater contribution to the stone-free rates in lower pole stones[17, 18]. Additionally, lower pole stones are an ideal indication for PNL because of easy access and low complication rates [17]. In fact, if consider the results of our study, a common scoring system involving stone density parameters may possibly contribute to making the surgeon more objective and successful in cases of lower pole stones and multiple caliceal stones [1, 19].The difference between our study and studies in the literature is related to adding the effects of stone density to these evaluations. We have noted in previous studies that reduction in stone density reduced the success of PNL operations and it may be useful to use flexible nephroscopy routinely to eliminate this issue [12,20]. Thus, we have seen that densities of lower than 677 HU reduced the success of mini-PNL but had no effect on RIRS. We attribute this to the difficulty in detecting stones by fluoroscopy, due to the reduction in density and the importance of this difficulty in PNL operations.

The most important limitation of our study was the subgroup comparisons included low numbers of patients. If we had access to a sufficient number of patients, we could achieve more reliable results by dividing the cases into density groups and stone location subgroups. Another limitation could be that we did not employ a smaller scale percutaneous surgery method (e.g. ultra mini PNL) for comparison. .

CONCLUSION

Consequently, lower pole stones of smaller than 2 cm, multiple caliceal stones and stone density parameters affected the stone-free rates significantly. While multiple stones or stone densities of < 677 HU affected success in mini-PNL negatively, lower calyx location affected RIRS results negatively. For this reason, a surgical preference that is made by considering the parameters in these groups may contribute optimal usage of these endourological techniques.

CONFLICT OF INTEREST

The authors report no conflict of interest.

Abbreviations used:

retrograde intrarenal surgery (RIRS)

percutaneous nephrolithotomy (PNL)

hounsfield unit (HU)

shock wave lithotripsy (SWL)

REFERENCES

1. Demirbas A, Resorlu B, Sunay MM, Karakan T, Karagöz MA, Doluoglu OG. Which should be preferred for moderate-size kidney stones? Ultramini percutaneous nephrolithotomy or retrograde intrarenal surgery? J Endourol. 2016;**30:** 1285-9.

2. Atis G, Culpan M, Pelit ES, et al. Comparison of percutaneous nephrolithotomy and retrograde ıntrarenal surgery in treating 20-40 mm renal stones. Urol J. 2017;16;2995-2999.
3. Jacquemet B, Martin L, Pastori J, et al. Comparison of the efficacy and morbidity of flexible ureterorenoscopy for lower pole stones compared with other renal locations. J Endourol. 2014;**28:**1183-7.
4. Ferakis N, Stavropoulos M. Mini percutaneous nephrolithotomy in the treatment of renal and upper ureteral stones: Lessons learned from a review of the literature. Urol Ann. 2015;**7:**141-8.
5. Karatag T, Buldu I, Inan R, Istanbulluoglu MO. Is micropercutaneous nephrolithotomy technique really efficacicous for the treatment of moderate size renal calculi? Yes. Urol Int. 2015;**95:**9-14.
6. Karakan T, Kilinc MF, Doluoglu OG, et al. The modified ultra-mini percutaneous nephrolithotomy technique and comparison with standard nephrolithotomy: a randomized prospective study. Urolithiasis. 2017;**45:**209-213
7. Resorlu B, Unsal A, Gulec H, Oztuna D. A new scoring system for predicting stone-free rate after retrograde intrarenal surgery: the "resorlu-unsal stone score" . Urology, 2012;**80:512-** 518,
8. Resorlu B, Oguz U, Resorlu E, Oztuna D, Unsal A.The impact of pelvicaliceal anatomy on the success of retrograde intrarenal surgery in patients with lower pole renal stones. Urology.
9. Maghsoudi R, Etemadian M, Kashi AH, Ranjbaran A. The association of stone opacity in plain radiography with percutaneous nephrolithotomy outcomes and complications. Urol J. 2016; 13:2899-2902.2012;**79:**61-66.

10. Desai J, Zeng G, Zhao Z, Zhong W, Chen W, Wu W. A novel technique of ultra-mini-percutaneous nephrolithotomy: introduction and an initial experience for treatment of upper urinary calculi less than 2 cm. Biomed Res Int. 2013;2013:490793.
11. Wilhelm K, Hein S, Adams F, Schlager D, Miernik A, Schoenthaler M. Ultra-mini PNL versus flexible ureteroscopy: a matched analysis of analgesic consumption and treatment-related patient satisfaction in patients with renal stones 10-35 m.m. World J Urol. 2015; **33:** 2131-6.
12. Gücük A, Uyetürk U, Oztürk U, Kemahli E, Yildiz M, Metin A. Does the hounsfield unit value determined by computed tomography predict the outcome of percutaneous nephrolithotomy? J Endourol.2012; **26:** 792-6.
13. Javanmard B, Kashi AH, Mazloomfard MM, Ansari Jafari A, Arefanian S. Retrograde ıntrarenal surgery versus shock wave lithotripsy for renal stones smaller than 2 cm: a randomized clinical trial. Urol J. 2016;13:2823-2828.
14. Turk C, Petrik A, Sarica K, et al. EAU guidelines on diagnosis and conservative management of urolithiasis. Eur Urol. 2016;**69:**468-74.
15. Ozgor F, Tepeler A, Elbir F, et al. Comparison of miniaturized percutaneous nephrolithotomy and flexible ureterorenoscopy for the management of 10-20 mm renal stones in obese patients. World J Urol 2016;**34:** 1169-73.
16. Zengin K, Tanik S, Karakoyunlu N, et al. Retrograde intrarenal surgery versus percutaneous lithotripsy to treat renal stones 2-3 cm in diameter. Biomed Res Int. 2015;2015:914231.
17. Kirac M, Bozkurt ÖF, Tunc L, et al. Comparison of retrograde intrarenal surgery and mini-percutaneous nephrolithotomy in management of lower-pole renal stones with a diameter of smaller than 15 mm. Urolithiasis. 2013;**41:** 241-6.
18. Lee JW, Park J, Lee SB, Son H, Cho SY, Jeong H. Mini-percutaneous nephrolithotomy vs retrograde intrarenal surgery for renal stones larger than 10 mm: a prospective randomized controlled trial. Urology. 2015;**86:** 873-7.
19. Pelit, ES, Atis G, Kati B, et al. Comparison of mini-percutaneous nephrolithotomy and retrograde intrarenal surgery in preschool-aged children. Urology.2017;**101:** 21-25.
20. Gücük A, Kemahlı E, Üyetürk U, Tuygun C, Yıldız M, Metin A. Routine flexible nephroscopy for percutaneous nephrolithotomy for renal stones with low density: a prospective, randomized study. J Urol.2013;**190:**144-8.

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Figure legends

Figure 1. Patients' enrollment algorithm

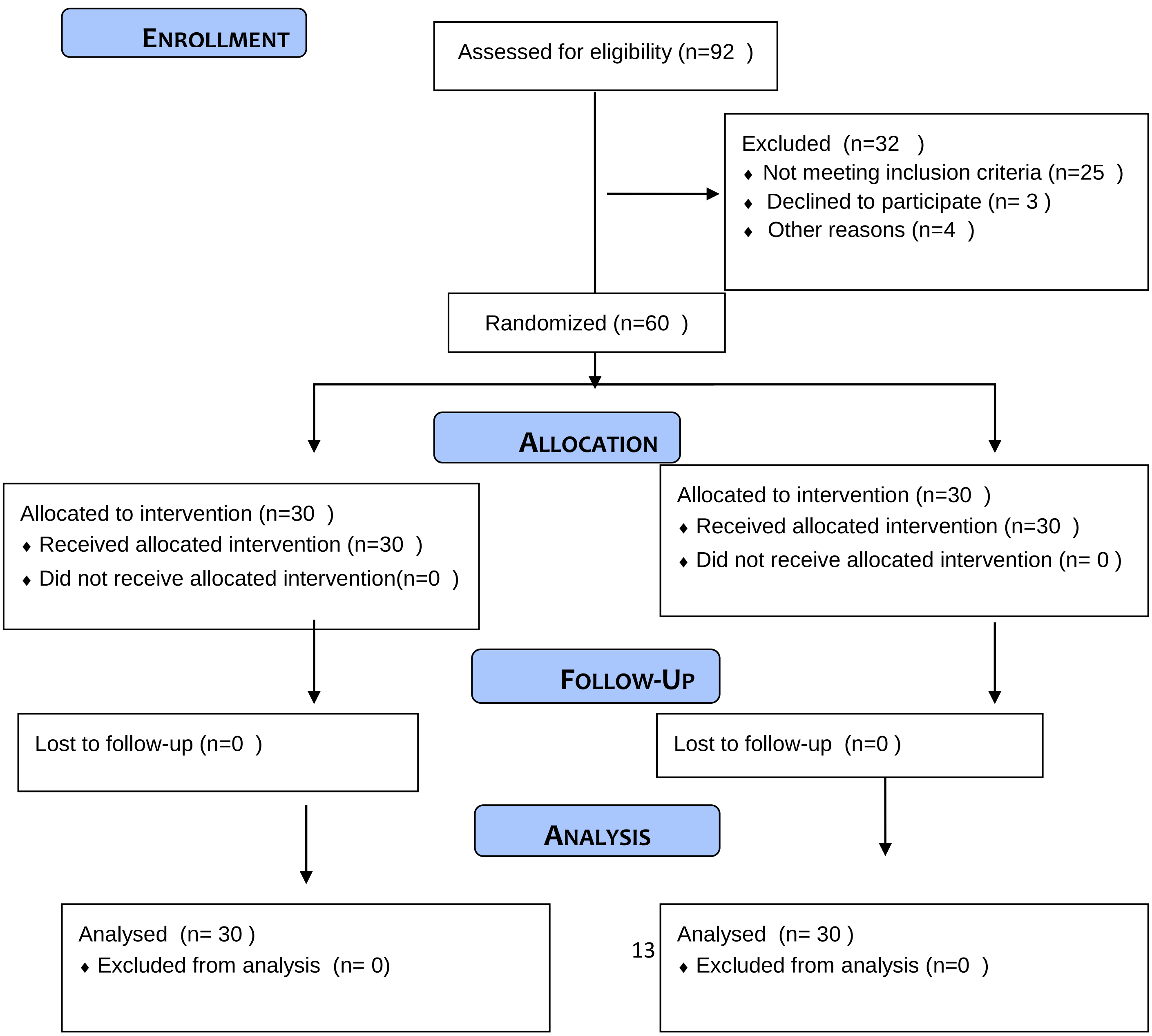

Table 1. Patient and stone characteristics

Variable	**Mini-PNL Group (N = 30)**	**RIRS Group (N = 30)**	**P-value**
Sex			0.771
Male	21	23	
Female	9	7	
Mean age (years)	46.1 ± 17.5	46.6 ± 13.5	0.902
Mean BMI (kg/m^2)	26.4 ± 3.3	27.2 ± 3.7	0.421
Stone localization			0.829
Upper calices	8 (% 26,7)	8 (26.7)	

Lower calices	14 (% 46.7)	12 (% 40)	
Multipl calices	8 (% 26.7)	10 (% 33.3)	
Mean stone density (HU unit)	845.3 ± 267.5	816.7 ± 251.2	0.671
Stone surface area (mm^2)	275.5 ± 75.,1	259.1 ± 65.2	0.368

Abbreviations: PNL, Percutaneous Nephrolithotomy; RIRS, Retrograde Intrarenal Surgery; BMI, Body Mass Index;

Table 2. Operative and postoperative data of Mini-PNL and RIRS groups and their comparisons

Parameters	**Mini-PNL group**	**RIRS group**	**p**
Mean total operative time (min)	98.3 ± 18.8	109.0 ± 33.8	0.134
Mean fluoroscopy time (sec)	121.7 ± 49	24.2 ± 7.9	0.0001
Hospitalization time (day)	2.1 ± 2.03	1.6 ± 134	0.0001
Stone free rate (%)	86.7	83.3	1

Mean Pain visual analog score (range: 1-10)	3.1 ± 1.4	3.0 ± 1.4	0.778
Complications	12 (%40)	9 (%30)	0.6
None	18 (% 60)	21 (% 70)	
Clavien grade 1	9 (% 30)	6 (% 20)	
Clavien grade 2	3 (% 10)	1 (% 3.3)	
Clavien grade 3	0	2 (% 6.6)	

Abbreviations: PNL, Percutaneous Nephrolithotomy; RIRS, Retrograde Intrarenal Surgery.

Table 3: The values of the parameters that can affect the stone-free state in the intergroup comparison.

Stone free rate (%)

Parameters	Mini-PNL group	RIRS group	P Fisher's Exact
Stone location			
Lower calyx	14 (% 100)	8 (% 66.7)	0.033
Upper calyx	7 (% 87.5)	8 (% 100)	1
Multiple	5 (% 62.5)	9 (% 90)	0.275
P value	0.037	0.156	
Stone density			
<677 HU	5 (% 55.6)	9 (% 81.8)	0.336
>677 HU	21 (% 100)	16 (% 84.2)	0.098
P value	0.005	1	

Abbreviations: PNL, Percutaneous Nephrolithotomy; RIRS, Retrograde Intrarenal Surgery.