ORIGINAL PAPER

UROLITHIASIS

Frequency and risk factors for antegrade ureteral stone migration after percutaneous nephrolithotomy

Hector S. Barba, Christian Isaac Villeda-Sandoval, Carlos E. Mendez-Probst

Department of Urology at Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico

Citation: Barba HS, Villeda-Sandoval CI, Mendez-Probst CE. Frequency and risk factors of antegrade stone migration into the ureter after percutaneous nephrolithotomy. Cent European J Urol. 2020; 73: 355-361.

Article history
Submitted: Aug. 14, 2019
Accepted: July 26, 2020
Published online: Aug. 29, 2020

Corresponding author
Carlos E. Mendez-Probst
Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran
Department of Urology
15 Vasco de Quiroga
Belisario Domingez sección XVI, Tlalpan,
Ciudad de Mexico
14080 Mexico
phone: +52 55 548 70 900, ext. 7252
probstmc@hotmail.com

Introduction Percutaneous nephrolithotomy (PCNL) is the minimally invasive procedure of choice for the treatment of large and/or complex nephrolithiasis. Migration of residual fragments (RFs) into the ureter after PCNL is presumed to be uncommon. However, should associated stone-related events (SREs) occur, ancillary procedures may be required. The objective of this study was to describe the frequency and to analyze predictors of antegrade migration of RFs after PCNL.

Material and methods A case-control study of patients who underwent PCNL for nephrolithiasis and had a postoperative computed tomography available within 48 hours was performed. Descriptive statistics and logistic regression analysis were carried out.

Results The final sample included 169 interventions. Mean age was 49 ±13 years, median maximum stone size was 26 (7 to 87) mm and mean stone density was 835 (70 to 2022) Hounsfield Units (HUs). 7.1% of the patients experienced migration of RFs into the ureter after PCNL, of whom 41.6% suffered SREs. Lithotripsy was performed using ultrasonic (67.5%), laser (23.7%), and pneumatic (14.8%) technologies. Univariate analysis found female gender (OR 4.1, p = 0.02) height ≥1.68 m (OR 5.52, p = 0.009), middle (OR 6.71, p = 0.01) and upper (OR 3.59, p = 0.04) caliceal location, staghorn calculi (OR 4.72, p = 0.02), stone area (OR 1.001, p = 0.03), lasertripsy (OR 3.61, p = 0.03) and operative time (OR 1.007, p = 0.02) statistically significant for migration of SFs into the ureter after PCNL. Of these, only height ≥1.68 m (OR 7.17, p = 0.01) and staghorn nephrolithiasis (OR 13.27, p = 0.02) remained independent predictors in the multivariate analysis with an area under the curve of 0.69.

Conclusions 71.% of patients undergoing PCNL had a SF migrating to the ureter. Of these 41% suffered a SRE that required ancilliary interventions. Staghorn nephrolithiasis and ≥1.68 mts of height were found to predict this event.

Key Words: percutaneous nephrolithotomy ‹› nephrolithiasis ‹› residual stone fragments ‹› endolithotripsy ‹› stone relocation

INTRODUCTION

Percutaneous nephrolithotomy (PCNL) is considered the standard treatment for most large and/or complex nephrolithiasis, due to its higher stone-free rate (SFR) [1, 2] and lesser number of interventions compared to other therapeutic modalities [3]. Stone-free rate ranges from 40% to 90% depending on the size, number, composition of calculi, surgeon´s experience [4], modality of endolithotripsy, as well as definition of SFR. In addition, limited visualization due to bleeding, difficult-to-access calices, prolonged operative time, and inappropriate technique selection have been identified as predictors of decreased SFR in PCNL [5].

Antegrade migration of residual fragments (RFs) into the ureter during PCNL is believed to occur rarely [6] and most stones are thought to pass spontaneously [7]. However, stone-related events (SREs) resulting from ureteric obstruction may require ancillary procedures [7–10]. These events prolong hospital stay, delay nephrostomy tube removal and increase costs.

The reported incidence of SREs due to RFs has been estimated between 0.83% to 3.5%. Nevertheless, variability in imaging studies including x-ray, ultrasound (US) or computed tomography (CT) kidney-ureter-bladder (KUB) scans, which have heterogenous sensitivities as well as high false-negative rates, are suspected to underestimate this phenomena [10–13]. The objective of this study was to describe the frequency and to analyse predictors of antegrade ureteric migration of RFs after PCNL using CT KUB scan, the current gold standard for stone imaging.

MATERIAL AND METHODS

We performed a case-control study of patients who underwent PCNL for nephrolithiasis and had a post-operative CT KUB within 48 hours of the intervention at a single reference centre from 2010 to 2016. All PCNLs were performed by a single surgeon in the standard prone position. Access was guided by fluoroscopy combining both Bull's eye and triangulation techniques using a two-piece needle and Sensor guidewire (Boston Scientific, Ireland), followed by Amplatz guidewire exchange through an angled hockey-stick catheter and up to 30-Ch balloon Nephromax (Boston Scientific, Ireland) dilatation of the tract. Nephroscopy was performed using an Amplatz 24-Ch instrument and lithotripsy was carried out using a Calcuson/Endomat LC (Karl Storz, Germany) ultrasonic technology with a 3.5 mm probe; or a Calcusplit (Karl Storz, Germany) pneumatic device. Additionally, Holmium laser technology using 272-micron SlimLine (Lumenis, Israel) fibres with fragmentation settings (0.8 J and 8 Hz) was employed when flexible nephroscopy was needed. Large stone fragments were extracted using endoscopic forceps and smaller RFs with tipless baskets. Thorough flexible nephroscopy was performed routinely procuring the distal aspect or renal cavities up to the proximal ureter segment until resistance was met. A 16-Ch latex Foley catheter was left as nephrostomy tube with 2–3 ml of contrast to the balloon at the renal pelvis under fluoroscopy guidance. A tubeless technique was used in cases of single stones extracted without fragmentation, as well as little or no bleeding at all. Double J stents were inserted selectively in cases of pelvic-ureteric junction obstruction or if a ureteric injury was identified during the procedure. We did not use any ureteric occlusive devises such as balloons or barriers.

Our local policy is to perform routine CT KUB within 48 hours of a PCNL to assess SFR, which we defined as no RFs at all. Provided symptomatic or ≥5-mm RFs were found on the postoperative CT KUB either in the kidney or the ureter, ancillary endoscopy of the urinary tract (nephroscopy or ureteroscopy) was carried out as soon as reasonably attainable within a few days (ideally previous to hospital discharge) before removing the nephrostomy to use it as the tract of entry to renal cavities. Asymptomatic patients with stones ≤5 mm were followed up with an x-ray and ultrasound KUB at 1 month.

The sample size was calculated at 140 patients considering the prevalence of stone-related events secondary to migration of RFs into the ureter after PCNL to be between 0.83% and 3.5% [7]. A 3% margin of error as well as a 95% confidence level was used. For descriptive statistics, absolute and relative frequencies, mean and standard deviation, as well as median and interquartile range were used accordingly. Univariate and multivariate analyses were executed looking for predictors of migration of RFs into the ureter after PCNL. Multivariate analysis' receiver operator characteristic curve (ROC) was plotted to establish the area under the curve. Additionally, a Mann-Whitney U test was performed to look for predictors of a secondary intervention considering preoperative maximum stone size and area. Finally, a Kruskall-Wallis test was carried out to look for associations between stone size, stone area, as well as SFs size and lithotripsy modality. Statistical significance was set at <0.05. SPSS statistics v20 was employed.

RESULTS

A total of 169 PCNLs from 155 patients were included. Females accounted for 65.1% of the cohort, the mean body mass index (BMI) was 27 kg/m^2 and the majority of the patients were shorter than 1.68 m. Preoperatively, 41 (24.3%) kidneys had a double J ureteric stent in place, 65 (38.5%) had hydronephrosis, 70 (41.4%) harbored staghorn calculi, and 110 (63.8%) had multiple stones. Location of calculi within the kidney was in descending order in the renal pelvis (68.6%), followed by the inferior (63.8%), middle (45.6%), and upper calices (30.2%). Stone volume was calculated according to the scalene ellipsoid formula (simplified as $L \bullet W \bullet H \bullet \varpi \bullet 0.167$) and the mean was 4.4 cm^3 (range 0.5 to 9.9 cm^3). Demographics are presented in Table 1.

Median operative time was 180 (57–540) minutes and lithotripsy was required in 160 (94.6%) procedures of which 82 (48.5%) was ultrasonic, 14 (8.2%) pneumatic, 4 (2.3%) laser and 60 (35.5%) a combination of these. More than 96% were left with a postoperative nephrostomy tube and 6 (3.5%) had a double J stent inserted. On the postoperative CT KUB, the SFR was 61% and 12 (7.1%) cases had RFs migrated into the ureter. Five of the latter migrated into the upper half of the ureter and seven into the

Table 1. *Demographic data and paired analysis between migration and non-migration of RFs into the ureter after percutaneous nephrolithotomy*

Variables	Total	Migration group	Non-migration group	p
Age (years)	49.1 ±9.8	45.6 ±9.5	49.3 ±13.7	
Gender				0.026
Women	110 (65.1)	4 (33.3)	106 (67.5)	
Men	59 (34.9)	8 (13.5)	51 (86.4)	
BMI (kg/m²)	26.5 (5)	27 (8)	27.5 (7)	0.34[b]
Comorbidities	73 (43.2)	4 (33.3)	69 (43.9)	0.55
Chronic renal failure	36 (21.3)	3 (25)	33 (21)	0.72
Preoperative ureteric stent	41 (24.4)	4 (33.3)	37 (23.7)	0.48
Abnormal urinary tract	45 (26.6)	5 (41.7)	40 (25.5)	0.3
Hydronephrosis	65 (38.5)	4 (33.3)	61 (38.9)	0.76
Staghorn nephrolithiasis	70 (41.4)	9 (75)	61 (38.9)	0.029
Stone burden[a] volume (cm^3)	5.9 (10.9)	14.2 (26.2)	5.9 (9.4)	0.16[b]
Stone burden[a] ≥12.88 cm^3	32 (26.4)	5 (62.5)	27 (23.9)	0.03
Stone(s) located in the renal pelvis or upper ureter	125 (74.4)	10 (83.3)	115 (73.7)	0.73
Number of tracts				1
1 tract	130 (81.8)	10 (83.3)	120 (81.6)	
≥2 tracts	29 (18.2)	2 (16.7)	27 (18.4)	
Endolithotripsy				0.004
Ultrasonic	19 (11.2)	1 (8.3)	18 (11.5)	
Laser	1 (0.6)	1 (8.3)	0	
Lithoclast	2 (1.2)	0	2 (1.3)	
Considerable bleeding	10 (6)	0	10 (6.4)	1
Perforation of the urinary tract during PCNL	12 (7.1)	0	12 (7.7)	1
Nephrostomy (postoperative)	163 (96.4)	10 (83.3)	153 (97.5)	0.059
Stone free rate	22 (64.7)	1 (50)	21 (65.6)	1

[a]Automated 3D-rendering software calculation; [b]Spearman'r rho correlation

lower one. Residual fragments' median maximum size was 4 (3) mm and had an area of 0.06 (0.13) cm^3. Overall, five of the twelve cases that migrated RFs into the ureter after PCNL needed ancillary interventions such as double J stent insertion or ureteroscopy within a few weeks due to SREs (one case of fever and two episodes of renal colic) or asymptomatic ≥5-mm RFs. Except for one case that failed to clear the calculus, the remaining stones passed spontaneously as there was neither evidence of their presence on the follow-up KUB film, nor hydronephrosis on an ultrasound KUB imaging performed at one month.
Mann-Whitney U and Kruskal-Wallis tests were not significant. The univariate analysis identified female gender, patient height ≥1.68 m, staghorn calculi, mid and upper calyx location, laser lithotripsy and operative time as significant predictors of antegrade migration of RFs into the ureter after PCNL. Only height ≥1.68 m and staghorn calculi remained statistically significant in the multivariate analysis as shown in Table 2. The model achieved an AUC of 0.69 as shown in Figure 1.

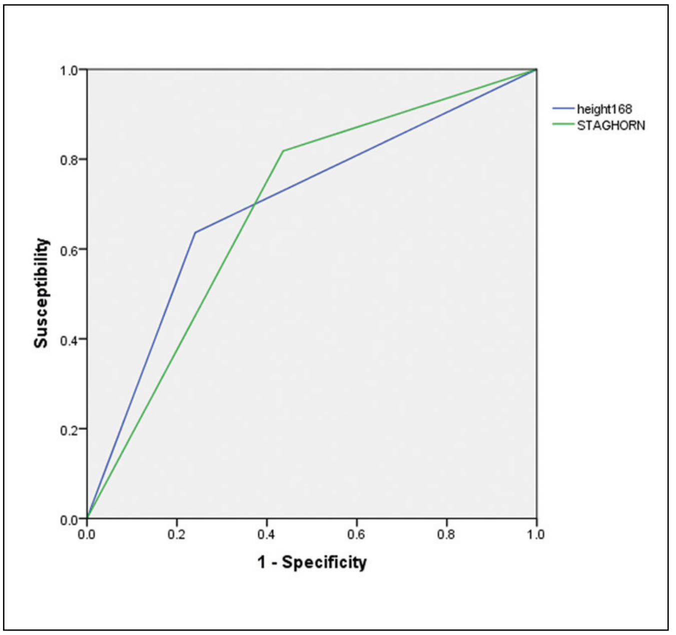

Figure 1. *Receiver operator characteristic curves for height ≥1.68 and staghorn calculi.*

Table 2. *Univariate and multivariate analysis of migration of SF into the ureter in PCNL*

Analysis	Univariate		Multivariate	
Variables	OR[a] (CI[a] 95%)	p	OR[a] (CI[a] 95%)	p
Female gender	4.1 (1.19–14.44)	0.02		
Age	0.98 (0.93–1.02)	0.37		
Height	1.01 (0.96–1.07)	0.53		
Height ≥1.68 m	5.52 (1.51–20)	0.009	7.17 (1.47–34.85)	0.01
BMIa	0.97 (0.86–1.09)	0.61		
Renal failure	1.25 (0.32–4.88)	0.72		
Preoperative hydronephrosis	0.78 (0.22–2.72)	0.76		
Preoperative double J stent	1.6 (0.45–5.64)	0.48		
Location				
Ureteropelvic junction	1.09 (0.13–9.24)	1		
Inferior pole	3.0 (0.63–14.21)	0.21		
Middle pole	6.71 (1.42–31.66)	0.01		
Superior pole	3.59 (1.08–11.92)	0.04	1.7 (0.35–8.15)	0.5
Renal pelvis	2.4 (0.5–11.38)	0.34		
Staghorn calculus	4.72 (1.23–18.13)	0.02	13.27 (1.36–129.5)	0.02
Maximum stone size (mm)	1.03 (0.99–1.06)	0.06		
Maximum stone area (mm²)	1.001 (1.0–1.001)	0.03		
Stone density (HU)	1 (0.99–1.002)	0.76		
Endolithotripsy				
Laser	3.61 (1.09–11.93)	0.03	2.17 (0.44–10.56)	0.33
Ultrasonic	0.65 (0.19–2.16)	0.52		
Pneumatic	1.16 (0.24–5.66)	0.69		
Number of tracts		0.87*		
Operative time (min)	1.007 (1.001–1.013)	0.02	0.99 (0.99–1)	0.6

[a]OR – odds ratio; CI – confidence interval; BMI – body mass index; HU – Hounsfield units; PCNL – percutaneous nephrolithotomy

DISCUSSION

In our series, 12 (7.1%) out of 169 PCNLs suffered migration of RFs into the ureter within the first 48 hours. Five of these twelve migrated stones required an ancillary intervention such as ureteric stent insertion or ureteroscopy. The univariate analysis suggested female gender, height ≥1.68 m, staghorn calculi, mid and upper calyx location, lasertripsy and operative time as statistically significant. However, only height ≥1.68 m, and staghorn calculi remained significance in the multivariate analysis with an AUC of 0.69.

The frequency of antegrade migration of RFs into the ureter in our study is twice the reported rate in literature [10–13]. This has two possible explanations: first, diagnostic imaging in other studies were based on x-ray and ultrasound KUB scans, which are known to be less sensitive for stone detection, in contrast to CT in ours. Nephroscopy has been used as the gold standard of RFs detection after PCNL and compared to it, x-ray and CT KUB underestimate SFR by 35% and 17%, respectively. Therefore, a 20% increase in detection accuracy was expected [14, 15]. Second and most importantly, only SRE resulting from relocation of RFs into the ureter after PCNL are acknowledged properly. As seen in our study, only around 40% of RFs relocated into the ureter and caused a SRE. Moreover, Raman et al. studied 537 PCNLs followed-up with CT KUB and found 8% of RFs within the kidney, of which, similarly to our findings, 43% had a SREs at some point. Residual fragments ≥2 mm in size or located either in the renal pelvis or the ureter predicted this outcome [6]. On the other hand, we decided to intervene nine of the cases with RFs in the ureter due to the size alone, though some of those fragments could have passed spontaneously without causing SREs.

In our cohort, most RFs relocated into the lower half of the ureter. This precludes the identification and the possibility of retrieving the stone with the flexible cystonephroscopy during the PCNL intervention. as antegrade ureteric exploration with a flexible cystoscope may miss these fragments, especially in obese subjects, these patients might be better served by using a flexible ureteroscope.

With regards to stone composition, major differences between females and males have been described

[16, 17]. The former gender has a higher calcium phosphate to calcium oxalate rate as compared to males [18]. Calcium phosphate calculi tend to be softer than calcium oxalate ones, which may render them easier to fragment. One theory of why women were found to have migrated RFs into the ureter after PCNL more frequently than men in the univariate analysis is that more fragmentation is produced in the former group as opposed to dusting in the latter. This also holds true considering ultrasonic dusting was the main lithotripsy modality. Unfortunately, stone composition was not investigated in all cases, so we decided to exclude this variable from the final analysis.

Surprisingly, height was a consistent predictor in our univariate and multivariate analyses. This variable has not been identified as predictor of stone outcomes in previous studies. Novaes et al. evaluated the ureteral length of 115 adult cadavers and found no differences regarding height or gender [19]. Moreover, Kieran et al. undertook a comprehensive assessment of 12 aspects of ureteric morphology across the developmental time in a murine model and found no consistent differences between kidneys in regards to gender or laterality [20]. Consequently, there is not a plausible explanation to our finding and warrants further investigation.

Lower pole calculi have a poorer clearance rate than upper or mid caliceal system stones due to its dependent position within renal cavities along with gravity [21]. This principle may not hold entirely true during a PCNL, as gravity in the position of decubitus does not exert the same force as in the standing position. Nevertheless, our univariate analysis did find calculi located in upper pole and middle calices to be associated with more antegrade migration of RFs. Ganpule et al. described a frequency of 7.5% RFs after 2,469 PCNLs, of which 57.7% were located in the inferior pole. Sixty-five percent of them cleared spontaneously within the following 3 months. Calculi <25 mm^2 and those located in the renal pelvis had the best chance for clearance [22]. Extrapolating the predictors from this study, we hypothesise that during PCNL, pelvic stones are prone to shed away fragments that relocate into the ureter. On the other hand, the aforementioned study's multivariate model revealed preoperative nephrostomy and ureteral stent variables as predictors of spontaneous clearance, which contrasts with our findings.

To answer the question of whether to observe or treat small RFs relocated into the ureter after PCNL we extrapolate evidence from other clinical scenarios such as spontaneous relocation of renal stones into the ureter causing renal colic or antegrade migration of RFs after ureteroscopy or shock-wave lithotripsy. Schatloff et al. compared intraoperative active fragment retrieval in ureteroscopy and lasertripsy versus spontaneous fragment expulsion in a relatively small cohort of 60 cases. The second group had higher rates of unplanned hospital visits (3% vs. 30%, OR 12.4, 95% CI 1.8–80.3, p = 0.01) and a trend of both re-hospitalizations (0% vs. 10%, p = 0.24) and ancillary treatments (0% vs. 7%, p = 0.49) [23]. Scholarikos et al. conducted a systematic review of 37 studies on the natural history of and the role of active monitoring for urinary stones in which the likelihood of spontaneous clearance was 87%, 72%, 47%, and 27% for ureteral stones measuring 1 mm, 4 mm, 7 mm, and 10 mm respectively. Also, the probability of spontaneous passage of RFs is higher for distal (45% to 71%) than mid (22% to 46%) and proximal (12% to 22%) ureteric calculi [24]. Several other factors have been described including longitudinal diameter [14], area and volume in addition to major diameter to better predict the heterogeneous behaviour of ureteric stones, particularly between 5 and 10 mm [25, 26]. The bottom line is that we are still far from predicting spontaneous passage accurately and we should individualise as much as possible.

The pulse settings of endolithotripsy seem to be associated with the size of stone fragments as well as the amount of retropulsion. Hemal et al. evaluated the impact of single or multiple pulse settings of a pneumatic lithotripter (Lithoclast, EMS) to fragment renal calculi and its effect on fragment size and clearance. They prospectively studied 153 patients of whom 69 were in the single and 84 in the multiple pulse mode groups. They found that immediate postoperative RFs were seen more frequently in the multiple pulse mode than in the single one (16 vs. 35, p ≤0.05). This suggests that single pulse mode is associated with controlled fragmentation of the stones, formation of larger fragments, less stone scatter and less postoperative RFs [27]. Bader et al. researched Holmium laser lithotripsy-induced stone fragmentation in vitro to identify the potential impact of different pulse duration on stone fragmentation characteristics. They showed a reduction in stone pushback and equal fragmentation with longer laser pulses compared with short pulse mode [28]. Sea et al. determined the optimal Holmium laser lithotripsy power settings to achieve maximal fragmentation, as well as minimal fragment size and retropulsion in stone phantoms irrigated in water with a wide range of laser settings. At lower energies, less fragmentation and retropulsion as well as smaller fragments were seen [29]. Lasertripsy was performed with short pulse power settings at our centre and the aforementioned studies may explain why this factor was statistically significant in the univariate analysis. Nevertheless, only 4 patients underwent Holmium lasertripsy in our series, which makes inference difficult.

The change in area between the renal pelvis and the ureter have flow dynamics implications on fluids. The same amount of volume of fluid coming from the renal pelvis accelerate as it goes into the funnel of the uretero-pelvic junction to compensate. This is known as the principle of Bernoulli [30]. This phenomenon may have an effect on the movement of RFs facilitating their relocation into the ureter. In addition, longer PCNL operative time may increase the volume of irrigated fluid, favouring dragging fluid dynamics. Identified predictive factors for longer operative times in PCNL are higher BMI, stone burden, type of access imaging as well as selected calyx for accessing and stone complexity as predicted by some nephrometry scores [31]. Furthermore, Hendlin et al. evaluated the forces exerted on a stone with different ureteroscopic irrigation systems that could impact stone migration during ureteroscopy, and found that gravity-based systems exert less force than handheld and foot pump devices [32]. In general, we hypothesise the more irrigation the higher the chances of stone relocation.

Several anti-migration devices have been studied [7, 8, 9], though clinical advantages have not been really proven. It is clear they increase costs and are not risk free. We do not routinely use them in our practice.

There are several study limitations starting with the retrospective nature of our analysis. Firstly, this is a single surgeon and centre experience with many different registrars contributing to the results of the interventions, which cannot be generalised until the results are confirmed. Secondly, many of the known predictive factors of spontaneous passage of stone in the ureter were not recorded and analysed. Thirdly, the composition of stones may have played a role in the form of fragmentation, as mentioned above, though it was not included in the analysis. Fourthly, the different power settings of different lithotripsy modalities were not categorised and may have predicted differently. Lastly, irrigation fluid volumes were not registered and may have proven a covariable for the analyses. On the other hand, the strengths are the following. To start with, CT KUB was the imaging scan used homogenously in all our cases, which is the known standard for urolithiasis evaluation. This allowed us to measure the density, area and volume of stones as well as the accurate location of even small RFs, instead of only including those RFs causing SREs. Secondly, timing of CT scans reflected the immediate effect of PCNL on antegrade migration of RFs into the ureter. Moreover, our stringent SFR criteria allowed us to analyse the natural history of the migrated RFs accurately during the follow-up period. Our cohort also was consistently followed in time, which allowed us to confidently tell asymptomatic from SREs.

Based on our findings, it seems reasonable to advocate for a two-pronged approach. Routine flexible nephroscopy and limited antegrade ureteroscopy (proximal ureter) with the flexible cystonephroscope for all patients undergoing PCNL and no high risk factors such as height ≥1.68 m and staghorn calculi. In high-risk patients, the use of an ureteral occlusive devices or either antegrade thorough ureteric exploration down to the ureteric-bladder junction with a flexible ureteroscope, or endoscopically combined renal surgery using retrograde semi-rigid ureteroscopy to ensure SFR. However, predictors of antegrade migration of RFs into the ureter must first be confirmed in order to justify this approach. Lastly, small fragments found in the ureter may be subjected to surveillance for a reasonable period of four weeks.

CONCLUSIONS

Antegrade stone migration of RFs into the ureter after percutaneous nephrolithotomy occurred in 7.1% of cases, of which less than a half require ancillary procedures due to stone-related events. Staghorn calculi and height ≥1.68 metres may predict high risk patients in whom a more thorough ureteric exploration may be warranted.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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