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Comparison of percutaneous nephrolithotomy and retrograde flexible nephrolithotripsy for the management of 2–4 cm stones: a matched-pair analysis

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What's known on the subject? and What does the study add?
Recently European Association of Urology 2011 guidelines on urolithiasis recommended retrograde intrarenal surgery as the second-line therapy for the treatment of kidney stones <10 mm in diameter.

This study shows that retrograde intrarenal surgery may be an alternative therapy to percutaneous nephrolithotomy, with acceptable efficacy and low morbidity for 2–4 cm stones.

OBJECTIVE

- Currently, the indications for retrograde intrarenal surgery (RIRS) have been extended due to recent improvements in endoscopic technology. In this study, we compare the outcomes of percutaneous nephrolithotomy (PCNL) and RIRS in the treatment of 2–4 cm kidney stones.

MATERIALS AND METHODS

- Between September 2008 and January 2011, 34 patients who had renal stones ranging from 2 to 4 cm in diameter were treated with RIRS. The outcomes of these patients were compared with patients who underwent PCNL using matched-pair analysis (1:1 scenario).
- The matching parameters were the size, number and location of the stones as well as age, gender, body mass index, solitary kidney, degree of hydronephrosis, presence of previous shock wave lithotripsy and open surgery.
- Data were analysed using Fisher's exact test, Student's *t* test and the Mann–Whitney *U* test.

RESULTS

- Stone-free rates after one session were 73.5% and 91.2% for RIRS and PCNL respectively ($P = 0.05$). Stone-free rate in the RIRS group improved to 88.2% after the second procedure.
- Mean operation duration was 58.2 (±) 13.4 min in the RIRS group but 38.7 (±) 11.6 min in the PCNL group ($P < 0.0001$). Blood transfusions were required in two patients in the PCNL group.
- Overall complication rates in the PCNL group were higher, but the differences were not statistically significant. Hospitalization time was significantly shorter in the RIRS group (30.0 + 37.4 vs 61.4 + 34.0 h, respectively; $P < 0.001$).

CONCLUSION

- Satisfactory outcomes can be achieved with multi-session RIRS in the treatment of 2–4 cm renal stones. RIRS can be used as an alternative treatment to PCNL in selected cases with larger renal stones.

KEYWORDS

percutaneous nephrolithotomy, retrograde intrarenal surgery, urolithiasis, flexible ureterorenoscopy, complication

INTRODUCTION

Currently, guidelines on urolithiasis recommend percutaneous nephrolithotomy (PCNL) as the first-line therapy for the treatment of kidney stones >20 mm in diameter [1,2]. Although high success rates exceeding 95% have been reported with PCNL, there are still significant complications including urinary extravasation (7.2%), bleeding necessitating transfusion (11.2–17.5%), postoperative fever (21–32.1%), septicaemia (0.3–4.7%), colonic injury (0.2–0.8%) or pleural injury (0.0–3.1%) associated with this procedure [3,4].

Because of technological improvements in the design of modern flexible ureteroscopes such as incorporation of a working channel, decrease in the diameter of the scope, greater resolution obtained, improved light diffusion and extended field of vision, retrograde intrarenal surgery (RIRS) has been frequently considered in the

management of larger renal stones as an alternative to PCNL [5,6]. In this study, outcomes of RIRS and PCNL in patients with 2–4 cm stones were compared, and applicability of RIRS in patients with greater stone burden was evaluated.

PATIENTS AND METHODS

Between September 2008 and January 2011, 34 patients who had 2–4 cm kidney stones were treated with RIRS at our institution. IVU and/or CT were performed for all patients. Patients' demographic parameters, including age, sex, body mass index (BMI), history of ipsilateral kidney surgery as well as the size, number and location of the stone(s) were recorded. Preoperative laboratory tests included serum creatinine and haemoglobin measurements, platelet counts, coagulation screen tests and urine cultures. All patients had sterile urine culture before the surgery. Before surgery all patients signed an informed consent form. Stone size was assessed as the surface area calculated according to European Association of Urology guidelines [2].

In the same period, PCNL was performed in 561 patients, and 145 of them had 2–4 cm kidney stones. From this cohort, we selected 34 patients to serve as the control group in the study. The 34 patients were retrospectively matched at a 1:1 ratio to index RIRS–PCNL cases with respect to the size, number and location of the stones as well as age, gender, BMI, presence of previous ipsilateral open surgery and shock wave lithotripsy (SWL) and solitary kidney.

PCNL TECHNIQUE

Briefly, access was performed under C-arm fluoroscopy using an 18 gauge needle with the patient in the prone position as previously described in detail elsewhere [7]. The tract was dilated with a high pressure balloon dilator (Nephromax™ Microvasive, Boston Scientific, Natick, MA, USA). Fragmentation of the stone burden was accomplished using a pneumatic (Vibrolith®, Elmed, Ankara, Turkey) or ultrasonic (Swiss Lithoclast®, EMS Electro Medical System, Nyon, Switzerland) lithotripter. A 14 F nephrostomy tube was placed inside the renal pelvis or the involved calix at the conclusion in the majority of cases. The operative time was calculated from the puncture for an access tract to the final placement of a nephrostomy tube.

RIRS TECHNIQUE

A standardized RIRS procedure was performed in all cases as described elsewhere [8]. A safety guidewire was placed into the renal pelvis in the lithotomy position after induction of general anaesthesia. Visual assessment of the ureter and ureteropelvic junction in all patients was performed with a 9.5 F semirigid ureteroscope, which was also used to dilate the ureter to facilitate placement of a ureteral access sheath when necessary. Ureteral balloon dilatation was performed when indicated. A ureteral access sheath was preferred in selected cases if possible. Accessible calices were determined under fluoroscopic guidance. A 7.5 F fibre-optic (Storz FLEX-X^2, Tuttlingen, Germany) or 8.7 F digital flexible ureteroscope (DUR-D Gyrus ACMI, Southborough, MA, USA) and a 200 or 273 μm laser fibre were used for treatment. We used a holmium laser machine set at an energy of 1.0–1.5 J and a rate of 8–10 Hz. At the end of laser lithotripsy, stone fragments smaller than 2 mm were left for spontaneous passage, and basket retrieval was performed for fragments larger than 2 mm. A systematic inspection of the collecting system was performed at the end of the procedure to confirm achievement of adequate fragmentation and stone clearance. A 4.8 F JJ stent was routinely placed in each patient and was removed 3 weeks after the procedure. The operative time was defined as the time passed from insertion of a cystoscope to the completion of stent placement.

Initial postoperative stone-free rates were determined at hospital discharge with a kidney–ureter–bladder radiogram. Afterwards, follow-up stone-free rates were determined in an outpatient clinic setting at 3 months postoperatively with IVU or low-dose spiral CT. The procedure was considered successful if the patient was stone free.

STATISTICAL ANALYSIS

Continuous variables were compared with Student's *t* and Mann–Whitney *U* tests as appropriate. Proportions of categorical variables were analysed using the chi-squared or Fisher's exact test. Statistical significance was set at $P < 0.05$, and all reported *P* values were two-sided. The data analysis was performed using SPSS 16.0 (SPSS, Chicago, IL, USA).

RESULTS

The baseline demographics were comparable between the two groups, in terms of the size, number and location of stones as well as age, gender, BMI, presence of previous ipsilateral open surgery and/or SWL (Table 1). All patients had sterile urinary culture before the surgery in both groups. However, preoperative urine cultures in four and three patients were positive in the PCNL and RIRS groups, respectively, and these infections were treated according to antibiotic sensitivity tests.

Perioperative and postoperative parameters are compared in Table 2. The mean operative times for the RIRS and PCNL groups were 58.2 ± 13.4 (range 30–85) and 38.7 ± 11.6 (range 14–60) min, respectively ($P < 0.001$). The mean fluoroscopy screening time was significantly longer in the PCNL group ($P < 0.001$). Overall complication rates in PCNL were higher, but the differences were not statistically significant. The mean drop in the postoperative haemoglobin level was 0.29 ± 0.17 (range 0.0–0.5) g/dL in the RIRS group, which was found to be statistically significant ($P < 0.001$) compared with the corresponding decrease (1.65 ± 1.20; range 0.1–5 g/dL) in the PCNL group. However, blood transfusion was required for two (5.6%) patients in the PCNL group. In this group, neither hydrothorax nor haemothorax developed in any patient. A JJ stent was inserted in one patient because of persistent leakage of urine after the removal of the nephrostomy tube. Transient fever was encountered in two and one patient(s) in the PCNL group and RIRS group, respectively. Urosepsis was detected in one patient who underwent RIRS. The patient was successfully treated with intravenous antibiotics. In the RIRS group, creatinine levels rose in a patient with a solitary kidney in the postoperative period and regressed to preoperative levels 7 days after the operation. Furthermore, rigid ureteroscopy was required due to the development of steinstrasse in another patient. A second-look ureteroscopic procedure was not required in the PCNL group. Average

hospital stay in the RIRS group was 30.0 + 37.4 h, which was significantly shorter than that for the PCNL group (61.4 + 34.0 h) ($P < 0.001$).

Stone analysis was obtained in 88.2% ($n = 30$) and 82.3% ($n = 28$) of the patients in the PCNL and RIRS groups, respectively. It revealed 70.0% and 75.0% calcium oxalate stones in the PCNL group and RIRS group, respectively (Table 3).

The stone-free rate was 73.5% for the RIRS group and 91.2% for the PCNL group after a single procedure ($P = 0.05$). Nine and three patients in the RIRS and PCNL groups, respectively, had residual stones. A second RIRS was required for five patients. All these patients were completely stone free, resulting in an overall success rate of 88.2%. Finally, stone-free rates at 3 months follow-up improved to 94.1% for the RIRS group and 97.0% for the PCNL group.

DISCUSSION

PCNL is the treatment modality of choice for most renal stones larger than 300 mm^2 and also for complex renal stones [2]. Although this procedure has the advantage of high stone clearance rates, it is still an invasive method with serious complications despite technological advancements. On the other hand, the recent development of new generation flexible ureteroscopes has enhanced the efficacy of these surgical instruments, and significantly decreased morbidity rates in the management of kidney stones [9–11]. Although several authors have compared the outcome of PCNL and SWL in the management of intrarenal stones [12,13], there are still few studies comparing the results of PCNL and RIRS in the treatment of kidney stones [14,15].

The overall success rate of RIRS has been reported to be between 77% and 93% after additional sessions for intrarenal calculi larger than 2 cm (Table 4) [6,11,16–21]. After second sessions, stone-free rates were comparable with those achieved using PCNL. When compared with PCNL, the most important disadvantage of RIRS is requirement for a second session. Grasso *et al.* [16] used a fibre-optic ureteroscope with a decreased inner diameter for

TABLE 1 Matched-pair analysis of PCNL vs RIRS

Parameters	PCNL	RIRS	*P*
Mean age	44.8 ± 17.1	44.5 ± 16.5	0.95
Gender			
Female	52.9 (18)	47.1 (16)	0.63
Male	47.1 (16)	52.9 (18)	
Mean BMI (kg/m^2)	26.4 ± 5.2	26.0 ± 2.9	0.70
Previous open surgery			
(–)	79.4 (27)	82.4 (28)	0.75
(+)	20.6 (7)	17.6 (6)	
History of SWL			
(–)	73.5 (25)	79.4 (27)	0.57
(+)	26.5 (9)	20.6 (7)	
Solitary kidney	8.8 (3)	14.7 (5)	0.71
Hydronephrosis			
Nil or mild	47.1 (16)	44.1 (15)	0.80
Moderate or severe	52.9 (18)	55.9 (19)	
Stone number			
Single	23	28	0.26
Multiple	11	6	
Stone localization			
Upper calices	6	6	
Middle calyx	2	2	1.0
Lower calices	14	15	
Pelvis	12	11	
Stone size (mm^2)	270.0 ± 53.6	268.3 ± 64.4	0.70

TABLE 2 Comparison of perioperative and postoperative data in PCNL and RIRS patients

	PCNL	RIRS	*P*
Mean operation duration ± SD (min)	38.7 + 11.6 (14–60)	58.2 + 13.4 (30–85)	<0.001
Mean fluoroscopic screening time ± SD (min)	4.9 ± 2.1 (1–12)	1.8 ± 0.6 (0.7–3)	<0.001
Mean hospitalization time ± SD (h)	61.4 ± 34.0 (24–192)	30.0 ± 37.4 (18–192)	<0.001
Mean drop in haemoglobin level ± SD (g/dL)	1.65 ± 1.20 (0.1–5)	0.29 ± 0.17 (0.0–0.5)	<0.001
Complications			
Fever	2	1	
Sepsis	–	1	
Need for blood transfusion	2	–	0.72
Prolonged urine leakage	1	–	
Steinstrasse	–	1	
Increase in creatinine levels	–	1	

TABLE 3 Stone composition in each group

Stone composition	PCNL group ($n = 30$)	RIRS group ($n = 28$)	*P*
Calcium oxalate monohydrate	18	17	
Calcium oxalate dihydrate	3	4	
Uric acid	2	3	0.88
Struvite	2	1	
Mixed	5	3	

TABLE 4 Review of the literature on RIRS treatment of kidney stones >2 cm

Authors	*n*	Stone size	Operative time	Mean number of procedures	Overall success rate	Complications
Breda *et al.* [6]	15	20–25 mm	83.3	2.3	93.3	1 fever 2 gross haematuria
El-Anany *et al.* [11]	30	>2 cm	85	1.0	77	1 haematuria 2 fever
Grasso *et al.* [16]	51	>2 cm	–	1.3	91.0	1 pyelonephritis 1 haematuria 1 cerebrovascular accident
Riley *et al.* [17]	22	2.5–5 cm	72	1.8	90.9	1 urosepsis
Mariani [18]	15	2–4 cm	47	1.5	92.0	1 colic
Breda *et al.* [19]	27	>2 cm	66	1.6	85.1	1 significant bleeding 1 ureteral perforation
	24	<2 cm	61	1.2	100	1 pyelonephritis 4 UTI
Hyams *et al.* [20]	120	2–3 cm	74	1.1	85	1 urethral perforation 1 febrile UTI 2 steinstrasse 1 subcapsular haematoma 1 fever 1 acute urinary retention 1 pyelonephritis
Mariani [21]	16	41–97 mm	49	2.4	88.0	3 fever 3 steinstrasse 1 pneumonia
Present study	34	2–4 cm	58.2	1.2	88.2	1 fever 1 urosepsis 1 steinstrasse 1 increase in creatinine levels

non-infectious stones of ≥2 cm, which are not suitable for PCNL. They reported a stone-free rate of 93%. Breda *et al.* [6] investigated the effectiveness and safety of ureteroscopic lithotripsy for single intrarenal stones measuring 20–25 mm in diameter. These investigators used a 7.2 F flexible ureteroscope and 200 μm laser fibre and reported a mean postprocedural success rate of 93% after an average of 2.3 sessions [6]. Riley *et al.* [17] showed a 90.9% success rate for an average stone size of 3.0 cm. They achieved a 91.6% success rate with an average of 1.9 procedures for stones larger than 3 cm, 80% success with an average of 1.8 procedures for stones larger than 3.5 cm, and 50% success with an average of two procedures for stones larger than 4 cm [17]. Chung *et al.* [14] compared outcomes of 15 PCNL and 12 RIRS patients who were treated for the clearance of 1–2 cm renal calculi. They reported that stone-free rates for PCNL and RIRS were 87% and 67%, respectively.

In the present study, the mean operation durations for the RIRS and PCNL groups were 58.2 + 13.4 and 38.7 + 11.6 min, respectively. Mariani [18] reported a mean operative time of 64 min for the ureteroscopic management of renal stones measuring 2 and 4 cm [18]. The association between operative time and complications related to PCNL has been reported in various studies [22,23]. Akman *et al.* [22] found that need for blood transfusion increased 2.82-fold when operative times were longer than 58 min for patients managed with PCNL. In another study, Kukreja *et al.* [23] found that diabetes mellitus and a multiple access tract procedure, together with prolonged operative time, were associated with blood loss during the PCNL procedure. The relationship between operative time and bleeding in RIRS is not acknowledged, and we do not think that any association exists. However, development of excessive intrarenal pressure in RIRS might lead to intrarenal reflux transiently affecting renal function. Schwalb *et al.* [24] found that high pressure irrigation during ureterorenoscopy (URS) in pigs caused irreversible, deleterious effects in the kidney parenchyma, and it is proposed that infectious complications may result from renal extravasation. Maintaining lower pelvic pressures during RIRS can be achieved by several manipulations, such as irrigation with isoproterenol, using a ureteral access sheath and limiting operative time [25,26]. In our study in the RIRS group, transient increase in creatinine levels in a patient with a solitary kidney was encountered on the first postoperative day, returning to preoperative levels 7 days later.

The mean duration of fluoroscopy was found to be longer in the PCNL group relative to the RIRS group. Similar to the present study, percutaneous nephrostomy under primary fluoroscopic guidance is the technique preferred by several investigators. The creation of percutaneous renal access generally requires longer fluoroscopy time

than the other steps of PCNL. However, the guidewires and ureteral access sheath were placed under fluoroscopy during RIRS. As an important advantage of RIRS over PCNL, creation of an access tract in the RIRS group is not required and significantly limits the duration of fluoroscopic screening time.

Complications arise mainly from percutaneous access and are associated with damage to the renal parenchyma and adjacent structures. The PCNL procedure is associated with several complications including bleeding requiring blood transfusion, septicaemia, colonic injury, haemothorax, fever and urinary infection. One of the most important complications is bleeding requiring transfusion, the incidence of which has been reported to vary between 0.8% and 45% in the PCNL literature [27–29]. Intractable bleeding requiring embolization or total nephrectomy could occur. On the other hand, URS and laser lithotripsy have a universally low complication rate compared with PCNL. A substantial decrease in the number of complications has been reported in modern series, especially related to the use of ureteroscopes of smaller size. Ureteral avulsion is exceedingly rare but the most important complication of ureteroscopy.

Steinstrasse is generally seen in patients with a greater stone burden post-SWL. In the present study, steinstrasse was not observed in the PCNL group but developed in one patient after RIRS and was managed using an additional rigid ureteroscopic procedure. Mariani [21] reported development of minimally symptomatic steinstrasse in 18.7% of patients with renal stones larger than 4 cm following retrieval by RIRS. These higher rates may be associated with the use of a laser lithotripter in combination with an electrohydraulic lithotripsy. Consistent fragmentation of greater residual stone burden during RIRS into smaller particles (<1–2 mm) substantially decreases the risk of steinstrasse. Therefore, vaporizing or melting of the stone using low energy and high frequency with the laser fibre over the stone's surface (painted technique) instead of trying to just fragment the stone into multiple small pieces should be preferred.

The hospital stay was longer in the PCNL group compared with the RIRS group. One of the most important reasons for this delay is nephrostomy tube placement for better drainage. Recent studies have shown that tubeless PCNL is the most important factor in decreasing hospital stay [30,31]. However, the decision to position a tubeless PCNL is usually made at the end of the procedure. It can be applied in the absence of a significant residual stone, pelvicaliceal system perforation, and significant bleeding. RIRS is typically an outpatient procedure. Technical improvements in flexible URS, including smaller calibre ureteroscopes with digital optics and dual deflection, have recently made RIRS a more popular and feasible option.

Limitations of our study include its retrospective nature, its limited power based on interest in a stone subgroup as well as the relatively shorter follow-up period of 3 months. Second, analgesic and postoperative pain scores were not evaluated. Postoperative pain can be related to the presence of a nephrostomy tube in patients who underwent PCNL. The analgesic dose used in tubeless procedures was lower than that seen in standard procedures in several studies [32,33]. However, studies are needed to compare the effect of tubeless PCNL and RIRS on postoperative pain. Currently, further prospective studies with high case volumes that compare RIRS vs PCNL with regard to outcomes, complications, cost and convalescence in long-term follow-up are required.

Currently, PCNL is the gold standard treatment modality for kidney stones larger than 2 cm in size. However, satisfactory outcomes can be achieved with multi-session RIRS in the treatment of 2–4 cm renal stones. Furthermore, hospital stay and morbidities of PCNL can be significantly reduced with RIRS. Therefore, RIRS with a holmium laser represents a good alternative treatment to PCNL in well selected cases with larger renal stones. However, these outcomes must be confirmed by further prospective randomized studies.

CONFLICT OF INTEREST

None declared.

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Abbreviations: **PCNL**, percutaneous nephrolithotomy; **RIRS**, retrograde intrarenal surgery; **BMI**, body mass index; **SWL**, shock wave lithotripsy; **URS**, ureterorenoscopy.