Journal of Pediatric Surgery (2013) **48**, 840–844

Journal of Pediatric Surgery

www.elsevier.com/locate/jpedsurg

Are small residual stone fragments really insignificant in children?

Nida Dincel[a], Berkan Resorlu[b,*], Ali Unsal[b], Abdulkadir Tepeler[c], Mesrur Selcuk Silay[c], Abdullah Armağan[c], Akif Diri[d], Ahmet Ali Sancaktutar[e], Tevfik Ziypak[f], Sevgi Mir[a]

[a]*Department of Pediatric Nephrology, Ege University, Faculty of Medicine, Izmir, Turkey*
[b]*Department of Urology, Kecioren Training and Research Hospital, Ankara, Turkey*
[c]*Department of Urology, Bezmialem Vakif University, Faculty of Medicine, Istanbul, Turkey*
[d]*Department of Urology, Ankara Training and Research Hospital, Ankara, Turkey*
[e]*Department of Urology, Dicle University, Faculty of Medicine, Diyarbakir, Turkey*
[f]*Department of Urology, Ataturk University, Faculty of Medicine, Erzurum, Turkey*

Received 23 May 2012; revised 21 July 2012; accepted 23 July 2012

Key words:
Children;
Follow-up;
Residual fragments;
Renal stone

Abstract

Objectives: To assess the significance of asymptomatic residual stone fragments of less than 4 mm (clinically insignificant residual fragments [CIRFs]) after shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PNL), and retrograde intrarenal surgery (RIRS) in children.

Patients and Methods: Eighty-five children were followed up for 6 to 50 months (median 22). Outcomes measured were fragment re-growth, stone events (emergency department visits, hospitalization, or additional interventions) and spontaneous fragment passage.

Results: During follow-up, 22 children (25.8%) passed residual fragments spontaneously. Highest spontaneous passage rate was found for renal pelvis stones and the lowest for the lower pole stones (57.1% vs. 16.1%; $p<0.001$). When the number of the fragments increased, the chance of the spontaneous passage decreased (30% vs 20%; $p<0.05$). Symptomatic episodes including renal colic, hematuria, or urinary tract infection were documented in 34 (40%) patients, and re-growth of fragments was observed in 18 (21.2%). Stone size had no significant effect on spontaneous passage ($p=0.079$), stone growth ($p=0.528$), and symptomatic episodes ($p=0.402$). Twenty-five patients (29.4%) required secondary intervention for stone re-growth or stone related events and the remaining 20 patients (23.5%) needed medical treatment for bothersome symptoms or complications.

Conclusions: Our results suggest that 40% of children with CIRFs will become symptomatic and 20% will develop stone re-growth over the following 6 months. Only one fifth of the fragments will pass spontaneously without any complications. Therefore, the use of the term "CIRF" is not appropriate for postoperative residual fragments in children.

* Corresponding author. Tel.: +90 5055025743; fax: +90 3123569003.
E-mail addresses: drberkan79@gmail.com, drberkan@yahoo.com (B. Resorlu).

0022-3468/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jpedsurg.2012.07.061

The management of upper urinary stone disease in children has changed dramatically in the last two decades due to improvements and miniaturization of instruments [1-4]. Currently, the three minimally invasive approaches available for pediatric patients with intrarenal stones are shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PNL) and retrograde intrarenal surgery (RIRS). SWL is a well-established treatment method and the majority of pediatric stone diseases can be managed effectively and safely with this technique. However, there are some stones that do not respond to SWL, and these can be managed by other treatment modalities such as PNL and RIRS.

These minimally invasive techniques have provided a new definition in reporting treatment results, that is clinically insignificant residual fragments (CIRFs) [5]. Residual fragments smaller than 5 mm which are asymptomatic, noninfectious and likely to pass spontaneously are termed CIRF [6]. However, this term has not been accepted by some authors because these fragments have the potential to cause ureteral obstruction and are important risk factors for stone re-growth and recurrence [7].

Although data are available regarding the outcomes of CIRFs in adults, no data is available for children and the fate of CIRFs is not known in the pediatric population. In this study, we evaluated the natural history of these fragments following SWL, PNL or RIRS in children.

1. Patients and methods

We retrospectively reviewed the medical records of 85 pediatric patients (1–17 years) who had CIRFs at 3 months after the last session of SWL (n=49) or 1–2 months after the RIRS (n=10) and PNL (n=26). CIRFs were defined as nonobstructive, noninfectious, asymptomatic residual fragments 4 mm or less in size [5]. Stone fragment size, location (upper-, middle-, lower-pole and renal pelvis) and presence of single or multiple fragments were assessed with the combination of ultrasonography (US) and plain radiography. Only patients with follow-up more than 6 months were included to study. The patients who had abnormal renal anatomy, musculoskeletal deformities, radiolucent stones and inadequate follow-up data were not included to study. Pretreatment evaluation included a careful medical history, physical examination, routine blood tests, urine analysis, urine culture, plain film, US and intravenous urography (IVU). Renal scintigraphy and computed tomography (CT) were not done routinely but they were performed whenever needed. Stone size was determined by measuring the longest axis on plain film; when multiple stones were present in the kidney stone size was reported as the sum of the diameters of each stone.

Stone-free status was determined in an outpatient clinic setting at 1–2 months postoperatively for PNL and RIRS, and at 3 months after SWL. Patients were evaluated by urinalysis, urine culture, renal function tests, plain abdominal radiography and urinary US every 3 months during the first year and every 6 months thereafter. Stone analyses were performed by X-ray diffraction crystallography. We routinely advised patients and their parents to maintain a high fluid intake and avoid excessive intake of salt and animal proteins. A primary metabolic evaluation included urine pH, stone analysis, serum calcium, phosphorus, uric acid and 24-hour urinary calcium, phosphorus, oxalate, citrate, uric acid, creatinine and electrolytes. Patients completing a metabolic evaluation were offered selective medical therapy. Medical therapy included potassium citrate for hypocitraturia, renal tubular acidosis, chronic diarrheal syndromes; thiazide diuretics for hypercalciuria; alpha-mercaptopropionylglycine for cystinuria; and allopurinol for hyperuricosuria [8]. However, some patients or their parents chose not to undergo selective medical therapy and opted for conservative measures alone.

Patients were followed for 6 to 50 months (median 22 months). During the follow-up, incidence of stone events (hospitalization, need for emergency room visit and additional interventions for removing the residual fragments or treat symptoms), growth in the size of fragments and spontaneous passage of these fragments were evaluated. For the developing complications, patients were treated conservatively or received appropriate ancillary treatment.

1.1. Statistical analyses

Data were processed using SPSS-16 for Windows (SPSS, Inc., Chicago, IL). Continuous variables were compared with the Mann–Whitney U test. The proportions of categorical variables were analyzed for statistical significance using the chi-square test. While the categorical variables were presented by frequency (percent), continuous variables were presented by median (range). Statistical significance was defined as $p<0.05$.

2. Results

The clinical and radiographic findings of the 85 children are summarized in Table 1. Forty-nine boys and 36 girls with a mean age of 9.2 years were included in the study. The median size of CIRFs was 3 mm (1–4 mm). The anatomical distribution of CIRFs was 36% lower pole, 31% middle or upper pole, 25% multiple caliceal and 8% renal pelvis. Most of the children had only one fragment (58.8%) followed by two and more than two fragments in 20% and 21.2% of the patients, respectively.

Stone analysis was available in 75 (88.2%) patients and showed that 41 patients had calcium oxalate or phosphate stones, 27 had mixed, 4 had cystine and 3 had uric acid stones. No patients with residual fragments had struvite calculi. Metabolic evaluation was performed in 66 patients

Table 1 Clinical and radiographic characteristics of children with residual fragments.

No. patients	85
Male/female	49/36
Median age (range)	9 years (1–17)
Median CIRF size (range)	3 mm (1–4)
No. of CIRFs	
Single (%)	50 (58.8%)
Multiple (%)	35 (41.2%)
Location of CIRFs (%)	
Renal pelvis	7 (8.2%)
Mid/upper pole calices	26 (30.6%)
Lower pole calices	31 (36.5%)
Multiple calices	21 (24.7%)
Stone Analysis (%)	
Ca oxalate/phosphate	41 (48.2%)
Mixed	27 (31.7%)
Cystine	4 (4.7%)
Uric acid	3 (3.5%)
Unknown	10 (11.7%)

(77.6%) of whom 44 (66.6%) had one or more predisposing disorders identified. Of these 17 had hypocitraturia, 14 hypercalciuria, 13 hypomagnesuria, 4 cystinuria, 3 had hyperoxaluria and 2 had hyperuricemia. Thirty patients (35.3%) underwent selective medical therapy whereas 53 (64.7%) chose not to undergo medical therapy and opted for conservative measures alone. Only 4 patients (13.3%) showed an increase in stone size during medical therapy compared to 14 of 53 (26.4%) patients without medical treatment.

After a median follow-up of 22 months (range, 6–50 months), 22 children (25.8%) passed residual fragments spontaneously. Highest spontaneous passage rate was found for renal pelvis stones and the lowest for lower pole stones (57.1% vs. 16.1%; $p<0.05$). For the lower pole stones, infundibulopelvic angle (IPA) measurement was a significant factor on stone clearance. The presence of an IPA of $<45^0$ was strongly related to a low spontaneous passage rate (46% vs 0% for IPA $\geq 45^0$ vs $<45^0$, $p=0.008$).

When the number of fragments increased, the chance of the spontaneous passage decreased. Among 50 patients with a single stone, 15 (30%) had spontaneous passage; in contrast, only 7 of 35 patients with multiple fragments (20%) had spontaneous passage ($p<0.05$). Stone size and patient age had no significant effect on the spontaneous passage rate ($p=0.079$ and $p=0.872$; respectively). Furthermore we did not find any significant correlation between stone size and stone growth ($p=0.528$) or stone size and symptomatic episodes ($p=0.402$).

Increase in the size of fragments was observed in 18 patients (21.2%), whereas the size of the fragments was stable in 45 (52.9%) patients. A total of 51 patients (60%) were asymptomatic during follow-up, while the remaining 34 (40%) developed symptomatic episodes including renal colic pain, hematuria or urinary-tract infection. Eleven children with stone growth were treated with SWL (n=6), RIRS (n=2), PNL (n=2) or open surgery (n=1), and 7 were observed. Of the 34 patients who experienced a stone related event 14 required a secondary intervention which included 7 SWL, 5 ureteroscopies, and 2 ureteral stenting and the other 20 patients were treated conservatively. The types of secondary interventions are listed in Table 2.

3. Discussion

Stone disease is not common in children but is often associated with anatomical and metabolic abnormalities or infection, and the risk of recurrence is high [9]. Therefore management of stone disease in children necessitates eradication of urinary tract infections, correction of any underlying metabolic or anatomical disorders and complete stone clearance. However, no minimally invasive treatment modality can achieve a 100% stone clearance rate, because stone fragments remain in a various proportion of the kidney.

Historically, with SWL, the term “CIRF” was used to refer to fragments ≤ 4 mm associated with sterile urine in an otherwise asymptomatic patient that would pass spontaneously [10]. However, this term was not accepted by some authors because fragments have the potential to cause obstruction and are an important risk factor for stone growth and recurrence [7]. Although various reports are available regarding long-term results of CIRFs in adults, the fate of

Table 2 Outcomes of residual fragments.

		p value
Spontaneous passage (%)	22/85 (25.8%)	
According to stone location		<0.05 *
Renal pelvis	4/7 (57.1%)	
Mid/upper pole	9/26 (34.6%)	
Lower pole	5/31 (16.1%)	
Multi-caliceal	4/21 (19.1%)	
IPA		<0.05 *
$\geq 45^0$	7/15 (46.7%)	
$<45^0$	0/11 (0%)	
According to no. fragments		<0.05 *
Single (%)	15/50 (30%)	
Multiple (% [median, range])	7/35 (20% [3, 2 – 4])	
Growth in size (%)	18 (21.2%)	
Stone related events (%)	34 (40%)	
Renal colic	21 (24.7%)	
Hematuria	14 (16.4%)	
Urinary tract infection	5 (5.8%)	
Secondary interventions (%)	25 (29.4%)	
SWL	13 (15.3%)	
Ureteroscopy	7 (8.2%)	
PNL	2 (2.3%)	
Ureteral stenting	2 (2.3%)	
Open surgery	1 (1.1%)	

* Significant at 0.05 level.

these fragments in children is not well known. This definition was made from adult experience, and may not hold true for pediatric patients. To our knowledge, this is the first study that examines the outcome of small stone fragments after PNL, RIRS and SWL in children.

In our series the incidence of growth in the size of CIRFs was 21.2% after a median follow-up of 22 months. These findings were comparable with adult series reporting re-growth rates from 2 to 59% [7,11,12]. Some studies have addressed the value of medical therapy on the outcome of residual fragments. Fine et al reported 50% stone re-growth in patients with CIRFs, was decreased to 16% with medical management [8]. Kang and coworkers also reported similar results after PNL in a more recent study [11]. In another two studies, Cicerello et al and Soygur et al demonstrated the benefit of potassium citrate therapy in the clearance of residual stone fragments [13,14]. In contrast, Osman and associates found no relation between metaphylaxis and stone re-growth [15]. Our data suggest that metabolic defects, if treated adequately, did not increase the re-growth rates. Only 11.4% of our patients showed an increase in stone size during medical therapy compared to 26.4% without medical management.

We observed stone related events such as renal colic, hematuria or urinary tract infection in 34 of 85 (40%) children. It is important to inform patients and their parents about the risks of stone-related symptomatic episodes and the eventual need for auxiliary treatments. Streem et al reviewed the natural history of CIRFs in 160 patients and observed that 43.1% of patients had a symptomatic stone event and/or required intervention after SWL [16]. In their opinion, the application of the term CIRF may not be appropriate. In a separate study by Khaitan, 81 patients were followed for 6–60 months (mean 15) after SWL to determine the fate of the CIRFs [7]. They concluded that term of CIRF is a myth, as 58.7% of their patients required intervention because of the development of one or more complications. The results of our study support this concept, because 34 of 85 (40%) became symptomatic in our series during the follow-up period. Furthermore 25 children (29.4%) required secondary interventions such as SWL, PNL, RIRS or ureteral stenting.

In our series, only 22 patients (25.8%) passed stone fragments spontaneously. This is less than the reported stone clearance rates after SWL in adults, which range from 30% to 98% in the literature [7,12,17]. We found that number and location of the fragments are important factors in predicting the spontaneous passage in children. The stone clearance rate was highest in the renal pelvis, followed by the middle or upper pole and then lower pole. These findings are in accordance with most previous reports; however, Zanetti et al and Moon et al found that the location of CIRFs did not significantly influence the clearance rate [7,15,18–20]. We think that the dependent anatomy of the lower pole acts as a hindrance to spontaneous passage of CIRFs. Resorlu et al evaluated the stone related factors and pelvi-calyceal anatomy for stone clearance after RIRS and they found that stone size and the lower pole infundibulopelvic angle (IPA) were important factors affecting stone clearance [21]. In our study presence of IPA of $<45^0$ was strongly related to a low spontaneous passage rates.

There are several limitations in our study owing to its multicentric and retrospective nature. Therefore, these findings must be confirmed by further prospective studies. But the most important limitation is that a combination of renal US and plain radiographs was used to assess the residual stones. US has limitations compared with CT scan, as it has less sensitivity and specificity [22]. However, US has clear advantages of convenience and lack of radiation exposure over the CT scan. This is important especially in children. Furthermore, routine imaging after stone surgery in children has recently been questioned, and studies regarding follow-up after this procedure are controversial. In a recent study, Resorlu et al reported that the combination of renal US and plain radiography are safe and effective imaging procedures in postoperative follow-up of children [22]. Despite these shortcomings, this is an important study, because there is no previous data in the literature about fate of CIRFs after endourologic surgery and SWL in children.

4. Conclusion

Our results suggests that 34 of 85 children (40%) with CIRFs will become symptomatic and 18 of 85 (21%) will develop stone re-growth over the following 6 months. Only 22 patients (25.8%) will pass stone fragments spontaneously without any complications. Therefore, the use of the term "CIRF" is not appropriate for postoperative residual fragments in children.

References

[1] Unsal A, Resorlu B. Retrograde intrarenal surgery in infants and preschool-age children. J Pediatr Surg 2011;46:2195-9.

[2] Lottmann HB, Traxer O, Archambaud F, et al. Monotherapy extracorporeal shock wave lithotripsy for the treatment of staghorn calculi in children. J Urol 2001;165:2324-7.

[3] Straub M, Gschwend J, Zorn C. Pediatric urolithiasis: the current surgical management. Pediatr Nephrol 2010;25:1239-44.

[4] Unsal A, Resorlu B, Kara C, et al. Safety and efficacy of percutaneous nephrolithotomy in infants, preschool age, and older children with different sizes of instruments. Urology 2010;76:247-52.

[5] Afshar K, McLorie G, Papanikolaou F, et al. Outcome of small residual stone fragments following shock wave lithotripsy in children. J Urol 2004;172:1600-3.

[6] Altunrende F, Tefekli A, Stein RJ, et al. Clinically insignificant residual fragments after percutaneous nephrolithotomy: medium-term follow-up. J Endourol 2011;25:941-5.

[7] Khaitan A, Gupta NP, Hemal AK, et al. Post-ESWL, clinically insignificant residual stones: Reality or myth? Urology 2002;59:20-4.

[8] Fine JK, Pak CY, Preminger GM. Effect of medical management and residual fragments on recurrent stone formation following shock wave lithotripsy. J Urol 1995;153:27-33.
[9] Oner A, Demircin G, Ipekcioglu H, et al. Etiological and clinical patterns of urolithiasis in Turkish children. Eur Urol 1997;31:453-8.
[10] Newman DM, Lingeman JE. Management of upper urinary tract calculi with extracorporeal shock wave lithotripsy. Compr Ther 1989; 15:35-40.
[11] Kang DE, Maloney MM, Haleblian GE, et al. Effect of medical management on recurrent stone formation following percutaneous nephrolithotomy. J Urol 2007;177:1785-9.
[12] Buchholz NP, Meier-Padel S, Rutishauser G. Minor residual fragments after extracorporeal shock wave lithotripsy: spontaneous clearance or risk factor for recurrent stone formation? J Endourol 1997;11:227-32.
[13] Cicerello E, Merlo F, Gambaro G, et al. Effect of alkaline citrate therapy on clearance of residual renal stone fragments after extracorporeal shock wave lithotripsy in sterile calcium and infection nephrolithiasis patients. J Urol 1994;151:5-9.
[14] Soygur T, Akbay A, Kupeli S. Effect of potassium citrate therapy on stone recurrence and residual fragments after shock wave lithotripsy in lower caliceal calcium oxalate urolithiasis: a randomized controlled trial. J Endourol 2002;16:149-52.
[15] Osman MM, Alfano Y, Kamp S, et al. 5-Year follow-up of patients with clinically insignificant residual fragments after extracorporeal shock wave lithotripsy. Eur Urol 2005;47:860-4.
[16] Streem SB, Yost A, Mascha E. Clinical implications of clinically insignificant stone fragments after extracorporeal shock wave lithotripsy. J Urol 1996;155:1186.
[17] Beck EM, Riehle RA. The fate of residual fragments after extracorporeal shock wave lithotripsy monotherapy of infection stones. J Urol 1991;145:6-9.
[18] Candau C, Saussine C, Lang H, et al. Natural history of residual renal stone fragments after ESWL. Eur Urol 2000;37:18-22.
[19] Zanetti G, Seveso M, Montanari E, et al. Renal stone fragments following shock wave lithotripsy. J Urol 1997;158:352-5.
[20] Moon YT, Kim SC. Fate of clinically insignificant residual fragments after extracorporeal shock wave lithotripsy with EDAP LT-01 lithotriptor. J Endourol 1993;7:453-6.
[21] Resorlu B, Oguz U, Resorlu EB, et al. The impact of pelvicaliceal anatomy on the success of retrograde intrarenal surgery in patients with lower pole renal stones. Urology 2012;79:61-6.
[22] Resorlu B, Kara C, Resorlu B, et al. Effectiveness of ultrasonography in the postoperative follow-up pediatric patients undergoing uretero-scopic stone manipulation. Pediatr Surg Int 2011;27:1337-41.