Examining Pediatric Cases From the Clinical Research Office of the Endourological Society Ureteroscopy Global Study

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OBJECTIVE To evaluate the characteristics and outcomes of ureteroscopy (URS) in children treated in several hospitals participating in the Clinical Research Office of the Endourological Society (CROES) Study, and to present the overall results of pediatric URS compared with adults.

PATIENTS AND METHODS The CROES Study collected data on consecutive patients treated with URS for urolithiasis at each participating center over a 1-year period. The collected prospective global database includes data for 11,885 patients who received URS at 114 centers in 32 countries. Of these URS-treated patients, 192 were ≤18 years old.

RESULTS Of the 114 centers participating in the study, 42% had conducted pediatric URS. Among the pediatric cases, 7 were infants, 53 were small children, 59 were school-aged children, and 73 were adolescents. A considerable number (37%) of the pediatric cases had previously undergone URS treatment. No differences in the surgical outcomes of the adults and children were reported. The URS-treated children had a greater number of positive preoperative urine cultures when compared with adult cases treated. A semirigid scope was used in the vast majority of pediatric cases (85%). According to the present data, within the group of URS-treated children, the younger the child, the more readmissions occurred.

CONCLUSION URS is as efficient and safe in children as it is in adults. The data suggest that readmissions among URS-treated children are associated with age, with the likelihood of readmissions greater among younger age groups. UROLOGY 101: 31–37, 2017.

Current trends in urolithiasis epidemiology are characterized by increased urolithiasis rates, combined with a shift toward a lower age of the first stone episode.[1,2] And although spontaneous passage is more likely in children than adults, some children benefit from active interventions.[2-7] The developments and experience made in the endoscopic treatment of adult stone disease also favorably affect pediatric cases. In the past, only mid-to-distal ureteral stones were treated. However, as a result of increased experience, recent clinical studies[1-4,8-10] have demonstrated the use of ureteroscopy (URS) in treating both upper ureteral and renal calculi.

Although minimally invasive interventions performed in adults and children may seem similar, there are also substantial differences. For example, in pediatric cases, the intervention is conducted on a still growing kidney and in smaller-sized anatomies,[6,11] for which different (smaller-sized) equipment is needed. Furthermore, anesthesia requirements for children are different from those of adults. In the pediatric population, diagnostic methods may differ, and the population has an increased hypothermia risk and is vulnerable to the long-term effects of ionizing radiation.[4,7] Finally, the pediatric population may have different clinical manifestations and a higher risk of lifelong recurrent interventions than adults.[12] Subsequently, the diagnosis, treatment, and follow-up protocols have to take these differences and challenges in pediatrics cases into account.

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Multicenter studies with large patient series can provide insights in the approaches used in different countries and medical centers, as well as surgeons' preferences. The Clinical Research Office of the Endourological Society (CROES) URS Global Study has established the world's largest URS database with 11,885 cases treated. This enables analyses of pediatric and adult URS cases within a prospective observational nature.[13] As the guidelines and clinical studies differ to some extent in defining patients eligible for URS treatment, the aim of the current study is to describe the "real-life" use of URS in the pediatric population in general clinical practice. The study compares the procedures and outcomes in children with the adult population to define similarities, differences, and limitations along with the safety and efficacy of the URS procedure.

PATIENTS AND METHODS

Study Population

Current study population is selected from the prospective, observational, international multicenter study initiated by the CROES in January 2010. The CROES URS Global Study collected data on consecutive patients treated with URS for urolithiasis at each participating center over a 1-year period. The study includes data from 11,885 patients who received URS at 114 centers in 32 countries. Of the URS-treated patients, 192 were ≤18 years old and treated in 54 centers in over 23 countries, which is described in more detail elsewhere.[13]

Patients' Characteristics

The age classification criterion of the World Health Organization was used to define age groups into infants (0-1 years), young children (2-4 years), school-aged children (5-14 years), and adolescents (15-18 years). The stone size was demarcated as the largest diameter in millimeter. The stone burden was defined as follows: $\sum$ stone length *$\sum$stone width *0.25*3.14159. Complications were categorized according to the Clavien-Dindo Classification of Surgical Complications system. The stone-free rate was defined as the proportion of success over failure. Treatment failure was defined as a stone still in situ, remaining stone fragments of >1 mm, and failed access. Subsequently, treatment success was defined as a patient free of stones of >1 mm.

Statistical Methods

Descriptive information is presented as the mean, with standard deviations for continuous normally distributed variables and median interquartile ranges for continuous skewed variables. Categorical variables are presented as percentages. In the case of small proportions, the actual number is also presented. Descriptive information and percentages were based on available data.

To compare the adults (>18) with children (0-18 years), an independent sample *t* test, in which unequal variances were assumed, was used for continuous variables. A log transformation was used for continuous skewed variables prior to a *t* test. A chi-square test was used for categorical or dichotomous variables. To compare the outcomes among different age groups (infants, young children, school-aged children, and adolescents), Pearson's chi-square analysis for dichotomous or categorical variables was used, and an analysis of variance was employed for continuous variables.

All statistical analyses were performed using Stata version 13 (StataCorp LP, College Station, TX; www.stata.com).

RESULTS

Of the 11,885 patients, 10,319 had complete information on age. Of these patients from the URS Global Study, only 192 (1.9%) were 18 years or younger. These patients were treated in 54 centers in over 23 countries. Of the 114 centers participating in the study, 42% had conducted pediatric URS. Most of the pediatric cases were treated in Turkey (46%), India (15%), and Iran (9%) (Fig. 1, Supplementary Table S1). Among the pediatric cases, 7 were infants, 53 were young children, 59 were school-aged children, and 73 were adolescents (Fig. 2, Table 1). The mean age of the children was 10.3 (6.3). Out of all the cases, 56.8% were male. Six pediatric cases had an anatomic anomaly. Seventy-one (37%) pediatric cases had undergone previous treatment, and 9 had undergone more than one previous treatment (Supplementary Table S2).

In addition to the expected differences in age and body mass index, the location of the stones differed between adults and children treated with URS. Furthermore, the URS-treated children had more positive preoperative urine cultures than did adults. During the operation, the vast majority of the pediatric group was treated with a semirigid scope (86%), whereas a semirigid scope was used in only 73% of adults. Regardless of age groups, for both semirigid and flexible ureteroscopes, smaller sizes (7-8F) were preferred (Table 1). No significant differences in ureteroscope size between adults and children, nor between the different age groups within the pediatric population, were found. Table 1 also shows that the most preferred method for access was guidewires in both adult and pediatric cases. In adults, however, guidewire is suggested to be often substituted with a balloon or an access sheath.

The overall mean duration of the intervention was 33 minutes (23-60 minutes) and 40 minutes (25-60 minutes) for children and adults, respectively. As can be seen in Supplementary Table S2, for residual stone evaluation, ultrasound (US) was preferred in 52.6% of children, kidney, ureter, and bladder X-ray in 28.1%, and computomography in 6.3%, and these rates were comparable with adult patients. Whereas intraoperative complications were reported in 1 (0.5%) case in the pediatric group and in 145 (1.4%) cases in the adult group, postoperative complications were reported in 1 (0.5%) case in the pediatric and in 247 (2.4%) cases in the adult group. Twenty-one (10.9%) patients required further treatment. Among the children, 9 underwent re-ureteroscopy, 9 underwent external shock wave lithotripsy, and 1 underwent percutaneous nephrolithotomy (PCNL).

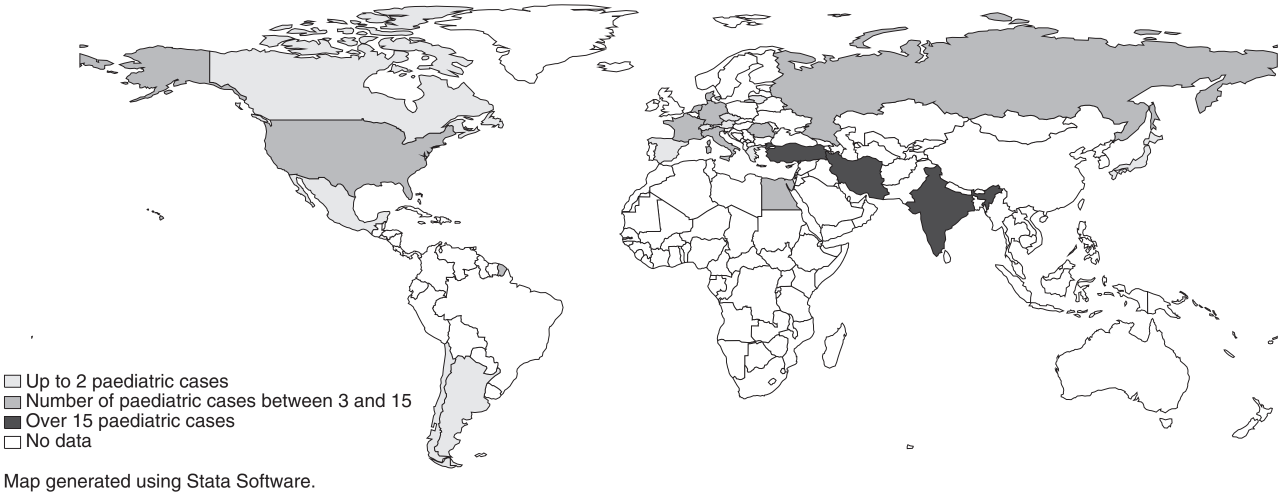

Figure 1. Pediatric cases worldwide.

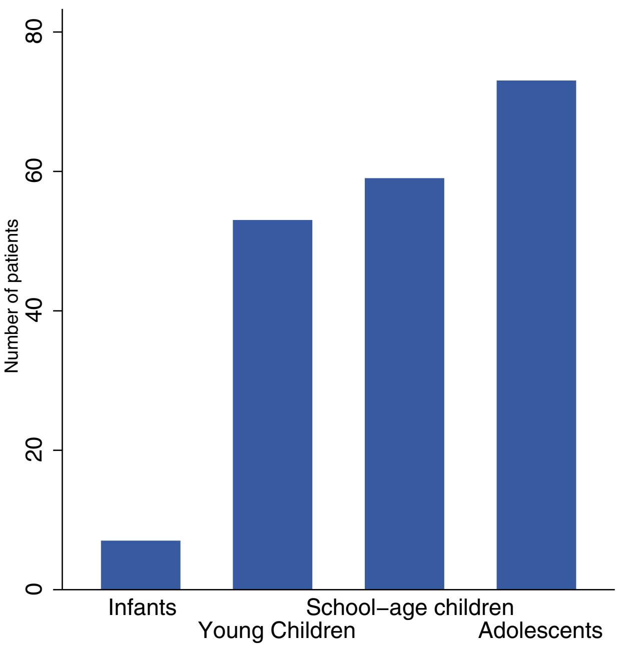

Figure 2. Number of pediatric patients according to the World Health Organization classification of age groups. (Color version available online.)

No differences in the surgical outcomes of the adults and children were reported. However, within the group of young children, as defined by the age categories of the World Health Organization, the younger the children are, the higher the readmission rates. Supplementary Table S2 presents the complete descriptive information.

DISCUSSION

Considering the aforementioned limitations in pediatric urolithiasis, the prevention of complications and morbidity is of utmost importance. To ascertain minimal damage with possible morbidity, the European Association of Urology guidelines safely suggest the use of diagnostic procedures comparable with those used in high-risk adult populations.[2] Several treatment options are available: renal stones of a diameter up to 20 mm are seen as ideal candidates for shock wave lithotripsy, percutaneous nephrolithotomy is the recommended treatment for renal pelvic or caliceal stones with a diameter of >20 mm, and URS has been shown to be effective in proximal ureteral calculi and small stones (<15 mm) in lower pole calices.[1,2] Recent clinical studies[1-7] have demonstrated the use of URS in treating both upper ureteral and renal calculi. Flexible URS was an effective and safe procedure for the management of urolithiasis in pediatric cases in both locations.[3,4] A study of treatment alternatives in urinary system stone disease confirmed earlier mentioned applications of minimally invasive techniques and suggested open surgery in only a small select patient group.[5]

The CROES URS Global Study consisted of 192 (1.9%) children aged 18 years or younger. The main finding of the CROES URS Global Study is the absence of differences in outcomes after URS treatment. The only suggested difference is increased readmission rate in children. Currently presented relatively small number of pediatric cases in the established database may be mainly due to the heterogeneity of the clinics dealing with pediatric cases, rather than a lower incidence of pediatric stone disease. These pediatric cases were treated in 54 of 114 centers in 23 countries, with most of the pediatric cases treated in Turkey (46%), India (15%), and Iran (9%). According to a recent report, beyond stone endemic countries, a worldwide increasing trend is present.[7] This increase has not been reflected in the proportion of pediatric cases in the CROES database. It should be noted that the study was conducted by endourologists, and pediatric urologists were not present in all participating centers. The low number of treated pediatric cases could be due to the core functions of the participating centers. Moreover, the present study

Table 1. Descriptive information on the pediatric CROES URS study population

	Infants (0-1) N = 7	Young Children (2-4) N = 53	School-aged Children (5-14) N = 59	Adolescents (15-18) N = 73	*P*	Total Children (0-18) N = 192	Adults (>18) N = 10127	*P*
Preoperative characteristics								
Age in years	1 (1.1)	2.8 (0.8)	9.6 (3.1)	17.1 (1.1)	<0.01	10.3 (6.3)	49.4 (15.1)	<.01
Gender (% F)	42.8%	39.6%	49.2%	41.1%	NS	43.2%	36.2%	NS
BMI	18.3 (5.0)	18.7 (4.5)	19.3 (4.7)	22.2 (3.8)	<0.01	20.2 (4.6)	26.8 (5.0)*	<.01
ASA								
I	86.8%	57.1%	92.0%	89.1%		84.3%	51.8%	
II	12.1%	42.8%	8.0%	9.1%		14.3%	38.0%	
III	1.1%	–	–	1.8%	NA	1.4%	9.7%	NA
Stone location								
Ureteral	71.4%	90.5%	79.7%	71.2%		79.2%	71.5%	
Renal	–	1.9%	6.8%	19.2%		9.9%	15.6%	
Both	28.6%	7.6%	5.1%	4.1%	NA	6.3%	9.4%	.03
Stone burden	78.5 (23.6-314.9)	49.5 (23.6-94.3)	44.0 (18.9-94.3)	47.1 (18.9-78.5)	NS	45.6 (19.6-94.3)	56.5 (27.5-103.7)*	NS
Congenital abnormalities								
Solitary kidney	–	1.9% (1)	1.7% (1)	–		1.1% (2)	3.0% (300)	
Horseshoe	–	–	1.7% (1)	–		0.5% (1)	0.2% (3)	
Ectopic	–	–	–	–		–	0.1% (2)	
Malrotation	–	–	–	–		–	0.1% (2)	
Other	–	–	1.7% (1)	2.8% (2)	NA	1.6% (3)	1.1% (17)	NA
Positive urine cultures	71.4%	68.0%	7.14%	4.23%	<0.01	9.2%	7.5%	.01
Previous treatment	28.6%	39.6%	40.7%	32.9%	NS	37.0%	41.4%	NS
Preoperative stent	–	17.0% (9)	10.2% (6)	11.1% (8)	NA	12.0% (23)	17.5% (1766)	NS
Intraoperative characteristics								
URS type								
Semirigid	71.4%	96.2%	88.1%	79.2%		86.4%	73.0%	
Flexible	14.3%	1.9%	8.5%	13.9%		8.9%	15.8%	
Both	14.3%	1.9%	3.4%	6.9%	NS	4.7%	11.3%	<.01
Size of semirigid scope								
Ch.7	2	12	18	17		25.5% (49)	25.3% (2578)	
Ch.8	1	35	27	27		46.9% (90)	33.6% (3400)	
Ch.9	2	1	4	8		7.8% (15)	16.5% (1676)	
Ch.10	–	–	–	–		–	1.6% (160)	
Other	1	3	4	10	NA	9.4% (18)	5.8% (585)	NA
Size of flexible scope								
Ch.7	2	2	3	8		7.8% (15)	13.6% (1382)	
Ch.8	–	–	1	3		2.1% (4)	7.4% (747)	
Ch.9	–	–	1	2		1.7% (3)	2.2% (225)	
Ch.10	–	–	–	–		0.5% (1)	0.2% (21)	
Other	–	–	2	2	NA	2.1% (4)	2.2% (224)	NA
Operation time (min)	34 (29-60)	38 25-60)	30 (20-47)	30 (20-60)	NS	33 (23-60)	40 (25-60)*	NS
Intraoperative complication	–	–	–	1.4% (1)*	NA	0.5% (1)	1.4% (145)	NA

Continued

Table 1. Continued

	Infants (0-1) N = 7	Young Children (2-4) N = 53	School-aged Children (5-14) N = 59	Adolescents (15-18) N = 73	*P*	Total Children (0-18) N = 192	Adults (>18) N = 10127	*P*
Access support								
Balloon	–	–	5.1% (3)	9.7% (7)		5.2% (10)	10.9% (1105)	
Access sheath	–	–	5.1% (3)	5.6% (4)		3.7% (7)	7.6% (770)	
Guidewire	85.7% (6)	88.7% (47)	83.1% (49)	75.0% (54)		81.7% (156)	76.0% (7681)	
Other	–	1.9%	–	2.8%		1.6% (3)	1.3% (130)	
None	14.3% (1)	(1) 9.4% (5)	6.8% (4)	(2) 6.9% (5)	NA	7.9% (15)	4.2% (426)	NA
Fragmentation device								
US	–	–	–	1.4% (1)		0.5% (1)	1.4% (136)	
Laser	14.3% (1)	45.3% (24)	54.2% (32)	54.8% (40)		51.3% (97)	53.0% (5319)	
Pneumatic	85.7% (6)	43.4% (23)	20.3% (12)	–		21.7% (41)	28.1% (2819)	
EHL	–	–	–	20.6% (15)		7.9% (15)	0.3% (34)	
Other	–	1.9% (1)	–	1.4% (1)		1.1% (2)	0.9% (85)	
None	–	9.4% (5)	22.0% (13)	20.6% (15)	NS	17.5% (33)	16.4% (1648)	NA
Postoperative stent	57.1% (4)	43.4% (23)	67.8% (40)	79.2% (57)	<0.01	64.9% (124)	81.4% (8237)	NS
Postoperative characteristics								
LOHS (d)	2 (1-6)	1 (1-2)	1 (1-2)	1 (1-2)	NS	1 (1-2)	1 (1-2)	NS
Stone-free	85.7%	86.5%	87.5%	92.9%	NS	89.2%	86.8%	NS
Retreatment	14.3% (1)	11.3% (6)	11.9% (7)	9.6% (7)	NS	10.9%	10.9%	NS
Readmission	42.9% (3)	17.3% (9)	7.0% (4)	4.5% (3)	<0.01	10.4%	9.4%	NS
Postoperative complication	–	–	–	1.4% (1)[†]	NS	0.5% (1)	2.4% (247)	NS
Evaluation method								
None	14.3% (1)	3.8% (2)	3.4% (2)	6.9% (5)		5.2% (10)	5.9% (598)	
US	57.1% (4)	52.8% (28)	49.2% (29)	54.8% (40)		52.6% (101)	49.3% (4992)	
KUB	28.6% (2)	39.6% (21)	33.9% (20)	15.1% (11)		28.1% (54)	25.2% (2552)	
CT	–	1.9% (1)	6.8% (4)	9.6% (7)		6.3% (12)	7.0% (711)	
IVU	–	–	1.7% (1)	1.4% (1)		1.0% (2)	2.6% (260)	
RP	–	–	–	1.4% (1)		1.5% (3)	0.3% (26)	
IOC	–	1.9% (1)	3.4% (2)	9.6% (7)	NA	5.2% (10)	7.8% (794)	NA

ASA, American Society of Anaesthesiologists score; BMI, body mass index; CROES, Clinical Research Office of the Endourological Society; CT, computomography; EHL, electrohydraulic lithotripsy; IOC, intraoperative confirmation; IVU, intravenous urography; KUB, kidney, ureter, and bladder X-ray; LOHS, length of hospital stay; NA, not available, not enough cases to perform a difference test; NS, not significant; RP, retrograde pyelogram; URS, ureteroscopy; US, ultrasound.

None of the patients used anticoagulants. Data are n (%) of patients for whom data were available. Percentages exclude missing values from denominators.

* Pediatric complication concerned a stricture.

† Pediatric complication concerned pain.

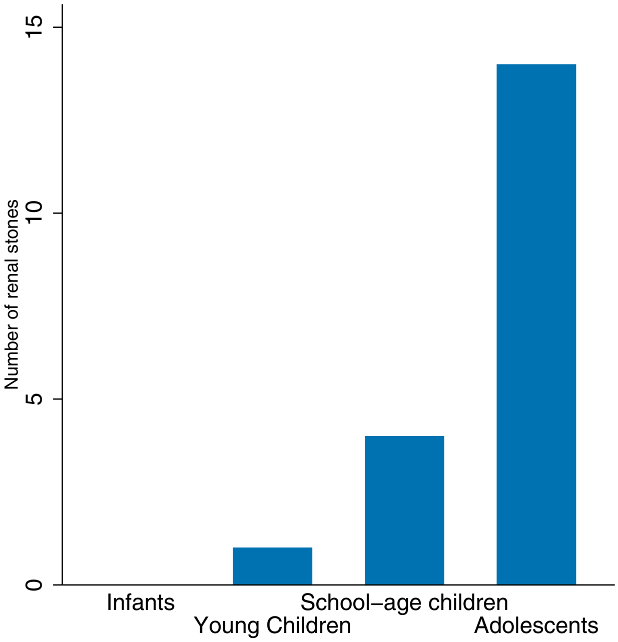

Figure 3. Renal stone intervention ratio in infants, young children, school-aged children, and adolescents. (Color version available online.)

does not conclude on what the treating physician's specialty is: endourologist, pediatric urologist, and possibly others such as pediatric surgeons.

Current presented worldwide application of URS in pediatric cases suggests a difference in the locations of stones between adults and children, with renal stones accounting for 15.6% of stone diseases in adults and 9.9% of stone diseases in children. A possible reflection made upon the higher incidence of kidney stones in the adults is that whereas the vast majority of children were treated with a semirigid scope (86%), this was 73% in adults. Previous studies on the use of URS in pediatric cases evaluated kidney and ureteral stones separately.[3,4,6] In the present study, in line with the increase in the age group, the renal stone intervention ratio also increased, with levels of 0%, 1.9%, 6.8%, and 19.2% in infants, young children, school aged-children, and adolescents, respectively, compared with ureteral stones (Fig. 3). The mean burden of the stones, 78.5 mm, in the small number of infant stone disease interventions (n = 7) seems to confirm this hypothesis because the mean renal stone size in the other groups was 44.0-56.5 mm in diameter. It seems that flexible URS was preferred only in cases where the indication for the intervention was obvious.

Several risk factors have been identified that need to be considered when choosing between alternative strategies. Among these factors, a prolonged operation time was shown to be an independent predictor of complications.[10] Although a higher failure rate (4.4 vs 1.7%) and a higher complication rate (24.0 vs 7.1%) were observed in previous reports in children whose mean age was <6 years,[14] current study shows comparable mean operation time and complications for all age groups. Also, in the infant and young children groups, the ratio of positive urine culture was higher than in the older groups, indicating underlying anomalies in these patients. The CROES URS Global Study, however, does not contain data on vesicoureteral reflux and accompanying pathologies. Moreover, previous treatment ratio was 28.6%-41.4% in all the age groups. This finding demonstrates the recurrent nature of pediatric stone disease and indicates that as the age for intervention decreases, the more important minimally invasive interventions, or minimal damage with high stone-free rates, becomes.

URS techniques used in pediatric cases are found to be very similar to those used in adults. During PCNL, miniaturized equipment is utilized in children compared with adult cases[15]; however, smaller size (7-8F) ureteroscopes are preferred in all age groups for semirigid and flexible scopes for URS. In fact, the only factor that could differ in pediatric cases would be the employment of shorter length equipment. Yet thinner size ureteral access sheaths might be used more commonly. However, current study did not capture any detailed information regarding the length of scopes or size of ureteral access sheaths.

No age-related difference in the preoperative stent ratio is found. The preoperative stenting ratio was 17.5% in adults and 12% in children. Earlier publications reported preoperative stenting ratios of between 0% and 100%.[3,5,6,11,12,16-20] A guidewire was found as the most used tool for access support in all age groups. The ratio of postoperative stenting was lower in the pediatric cases than in the adult cases. Possibly, the better spontaneous passage of stones in children and the necessity of general anesthesia for stent removal may have led to refrain from postoperative stent placement.

The postoperative outcomes among the age groups were also comparable, except the readmission rate of infants which was higher than in adults. However, as the number of infants was quite limited, this suggestion needs to be confirmed in studies including larger numbers of infants. The stone-free rates reported in children (89.2%) and adults (86.8%) were comparable with those reported in an earlier pediatric URS study.[4] Residual stones were evaluated with US or kidney, ureter, and bladder X-ray (80.7%) in most pediatric cases. The determination method of stone clearance still remains controversial.[21] Because of radiation exposure concerns in pediatric renal stone cases, contrast-enhanced computerized tomography or intravenous urogram imaging is not considered in the routine initial and postoperative radiological evaluation. Postoperative residual stone evaluation method was comparable for children and adult patients in the CROES database.

According to a recent study,[22] flexible URS and laser lithotripsy lead to high intrarenal pressure and fluid absorption, in addition to other reported complications.[10] Therefore, beyond showing URS use in pediatric renal and ureteral stones technically, the lack of complications in small children and the comparable rate of complications in adolescents compared with adults are important. Previous reviews of rigid and flexible URS reported a mean of 10.5% and 12.4% of complications, respectively, according to the Clavien-Dindo classification system.[4] The reported complication rates of 0.5% and 2.2% for children and adults, respectively, in the present study were lower than those reported earlier. Regarding intra- and postoperative complications, only a few cases were reported in each group. Hence, statistical tests could not be performed. To be able to compare these categorical variables between adults and children, more cases are needed, specifically in the category of small children. Future studies should include greater numbers of small children.

Last, a limitation of the CROES URS Global Study is the study setup, as the setup of the study is per treatment and not per patient. The retreatment and readmissions during the life course can be different for young treated children. "Also the comparably small numbers of paediatric cases and the heterogeneity of the clinics dealing with pediatric cases should be taken into consideration." Life course treatment outcomes of early treated children should be considered in future research.

CONCLUSION

Given the absence of a difference in the outcomes in worldwide use of URS in adults and children, we conclude that semirigid and flexible URS can be applied as successfully in children as in adults, assuming sufficient experience, equipment, and care. Within the group of URS-treated children, data suggest that the younger the children are, the more readmissions take place. However, this finding needs to be confirmed, especially for infants, in studies with larger numbers of children. Overall, the use of flexible URS is suggested as a valid alternative to external shock wave lithotripsy and PCNL.

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APPENDIX

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.urology.2016.11.020.