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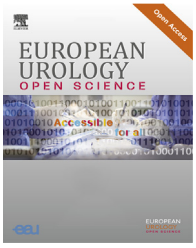

Pediatric Urology

Personalized Surgical Management Offers Full Restitution and Unimpaired Quality of Life to Patients with Duplex Kidneys and Associated Pathologies: 30-year Follow-up at a Tertiary Referral Center

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Article info

Article history:
Accepted September 20, 2023

Associate Editor:
Véronique Phé

Keywords:
Duplex kidney
Ureterocele
Ectopic ureter
Heminephrectomy
Ureterocystic reimplantation

Abstract

Background: Duplex kidneys may be associated with additional pathologies with an indication for surgery. Various surgical approaches have been described. However, little is known about long-term outcomes and quality of life (QoL) for these patients.
Objective: To present long-term outcomes and QoL data up to 30 yr after surgical treatment of duplex kidneys and associated pathologies.
Design, setting, and participants: We collected clinical and operative data for all patients who underwent surgery for complicated duplex kidney at our institution from 1990 to 2018. All patients were invited for a follow-up examination or telephone interview.
Outcome measurements and statistical analysis: We evaluated renal function, clinical outcomes, residual dilation of the upper urinary tract, and health-related QoL.
Results and limitations: Of the 176 patients included, 173 were available for follow-up (mean 140.5 mo). Surgical treatment involved an upper-tract, lower-tract, or combined approach in 11%, 56%, and 33% of cases, respectively. Rates of perioperative complications (8%) and secondary surgery (10%) were low. Overall, 95% of our patients achieved full restitution. Renal function was preserved in all cases, with recurrent urinary tract infections reported by just 2% and urinary incontinence by 1%. Good health-related QoL was reported by 98% of patients. Those without full restitution included six patients who underwent total nephrectomy and two boys who underwent multiple surgeries and urinary diversion. Our results are limited by their retrospective nature, including partly incomplete data sets.
Conclusions: Management of duplex kidneys and associated pathologies is complex and highly individual. By planning a personal approach for each patient it

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https://doi.org/10.1016/j.euros.2023.09.012

is possible to achieve full bodily integrity and good QoL for most of these patients.

Patient summary: Almost all patients undergoing surgery for duplex kidneys and associated pathologies will lead a life without body impairment and good quality of life.

This trial is registered in the German Clinical Trials Register as DRKS00022542.

1. Introduction

Duplex kidneys (DKs) represents the most common congenital abnormality of the urinary tract, with an overall incidence of 1% and accounting for 7.2% of urinary tract anomalies [1,2]. Although DKs are benign in most cases, they can be complicated by pathologies such as obstruction, vesicoureteral reflux (VUR), or ectopic insertion, which can eventually lead to renal impairment and scarring [3]. Owing to the large variety of pathologies associated with DK, management is highly individual and depends on factors such as the anatomic configuration, the function of the renal units, patient age, and clinical presentation. Even though renal resection is necessary in some cases and is widely used as a management option for nonviable or hypofunctional renal moieties, preservation of renal function and minimization of morbidity remain the central goals for surgical management of complicated DK. Several studies have described patient outcomes after different surgical procedures for DK, often focusing on specific pathologies, but there are few data on long-term outcomes for large cohorts with a variety of pathologies and managed via different surgical methods.

The aim of this retrospective single-center study was to evaluate clinical outcomes and quality of life (QoL) for children with symptomatic DK surgically treated at our institution over a period of 30 yr.

The primary objective of the trial was to assess long-term clinical outcomes for a surgically treated cohort with DK and associated pathologies (APs). The secondary objectives were: (1) to assess long-term QoL for these patients; (2) to describe the symptoms and complications leading to an indication for surgery; and (3) to describe the number, timing, and complications of surgical treatments.

2. Patients and methods

We conducted a retrospective, single-center, single-arm cohort study of patients with unilateral or bilateral DK who underwent surgical treatment at our institution. We identified eligible patients by searching our local hospital information system from 1990 to 2018 using the corresponding ICD (International Classification of Diseases) and OPS/ICPM (Operationen- und Prozedurenschlüssel/International Classification of Procedures in Medicine) codes.

We included patients with unilateral or bilateral DK with associated anomalies requiring surgical treatment who were aged <18 yr at the time of primary surgery. Patients or their caregivers without legal capacity or with insufficient language skills unable to understand the nature, significance, and consequences of the study were excluded.

We wrote to eligible patients inviting them to participate in the follow-up for the study. If patients or their caregivers agreed, we scheduled a visit to obtain informed consent and to carry out follow-up examinations.

2.1. Outcome measures

Owing to the lack of an established classification of pathologies associated with DK, we grouped patients with similar pathologies as follows: unilateral or bilateral DK; hydroureteronephrosis of an upper or lower renal unit [4]; presence of vesicoureteral reflux (VUR); presence of an ureterocele; ectopic ureter; and ureteropelvic junction obstruction (UPJO).

We grouped surgical treatments as follows: unilateral or bilateral surgery for pathologies in unilateral or bilateral DK; an upper, lower, or combined approach; endoscopic treatment (alone or preceding open surgery); a single or staged procedure; and additional surgery on the contralateral nonduplex kidney.

We assessed the long-term outcome for all patients during a study-associated follow-up visit or telephone interview after obtaining informed consent. In the case of missing parameters, we contacted the patient's primary caregiver or urologist or retrospectively reviewed our hospital information system (HIS) for the latest medical records.

Full restitution was defined according to the following outcome measures:

I. Renal function

- Serum creatinine less than or equal to the age-adjusted upper bound of the reference range [5,6] (Supplementary Table 1)

or

- Estimated glomerular filtration rate (eGFR) ≥90 ml/min/1.73 m^2 ("normal" using the Schwartz or Chronic Kidney Disease Epidemiology Collaboration [Kidney Disease Improving Global Outcomes] equation [7–11]; Supplementary Tables 2–4)
- If eGFR <90 ml/min/1.73 m^2: no additional loss of function of ≥10% in comparison to preoperative values

II. Urinary tract dilation

- Normal or hydronephrosis grade 1 (ultrasound grading, European Society of Paediatric Radiology Uroradiology Working Group 2008 scheme adapted from the Society of Fetal Urology classification [4]; Supplementary Table 5)

III. Symptoms

- No recurrent febrile UTIs within 2 yr before follow-up (<2 episodes within 6 mo or <3 episodes within 1 yr)
- No symptoms of incontinence or merely sporadic dribbling during the day or night in toilet-trained individuals (<1 pad/d)

IV. Quality of life

- EuroQol EQ-5D Utility Index ≥0.8 (good QoL) [12,13]
- EQ Visual Analog Score (EQ-VAS) ≥70

We calculated the proportion of patients with full restitution (positive outcome measures I + II + III + IV, no surgical outcome compromising bodily integrity). Six patients who underwent primary nephrectomy were excluded from this analysis. In cases with missing data (eg, no laboratory data on renal function), the results were extrapolated to the full number of patients included.

Follow-up was defined as the time between the primary surgery (or date of completion of the primary surgery for staged procedures) and the date of follow-up visit, interview, or latest medical record entry. Results are stratified by sex and underlying pathology (reflux, obstruction, combined pathology, UPJO). The pathology was defined as combined if obstruction and concomitant VUR were present (in patients with bilateral APs on at least one side).

2.2. Data analysis

A descriptive analysis was performed. Continuous data are summarized using the arithmetic mean, median, and range. Categorical data are summarized using the total number of patients in each category, with relative frequencies reported as the valid percentage. Statistical analysis was conducted using χ^2 and two-tailed Fisher's exact tests, with $p < 0.05$ considered statistically significant. SPSS (IBM, Armonk, NY, USA) was used for both descriptive and statistical analysis.

3. Results

From 1990 to 2018, 176 patients underwent surgical treatment for DK and APs at our institution. Two-thirds of the patients were female (66.5%) and approximately one-quarter (46 patients) had bilateral DKs, including 27 (15%) with bilateral APs. Clinical presentations and indications for surgery included severe hydroureteronephrosis or megaureter in 101 patients, high-grade VUR (grade ≥4) in 37, an impaired or nonfunctioning renal moiety in 87, (recurrent) UTI in 100 (including 5 patients with urosepsis and 2 with renal abscess), prolapsed ureterocele/outflow obstruction in eight, and urinary incontinence/dribbling in 10 (including multiple indications per patient; Table 1). The mean age at the time of initial treatment was 30.3 mo (range 1 wk–197 mo).

The distribution of surgical treatments using different approaches in the 176 patients was as follows. An upper-tract approach was used in 20 patients, including nephrectomy ($n = 2$), unilateral heminephrectomy (HN; $n = 13$), unilateral pyelopyeloplasty ($n = 1$), and unilateral ureteropyeloplasty ($n = 4$). A lower-tract approach was used in 98 patients, including unilateral ureteroneocystostomy ($n = 70$), bilateral ureteroneocystostomy ($n = 16$), bilateral distal ureteroureterostomy ($n = 1$, staged procedure), unilateral endoscopic ureteral bulking ($n = 8$), and unilateral endoscopic ureterocele decompression ($n = 3$). A combined approach was used in 58 patients, including a unilateral upper-tract procedure and ureteral stump excision (USE; $n = 22$), a unilateral upper-tract procedure and ureteroneocystostomy ($n = 30$), and bilateral HN and ureteroneocystostomy ($n = 6$). Fourteen of these combined surgeries were performed as staged procedures.

Table 1 – Patient characteristics, pathologies, and indication for surgery in duplex kidneys ($n = 176$)

Parameter	Result
Sex, *n* (%)	
Female	117 (66.5)
Male	59 (33.5)
Mean age at initial treatment, mo (range)	30.3 (0.25–197)
Laterality of duplex kidney, *n* (%)	
Unilateral	130 (73.9)
Bilateral	46 (26.1)
Bilateral pathologies	27 (15.3)
Primary pathology, *n* (%)	
Unilateral obstruction (upper pole)	76 (43)
Unilateral VUR (lower pole)	56 (32)
Unilateral UPJO	4 (2)
Bilateral obstruction (upper pole)	9 (5)
Bilateral VUR (lower pole)	15 (9)
Ureterocele (114 obstructed renal unit)	62/114 (54)
Ureterocele and ipsilateral VUR (62 ureterocele)	20/62 (32)
Ureterocele and contralateral VUR (53 unilateral ureterocele)	6/53 (11)
Megaureter (114 obstructed renal unit)	107/114 (94)
HUN ≥4 (90 refluxing renal unit)	42/110 (38)
Hutch diverticula (90 refluxing renal unit)	10/110 (8)
Additional pathologies in the contralateral nonduplex kidney, *n*/*N* (%)	25/130 (19)
Clinical presentation and indication for surgery (*n*) [a]	
Severe hydroureteronephrosis and/or megaureter	101
High-grade VUR (grade ≥4)	37
Poorly or nonfunctioning renal unit	87
Recurrent or severe urinary tract infection	100
Prolapsed ureterocele/outflow obstruction	8
Urinary incontinence/dribbling	10

UPJO = ureteropelvic junction obstruction; VUR = vesicoureteral reflux.
[a] Including multiple indication per patient.

We found markedly different rates of extirpative and reconstructive surgery in the different primary pathology groups (Fig. 1).

The overall 30-d complication rate (Clavien-Dindo ≥2) was 8.5%, including five patients with a grade 3b complication. We observed no grade >3b complications and no marked differences between surgical approaches, except that there were no complications after endoscopic procedures (Supplementary Table 6).

Rates of secondary surgery were higher for reconstructive than for extirpative surgery (11% vs 5%; $p = 0.177$), whereas none of the combined approaches was followed by secondary surgeries. Notably, the rate of secondary surgery after reconstructive surgery was significantly higher for patients with both upper-pole obstruction and lower-pole reflux than for those with an obstructive or refluxing pathology alone (33% vs 8%; $p = 0.024$; Supplementary Table 6).

We were able to invite 95 of 176 eligible patients for an outpatient follow-up visit. For 47 patients who declined personal participation, a telephone interview was carried out. We were unable to reach the remaining 34 patients because of invalid contact details. Medical records from regular postoperative care follow-up visits were available for 31 of these 34 patients, with three patients lost to follow-up. Thus, the follow-up rate was 98.3%. The mean follow-up time was 140.5 mo (range 2–371). The mean age at follow-up was 171.0 mo (range 8–445).

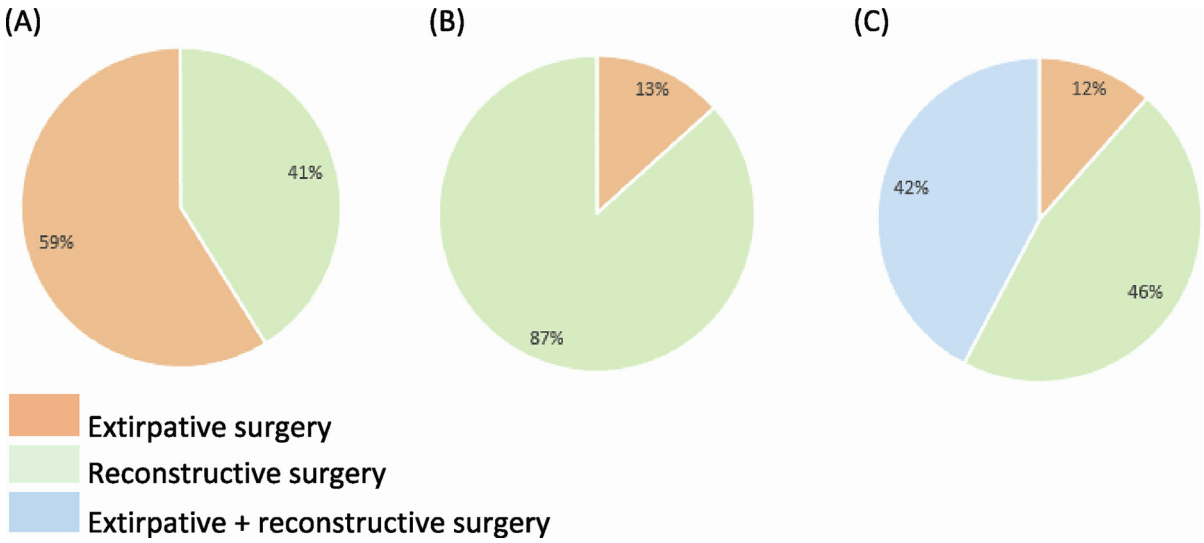

Fig. 1 – Distribution of surgical approaches by duplex kidney pathology: (A) obstructing pathology, (B) refluxing pathology, and (C) obstructing and refluxing pathology.

Renal function was assessed in 123 patients, of whom 81% had an eGFR within the normal range (mean 109 ml/min/1.73 m^2). Renal function was slightly reduced in 18% and moderately reduced in 1% of patients. None of the patients with reduced renal function at the time of follow-up had a ≥10% loss in comparison to preoperative values (Table 2, Fig. 2, and Supplementary Table 7).

The majority of patients (94%) had no or mild urinary tract dilation on follow-up ultrasound (grade 0 or 1, n = 165). The rate of persisting grade 2–3 hydronephrosis was highest in the group with preoperative combined pathologies in comparison to the refluxing and obstructing groups (20% vs 7.5% vs 1.3%; p = 0.009).

Some 9% of the follow-up population had febrile UTIs in the year before follow-up, with the majority of cases nonrecurring (13 of 16). All patients with febrile UTIs were female (p = 0.002). We found no significant differences in the rates of febrile and nonfebrile UTIs according to the underlying refluxing or obstructing pathologies, except for a lower rate of nonfebrile UTIs in the obstructing group than in the combined group and the refluxing group (2.6% vs 13% vs 9.1%; p = 0.044).

Urinary incontinence was reported by 17 patients (9.8%, 13/17 female). Half of these patients reported only sporadic dribbling during the day and one-third reported nocturnal wetting (4 male, 1 female). Daily incontinence was reported by three female patients (2%), including one patient with severe incontinence (>1 pad/d).

We were able to assess health-related QoL (HRQoL) using the validated EuroQol EQ-5D questionnaire in 120 patients. The mean EQ-5D Utility Index score was 0.98 (range 0.72–1.0), with 98% of patients reporting a high score (>0.8, good HRQoL). The mean EQ-VAS was 90.5 (range 38–100, where >80 represents good HRQoL). Mean scores were similar across genders, pathology types, and patient ages.

We found that the vast majority of our patients (95%) experienced full restitution after surgical management of their DK (87% after primary surgery, 8% after secondary surgery; Table 3). Those without full restitution included two boys with severe bilateral VUR who underwent multiple surgeries, resulting in an incontinent urostomy (definitive reconstruction pending) in one case and a continent urinary diversion with bladder augmentation in the other.

Table 2 – Outcomes for 173 patients at a mean age of 171.0 mo (range 8–445) at mean follow-up of 140.5 mo (range 2–371)

Outcome	Result
Renal function (*n* = 123) [a]	
Mean eGFR, ml/min/1.73 m^2 (range)	109.0 (49.4–144.3)
eGFR category, *n* (%)	
≥90 ml/min/1.73 m^2	100 (81.3)
60–89 ml/min/1.73 m^2	22 (17.9)
30–59 ml/min/1.73 m^2	1 (0.8)
Urinary tract dilation (*n* = 165)	
Ultrasonography, *n* (%)	155 (93.9)
Persistent hydronephrosis, *n* (%)	
Grade 0 or 1	10 (6.1)
Grade ≥2	0
Nephrectomy	6
Symptoms (*n* = 173) [b]	
UTI, *n* (%)	29 (16.7)
Recurrent nonfebrile UTIs	13 (7.5)
Febrile UTIs/pyelonephritis	16 (9.2)
Once	13 (7.5)
Recurrent	3 (1.7)
Incontinence, *n* (%)	17 (9.8)
Daytime, sporadic	9 (5.2)
Daily, minimal (<1 pad/d)	2 (1.2)
Daily, severe (>1 pad/d)	1 (0.6)
Enuresis nocturna	5 (2.9)

eGFR = estimated glomerular filtration rate; UTI = urinary tract infection.
[a] A serum creatinine result was available for just one patient and was within the reference range.
[b] Multiple symptoms per patient possible.

4. Discussion

DKs is the most common congenital abnormality of the genitourinary tract and may be complicated by APs, necessitat-

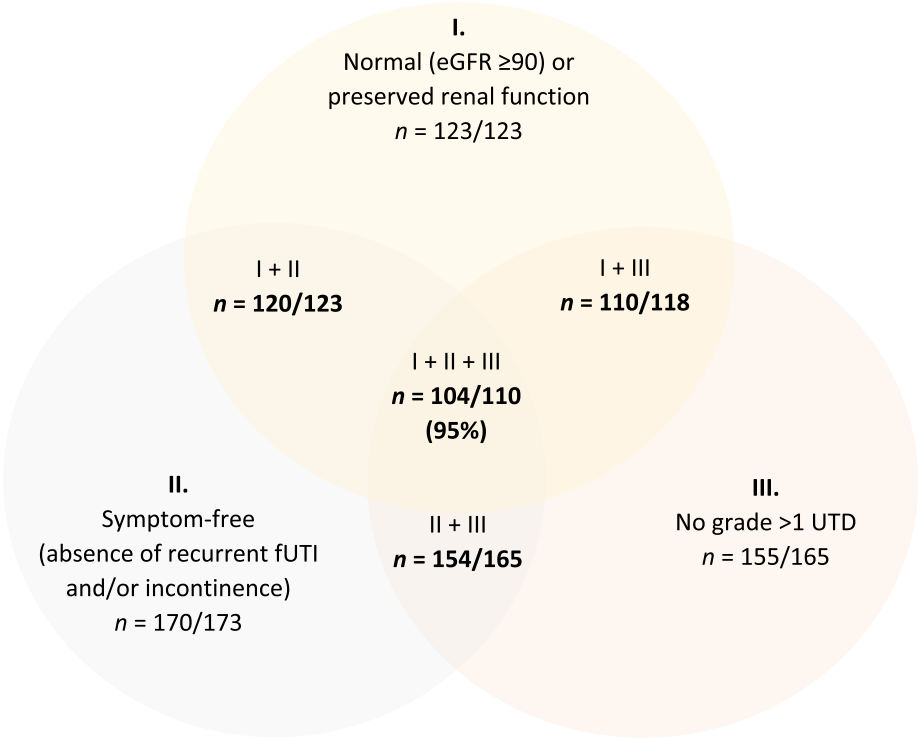

Fig. 2 – Outcome measures for 173 patients. The intersecting areas represent patients fulfilling outcome criteria for different measures. eGFR = estimated glomerular filtration rate (measured in ml/min/1.73 m^2); fUTI = febrile urinary tract infection; UTD = urinary tract dilation.

Table 3 – Final patient outcome at mean follow-up of 140 mo (range 2–371)

Outcome	Patients, *n*/*N* (%)
I. Preserved renal function	123/123 (100) [a]
II. Absence of recurrent urinary tract infections	170/173 (98)
III. Urinary continence	169/171 (99) [b]
IV. Good health-related quality of life	117/120 (98)
Full restitution (I + II + III + IV, no nephrectomy or diversion)	159/167 (95) [c]

eGFR = estimated glomerular filtration rate; *N* = number of patients for whom the relevant outcome data were available.

[a] Including 22 patients with slightly reduced and one with moderately reduced eGFR but with <10% additional loss from preoperative baseline (unknown in 5 patients).

[b] Including nine patients with sporadic, mild urinary dribbling and five patients with enuresis nocturna.

[c] Missing data were extrapolated and six patients who underwent unilateral total nephrectomy were excluded. Two patients had partial restitution, one with an incontinent urostomy (definitive reconstruction pending) and the other with a continent urinary diversion with bladder augmentation.

ing surgical intervention at an early age [2,14]. Treatments and surgical management are tailored to the underlying pathologies and thus are highly individual. Treatments are aimed at reversing clinical symptoms, avoiding progressive renal damage, and restoring upper and lower urinary tract functionality.

Although DKs are a rather common entity in pediatric urology, data on long-term outcomes and specifically HRQoL in this patient population are scarce or nonexistent. In fact, we believe that this is the first long-term follow-up of a large DK cohort involving all AP subtypes. Series published to date describe only small groups of patients [15,16] or specific APs and treatments, including UPJO [17], ectopic ureter [18], and ureterocele decompression [19,20]. In addition, most of these studies had short follow-up periods.

Concerning the AP distribution in our cohort, we found some striking similarities to historical pathology and radiology series (in light of missing comparable clinical series) [14,21,22]. Two-thirds of the patients were female (66.5%) and 26% had bilateral DKs, including 15.3% with bilateral APs. In 6/10 patients, surgery was performed for hydroureteronephrosis due to upper-pole obstruction, and unilateral or bilateral ureterocele in 6/10. Approximately half of the group with obstructing pathology had an ectopic ureteral insertion (with or without ureterocele). Almost all ureters in this group were described as megaureters. The number of ureteroceles associated with ipsilateral (1/3 cases) or contralateral (1/10 cases) VUR was similar to that in an earlier publication [23].

The extent of our ability to categorize and compare surgical approaches was somewhat limited. Both obstructive and refluxing pathologies were treated using an upper-tract, lower-tract, or endoscopic approach to perform endoscopic, extirpative, or reconstructive surgery or a combination thereof. However, earlier attempts to draw general conclusions from comparative studies on these approaches have been questioned in view of the complexity of the underlying pathologies [24,25]. In fact, our data support the view of Menon et al [25] that any generalization leads

to oversimplification. For example, we found lower rates of complications and secondary surgery after extirpative rather than reconstructive surgery, unlike the results and recommendations of Keene and Subramaniam [24]. We believe that the AP complexity precludes a comparison of studies. The indication for a specific surgical approach is based on multiple factors, such as the age and mode of presentation, ureterocele size and type or reflux grade, and differential function of the renal units affected rather than the superiority of a particular technique [23,25].

Despite these general limitations, we want to emphasize some important aspects of the surgical care for our young patients. The rates of extirpative surgery (nephrectomy or HN) were significantly higher for DK with upper-pole obstruction or both upper-pole obstruction and lower-pole VUR than for DK with lower-pole reflux. Lower-pole extirpation was only rarely performed. Apart from UTIs, 30-d complication rates were low after both open extirpative surgery and reconstructive surgery (both 3%). Likewise, the rates of secondary surgery were low for both approaches, albeit higher for the reconstructive than for the extirpative group (11% vs 5%). In part, the low number of secondary operations may be a result of the significant number of combined approaches for primary surgery (eg, HN + USE), in contrast to results reported by Keene and Subramaniam [24]. However, the number of DKs treated with combined HN + USE was lower in those with VUR and hydroureteronephrosis of the lower pole (2/7 vs 40/48 in the obstructing group), which supports the conclusion of De Caluwé et al [26] that the majority of patients do not need USE in this particular setting.

Most important, our series features long-term follow-up of clinical outcomes and a solid assessment of HRQoL in these patients. It is pleasing that 95% of the patients experienced full restitution and unimpaired HRQoL. The vast majority of patients lead a life with full bodily integrity (no nephrectomy or urinary diversion), unimpaired overall renal function, functional integrity of the upper and lower urinary tract, and no UTIs. Even potentially specific associated symptoms such as recurrent UTIs or incontinence do not appear to be more frequent than in the general population. The same applies to overall HRQoL which was good in 98% of patients.

Our study has some limitations. Owing to the long recruitment and follow-up periods, only slightly more than half of the patients were examined in person. However, 77% of those with follow-up >20 yr have been seen in the outpatient clinic. Owing to the retrospective nature, not all clinical data were available for all patients or was derived from various (external) sources with all inherent uncertainties. To calculate the proportion of patients with full restitution, we had to extrapolate renal function and HRQoL data. It was not possible to draw conclusions regarding the success rates for specific surgical approaches or compare these because of the AP heterogeneity, missing functional studies (renal scans, urodynamic studies), and the single-center, single-surgeon design of the study. We do not know if the same excellent results may be achievable with a more conservative or less invasive approach such as pure endoscopic treatments or waiver of USE.

5. Conclusions

Management of DK and APs is complex and highly individual. However, the common surgical approaches are well established and complication and reoperation rates are generally low. If a personalized approach is for each patient, it is possible to achieve full bodily integrity and good QoL in most cases. However, future activities should aim to launch prospective trials to compare various approaches in specific settings.

Author contributions: Lidija Ujkic had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Schoenthaler, Ujkic, Frankenschmidt, Gratzke, Pohl, Praus, Kroenig.
Acquisition of data: Ujkic, Pohlmann, Haeffner, Pohl, Pohlmann, Praus.
Analysis and interpretation of data: Ujkic, Schoenthaler.
Drafting of the manuscript: Schoenthaler, Ujkic.
Critical revision of the manuscript for important intellectual content: Gratzke, Haeffner.
Statistical analysis: Schoenthaler, Ujkic.
Obtaining funding: None.
Administrative, technical, or material support: Gratzke, Pohl, Haeffner.
Supervision: Schoenthaler, Pohl, Haeffner, Frankenschmidt, Kroenig.
Other: None.

Financial disclosures: Lidija Ujkic certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

Ethics considerations: The ethics committee approval reference for this study is 423/19.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.euros.2023.09.012.

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