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Diagnostic and therapeutic management of vesico-ureteral reflux in pediatric kidney transplantation—Results of an online survey on behalf of the European Society for Paediatric Nephrology

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Abstract

Background: Vesico-ureteral reflux (VUR) is considered to be a risk factor for recurrent febrile urinary tract infections and impaired renal transplant survival.

Methods: An online survey supported by the European Society for Paediatric Nephrology was designed to evaluate current management strategies of VUR in native and transplanted kidneys of recipients aged <18 years.

Results: Seventy-three pediatric transplant centers from 32 countries contributed to the survey. All centers performed urological evaluation prior to pediatric kidney transplantation (KTx) with subsequent interdisciplinary discussion. Screening for VUR in native kidneys (30% in all, 70% in selected patients) led to surgical intervention in 78% (11% in all, 89% in selected patients) with a decided preference of endoscopic intervention over ureterocystoneostomy. Following KTx, continuous antibiotic prophylaxis was applied in 65% of the patients and screening for allograft VUR performed in 93% of selected patients. The main management strategies of symptomatic allograft VUR were continuous antibiotic prophylaxis (83%) and surgical treatment (74%) (endoscopic intervention 55%, redo ureterocystoneostomy 26%).

Conclusions: This survey demonstrates the high variability in the management of VUR in pediatric KTx recipients, points to knowledge gaps, and might serve as a starting point for improving the care for patients with VUR in native and transplanted kidneys.

KEYWORDS
febrile urinary tract infection, online survey, pediatric kidney transplantation, therapy, ureteral implantation, vesico-ureteral reflux

Abbreviations: CAP, continuous antibiotic prophylaxis; ESPN, European Society for Paediatric Nephrology; fUTI, febrile urinary tract infection; KTx, kidney transplantation; UCN, ureterocystoneostomy; VCUG, voiding cystourethrography; VUR, vesico-ureteral reflux; VUS, voiding urosonography.

Collaborators including physicians who completed the survey are listed at Appendix A.

1 | INTRODUCTION

Although data are conflicting regarding the impact of vesico-ureteral reflux (VUR) on renal transplant function, febrile urinary tract infections (fUTI) associated with VUR in the renal allograft still remain an important morbidity factor in pediatric kidney transplantation (KTx).[1,2] Pre-existing VUR in the native kidneys, bladder dysfunction, and urological technical challenges contribute to the reported high prevalence rates of VUR up to 58% in pediatric renal transplant recipients.[3] The lack of well-designed studies in the population of renal transplant patients with VUR prevents to draw firm conclusions on the best diagnostic and therapeutic strategy.[2,3]

Surveys may serve as an advantageous method to collect data of a large sample in a time efficient manner to develop a better understanding of the field of interest. Furthermore, they often represent a major driving force for developing consensus statements, particularly if evidence is scarce and practice patterns seem to vary considerably.[4] In addition, the knowledge gained is an important starting point for the design of future studies. Therefore, an online survey was conducted to gather more information about the current management strategies for VUR in pediatric renal transplant patients, especially to what extent the procedures differ in the preparation for kidney transplantation and after kidney transplantation.

2 | MATERIALS AND METHODS

2.1 | Study design

An electronic, questionnaire-based survey was developed on behalf of the "Transplantation Working Group" of the European Society for Paediatric Nephrology (ESPN) and distributed to the mailing list contacts (ESPN members [state 12/2020]: $n = 656$) including study information and a personal link to the survey website (SurveyMonkey Inc., San Mateo, California, USA, www.surveymonkey.com) (Supporting Information S1, S2, and S3).[5]

The questionnaire was structured into four sections with 33 items (open and multiple-choice questions): (I) demographic and general characteristics about the responding transplant center; (II) detailed questions addressing urological assessment during pre-transplant evaluation including management of VUR in the native kidneys; (III) data on intra- and post-transplant urological management; and (IV) comprehensive information about diagnostics and management strategies of renal transplant VUR including type of imaging, timing, monitoring, and selection criteria for intervention (Supporting Information S1). Supplemental questions were sent to survey participants to clarify more specific aspects, which had arisen from the primary survey. (Supporting Information S4, S5 and S6).

Both surveys were tested in advance by four transplant experts for clarity, utility, and redundancy. Comments and improvements were implemented and the adapted surveys evaluated again by five and four transplant experts, respectively. The research project was not approved by an ethics committee, because the study neither involved patients directly nor any specific patient data information was required.

2.2 | Study duration and study population

The survey was carried out between May 25, 2020 and October 21, 2020. Overall, 100 responses were retrieved. Following the elimination of multiple data entries (double: $n = 11$; fourfold: $n = 2$), 83 participating pediatric nephrology centers were identified. Responders who did not perform renal transplantation in the pediatric population < 18 years ($n = 6$), could not be assigned to a particular institution ($n = 2$), or had completed <10% of the survey ($n = 2$) were excluded from the analysis. Finally, 73 pediatric KTx centers were included for data evaluation.

The additional survey questions were sent out between November 11, 2021 and February 27, 2022, and obtained a total of 57 usable data from 64 responses (critically incomplete dataset: $n = 1$; multiple data entries: $n = 5$).

2.3 | Statistical analyses

The responses were collected in an electronic database and checked before the final analysis. Double, triple and fourfold response from one center were combined into a single answer. Statistical analyses were conducted based on the number of total answers for each question. The overall completion rate of the questions within the entire original and additional survey was 92% (67/73) and 63% (36/57), respectively, unavoidable resulting in changing denominators or total numbers of the responding centers. Details of data completion including missing and valid data for all items are provided in the Supporting Information S8 and S9. If data were missing or ambiguous, responders were contacted via e-mail for further information.

Data were analyzed using the statistical package SPSS for Windows, release 27 (IBM Corp., New York, NY). Categorical variables were expressed as frequencies and percentages.

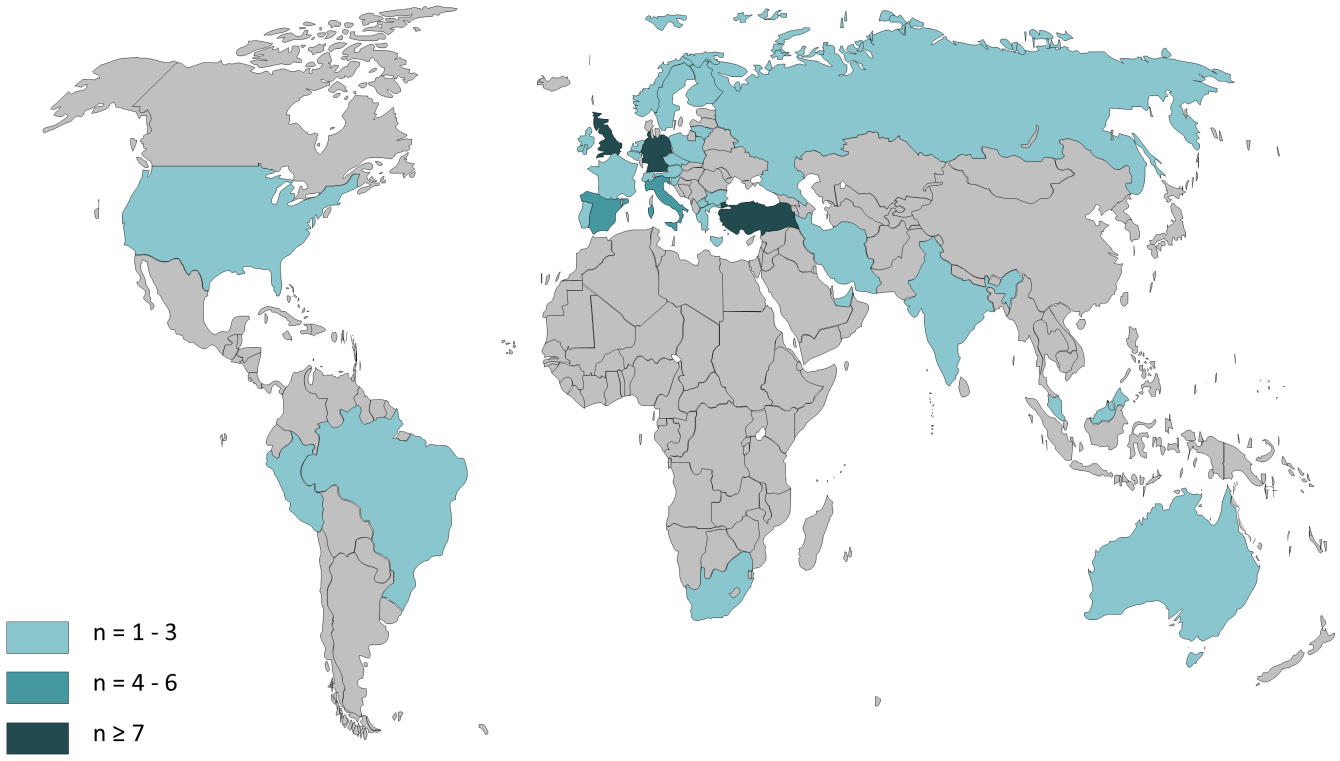
3 | RESULTS

3.1 | General information about the participating centers

3.1.1 | Demographic and institutional characteristics

In total, 73 centers from 32 countries participated in the survey, of which 85% (62/73) were European (Figure 1). Of those, 57 centers from 28 countries also answered the additional survey questions (Supporting information S7).

A standardized pre-transplant assessment protocol was used in 99% (72/73) of the centers. The average annual number of pediatric



Geographic location of participating centers (N = 73)					
	n		n	n	% of total
Europe				**62**	**85**
Turkey	10	Austria	1		
Germany	8	Bulgaria	1		
United Kingdom	7	Czech Republic	1		
Italy	5	Finland	1		
Spain	4	Ireland	1		
Belgium	3	Lithuania	1		
Netherlands	3	North Macedonia	1		
Switzerland	3	Norway	1		
France	2	Poland	1		
Greece	2	Portugal	1		
Slovenia	2	Russia	1		
Sweden	2				
Asia				**5**	**7**
Iran	2	India	1		
United Arabic Emirates	1	Malaysia	1		
Australia				**2**	**3**
South America				**2**	**3**
Brazil	1	Peru	1		
North America				**1**	**1**
United States of America	1				
Africa				**1**	**1**
South Africa	1				

FIGURE 1 Geographic location of participating centers (*N* = 73). *n*, number

KTx was stated as following: <5: 30% (22/73); 5–10: 40% (29/73); 11–20: 23% (17/73) and >20: 7% (5/73).

In 74% (54/73) of all centers, a surgeon specialized in pediatric transplantation, and in 90% (66/73) a surgeon or urologist specialized in pediatric urology was available.

3.1.2 | Grading of VUR

High-grade VUR was considered as the presence of VUR grade III by 32% (18/57), grade IV by 98% (56/57) and grade V by 100% (57/57) of the corresponding centers.

3.2 | Pre-transplant assessment

3.2.1 | Urological assessment prior to pediatric KTx

The pre-transplant assessment protocol included a urological work-up either for all patients (61% [43/71]) or selected recipients only (39% [28/71]). Both centers without a standardized pre-transplant or urological assessment protocol, also performed a urological work-up. The urological evaluation prior to KTx is displayed in Figure 2.

3.2.2 | Multidisciplinarity in the pre-transplant urological evaluation process

Overall, 99% (72/73) of the centers discussed the results of the urological work-up in interdisciplinary pre-transplant meetings for either all (58% [42/72]) or selected recipients only (42% [30/72]). The multidisciplinary team involved in the pre-transplant urological evaluation is depicted in Figure 3.

3.2.3 | Screening for VUR in the native kidneys

Screening for VUR in the native kidneys was carried out in all recipients by 30% (22/73), and in selected patients by 70% (51/73) of the centers with reasons provided in Figure 4. The main imaging methods for VUR screening were voiding cystourethrography (VCUG) (90% [65/72]) and voiding urosonography (VUS) (4% [3/72]), followed by less frequently used imaging techniques (6% [4/72]; that is, scintigraphy or video-urodynamics).

3.2.4 | Non-surgical management in native kidneys with VUR

Nine centers (16% [9/57]) stated not to screen for VUR in asymptomatic KTx candidates. In the remaining centers, non-surgical treatment strategies of asymptomatic VUR in native kidneys focused on surveillance (77% [37/48]), bladder training (63% [30/48]), continuous antibiotic prophylaxis (CAP) (19% [9/48]) and individual approaches (alpha-blocker therapy: $n = 1$; age- and VUR grade- dependent strategies: $n = 2$; CAP until potty training completed: $n = 1$). Patients with symptomatic VUR in the native kidneys were managed by bladder training (86% [49/57]) and CAP (75% [43/57]), followed by surveillance (12% [7/57]) and several individual strategies based on age, VUR grade and associated urinary tract anomalies ($n = 3$), while one center (2% [1/57]) indicated surgical treatment exclusively. Detailed information on CAP in asymptomatic and symptomatic native kidney VUR is provided in Table 1.

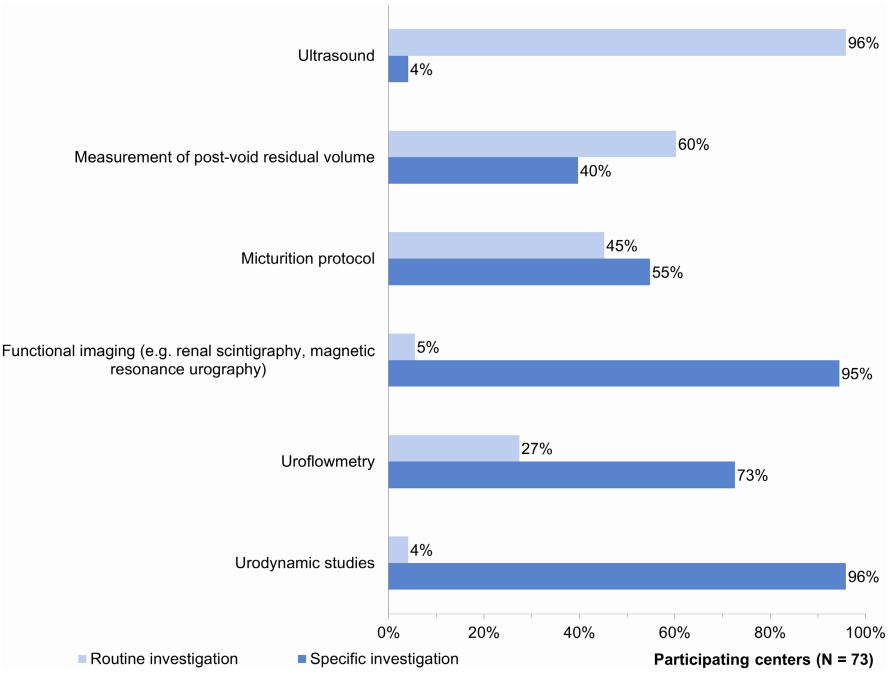


FIGURE 2 Urological assessment prior to kidney transplantation. *n*, number

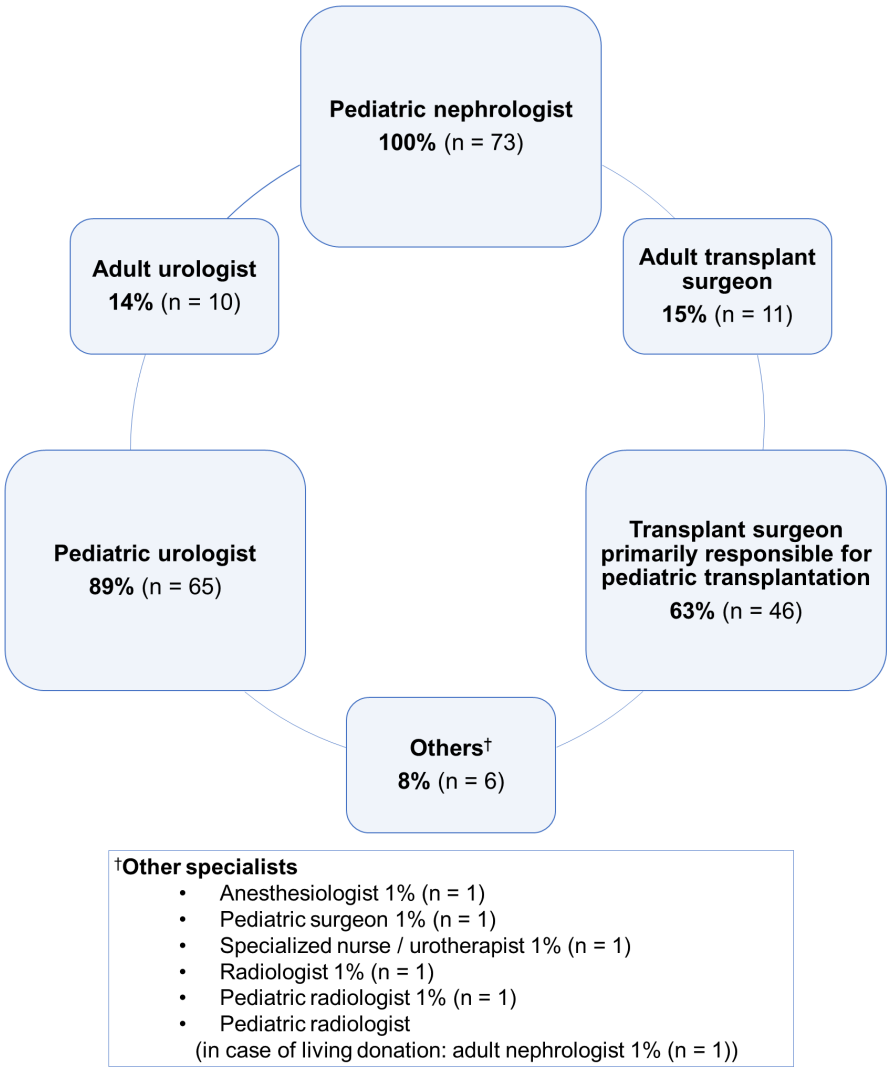


FIGURE 3 Specialists involved in the pre-transplant urological work-up ($N = 73$). *n*, number

3.2.5 | Surgical management in native kidneys with VUR

Surgical management of VUR in the native kidneys was reported by 78% (57/73) of the centers, with 11% (6/57) in all and 89% (51/57) in selected transplant candidates only (Figure 5a).

Nineteen of 48 (40%) centers indicated surgical management of asymptomatic VUR in all (11% [2/19]) or selected patients (89% [17/19]) (Figure 5b). Of those, 79% (15/19) preferred endoscopic intervention and 5% (1/19) ureterocystoneostomy (UCN); the remaining (16% [3/19]) did not determine or stated individual decisions (Figure 6a). In case of surgical intervention, all centers aimed to correct asymptomatic native kidney VUR before KTx with reasons listed in Supporting information S10.

Eight of 56 (14%) centers did not perform surgical intervention of symptomatic VUR in the native kidneys, while 86% (48/56) of the centers used surgical intervention, with 38% (18/48) in all and 63% (30/48) in selected KTx recipients (Figure 5c); one center did not specify. A total of 67% (32/48) of these centers favored endoscopic treatment, 19% (9/48) UCN, and 15% (7/48) did not specify due to individualized approaches including nephroureterectomy ($n = 3$) in particular cases. Detailed information is provided in Figure 6b,c. Overall, 85% (41/48) of the centers aimed to correct symptomatic native kidney VUR prior to KTx, followed by 8% (4/48) during and 4% (2/48) after KTx; one center did not determine (Supporting information S10).

The follow-up strategies after native kidney VUR correction are summarized in Supporting information S11.

3.3 | Transplant procedure

3.3.1 | Ureteral implantation and stenting during pediatric KTx

During renal transplantation, the ureteral implantation was mainly performed by a transplant surgeon primarily responsible for pediatric KTx (47% [33/70]), followed by a pediatric urologist (21% [15/70]), adult transplant surgeon (21% [15/70]) or adult urologist (10% [7/70]); three centers did not report these data.

Ninety percent (66/73) placed a ureteral stent in the transplant ureter by using a double-J-stent (68% [45/66]), percutaneous ureteral stent (15% [10/66]), mono-J-stent (6% [4/66]) or transurethral ureteral stent (2% [1/66]); the remaining centers did not specify.

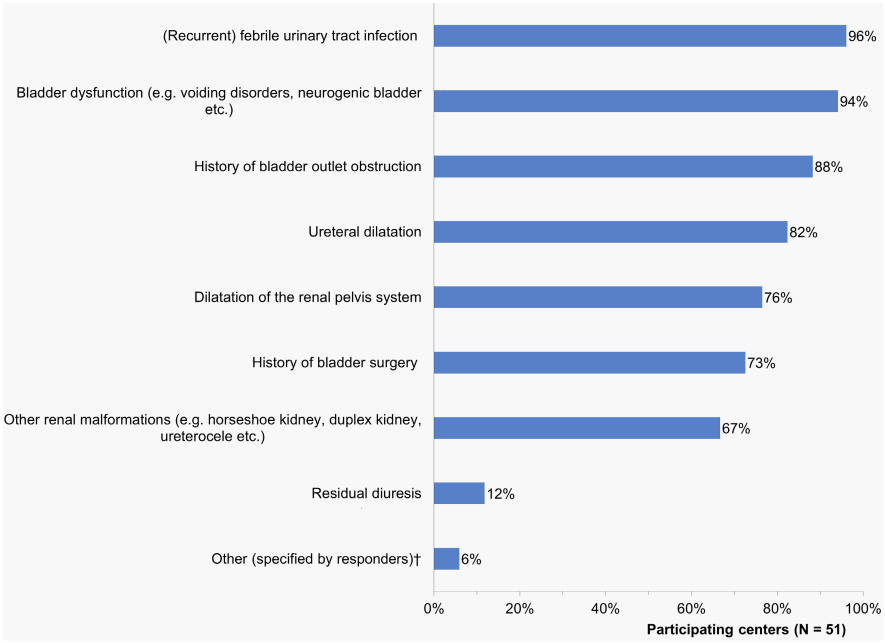


FIGURE 4 Criteria for pre-transplant VUR screening in native kidneys. †Other reasons: posterior urethral valves; renal scarring diagnosed by dimercaptosuccinic acid scintigraphy; pediatric urologist's decision. *n*, number; VUR, vesico-ureteral reflux

TABLE 1 Criteria for CAP in patients with native kidney VUR prior to KTx

Reasons, indications or conditions for	*n*	% of total
CAP in asymptomatic native kidney VUR (*N* = 9)		
Additional morphological or functional anomalies on renal pelvis system and ureter	2	22
Pre-existent pathologies of bladder morphology/function	5	56
Previous surgery on kidney or urinary tract	3	33
Low grade VUR (grade I–II)	0	0
High-grade VUR (grade III–V)	6	67
Unknown	0	0
Other reasons, specified by responders[a]	4	44
CAP in symptomatic native kidney VUR (*N* = 42)		
Additional morphological or functional anomalies on renal pelvis system and ureter	28	67
Pre-existent pathologies of bladder morphology / function	29	69
Previous surgery on kidney or urinary tract	10	24
Low grade VUR (grade I–II)	9	21
High-grade VUR (grade III–V)	35	83
Unknown	1	2
Other reasons, specified by responders[b]	9	21

Abbreviations: CAP, continuous antibiotic prophylaxis; fUTI, febrile urinary tract infection; *n*, number; UTI, urinary tract infection; VUR, vesico-ureteral reflux.

[a]Other reasons for CAP in asymptomatic native kidney VUR: recurrent UTI (*n* = 2); CAP until potty trained; persistent bladder incontinence.

[b]Other reasons for CAP in symptomatic native kidney VUR: recurrent UTI without further specification (*n* = 6); recurrent fUTI; recurrent fUTI and bladder bowel dysfunction; UTI associated with deterioration in kidney function.

3.4 | Post-transplant management

3.4.1 | CAP following pediatric KTx

Continuous antibiotic prophylaxis at pediatric KTx to prevent fUTI was administered in 65% (47/72) of the centers, with 49% (23/47) in all and 51% (24/47) in selected patients; one center did not specify. The main indications for CAP in selected recipients were pre-existing pathologies of bladder morphology and dysfunction (83% [20/24]) and recurrent fUTI (75% [18/24]). CAP was usually discontinued after removing the ureteral catheter (45% [21/47]), after exclusion of VUR (11% [5/46]), according to the center-specific protocol (30% [14/46]) or due to other (individualized) reasons (9% [4/46]); 2 centers did not specify (7% [3/46]).

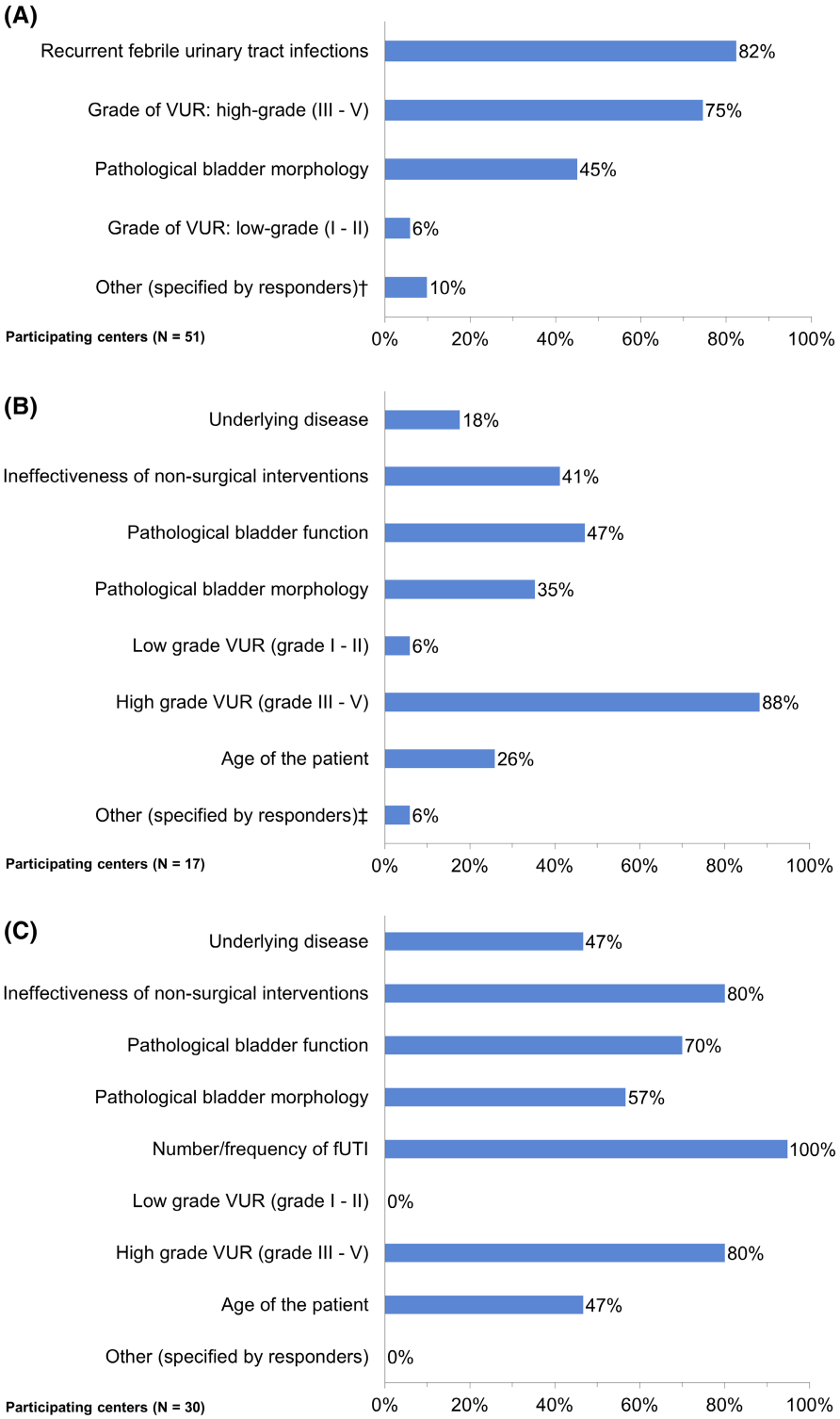


FIGURE 5 Reasons for surgical correction of VUR in the native kidneys. (A) Overall reasons for correction of native kidney VUR. (B) Reasons for surgical management of asymptomatic VUR in native kidneys. (C) Reasons for surgical management of symptomatic VUR in native kidneys. †Other reasons: combination of VUR, recurrent urinary tract infections and possibly pathological bladder morphology; individual multidisciplinary decision ($n = 2$); consideration of nephroureterectomy instead of surgical VUR correction. ‡Other reasons: in case of feasible low-risk surgery. fUTI, febrile urinary tract infection; n, number; VUR, vesico-ureteral reflux

3.4.2 | Urological work-up following pediatric KTx

An overview of routine and specific urological investigations conducted after KTx is displayed in Figure 7.

3.4.3 | Screening for VUR in the renal transplant

In the post-transplant period, 7% (5/73) screened for allograft VUR routinely. The remaining centers (93% [68/73]) limited VUR diagnostics mainly to the following conditions: (recurrent) fUTI (93% [63/68]), bladder dysfunction (56% [38/68]), and dilatation of the renal pelvis system (51% [35/68]) or ureter (47% [32/68]); further reasons are summarized in Table 2.

Two centers (3%) reported VUR in all renal allografts as a consequence of the surgical technique, that is, refluxing ureteral anastomosis, resulting in no need for VUR screening.

A pre-determined time-point to investigate VUR was indicated by 6% of the centers (4/71) (Supporting information S12); the remaining (94% [67/71]) did not specify.

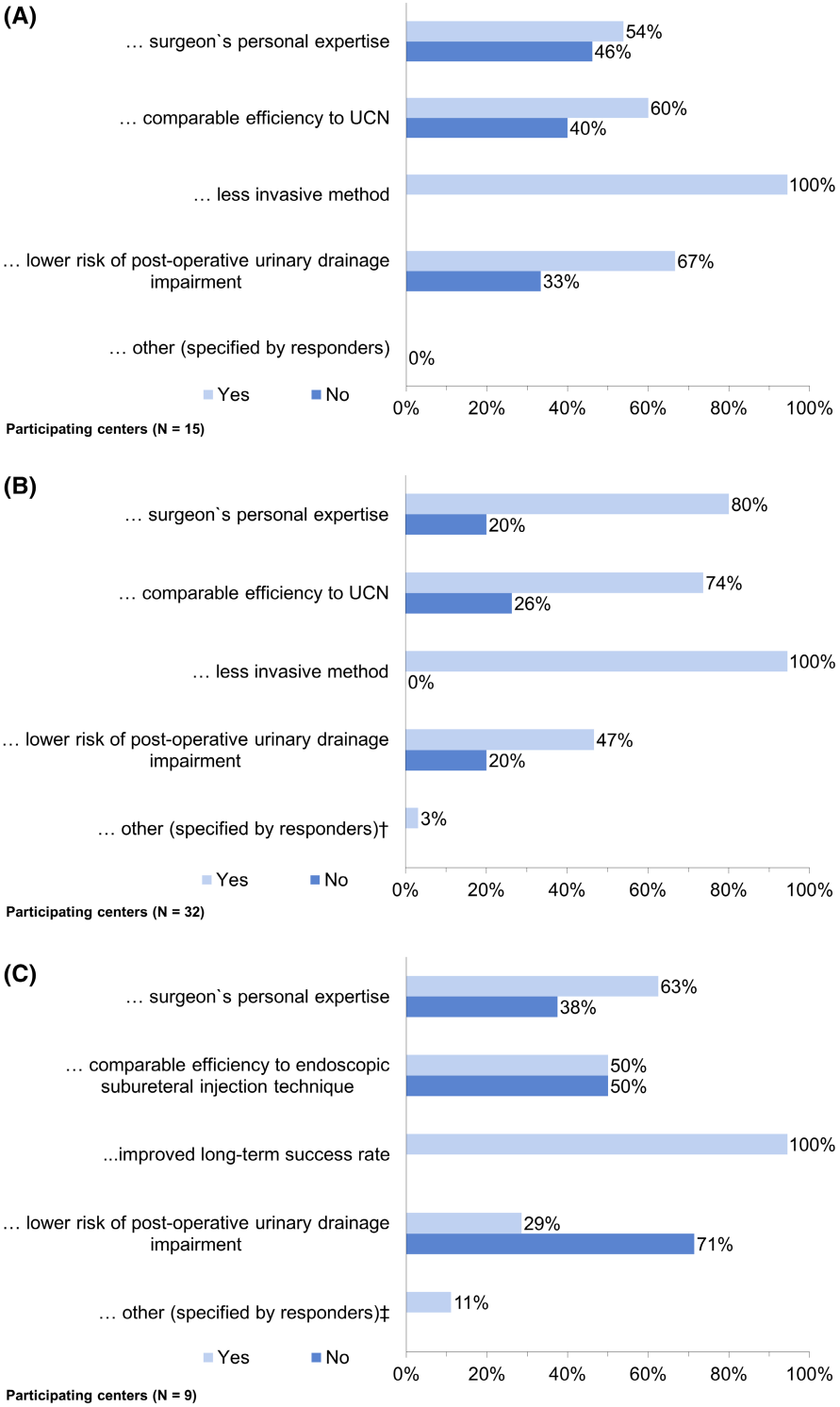


FIGURE 6 Statements addressing surgical management of VUR in native kidneys. (A) Opinions about endoscopic treatment of asymptomatic native kidney VUR. (B) Opinions about endoscopic treatment of symptomatic native kidney VUR. (C) Opinions about UCN in symptomatic native kidney VUR. †Other reasons: shorter hospital stay. ‡Other reasons: discussion of nephroureterectomy in patients with high-grade VUR and frequent febrile urinary tract infections. *n*, number; UCN, ureterocystoneostomy; VUR, vesico-ureteral reflux

3.4.4 | Management of symptomatic VUR in the renal transplant

The number of fUTI (96% [70/73]) and the presence of high-grade VUR (78% [57/73]) were the main determining factors for the management of VUR in the renal allograft, followed by bladder morphology (59% [43/73]), time-point of fUTI manifestation (51% [37/73]), underlying disease (47% [34/73]), presence of low grade VUR (10% [7/43]), bladder (dys)function (3% [2/73]), decreased glomerular filtration rate associated with bladder dysfunction (1% [1/73]) and presence of postvoid residual urine (1% [1/73]).

The following treatment strategies for allograft VUR were considered: CAP (83% [60/72]); surgical intervention (74% [53/72]) including the consideration of endoscopic intervention only (47% [25/53]), redo ureteral implantation only (15% [8/53]) or both methods (37% [20/53]); surveillance only (24% [17/72]) and other (*n* = 11 other interventions; Supporting information S13).

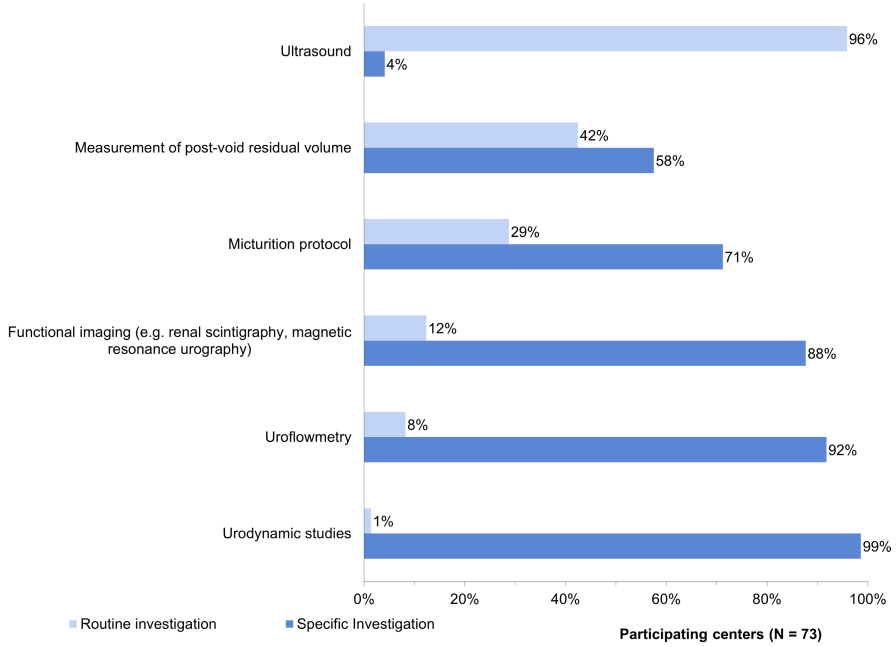


FIGURE 7 Urological assessment after KTx. KTx, kidney transplantation; *n*, number

TABLE 2 Criteria for post-transplant VUR screening ($N = 68$)

Reason/indication/condition	*n*	% of total
(Recurrent) febrile urinary tract infection (fUTI)	63	93
Bladder dysfunction (e.g., voiding disorders, neurogenic bladder, etc.)	38	56
Dilatation of the renal transplant pelvis system	35	51
Ureteral dilatation of transplant kidney	32	47
History of bladder outlet obstruction	17	25
History of bladder surgery	9	13
Other conditions, specified by responders[a]	2	3

Abbreviations: fUTI, febrile urinary tract infection; n, number; VUR, vesico-ureteral reflux.

[a]Other reasons: individual decision; renal scarring diagnosed by dimercaptosuccinic acid scintigraphy.

3.4.5 | Surgical management of VUR in the renal transplant

Of those 53 centers considering surgical intervention of symptomatic VUR in the KTx recipients, 55% (29/53) favored endoscopic intervention, and 26% (14/53) redo ureteral implantation. The remaining 19% (10/53) did not determine a preferred technique. Further information about the decision-making regarding the surgical procedures in transplant VUR is provided in Figures 8 and 9.

3.4.6 | Follow-up after surgical management of VUR in the renal transplant

Routine investigations to exclude VUR or drainage impairment following post-transplant VUR correction were performed by 66% (19/29) and 78% (11/14) of centers, respectively. These investigations were carried out in centers favoring surgical correction more often than in those preferring endoscopic treatment of allograft VUR. A comparison of the routine follow-up after post-transplant VUR intervention is depicted in Figure 10.

4 | DISCUSSION

The results of this survey clearly reveal the high variability in center-specific policies regarding the diagnostic and therapeutic management of VUR in renal transplant recipients. The heterogeneous practice patterns are rather due to the lack of consensus guidelines than to a non-standardized management of the participating pediatric transplant centers, since almost all corresponding centers had a pre-transplant protocol serving as a basis for diagnostics and treatment approaches. The center-specific standardization of the transplant procedure is not only a marker of good quality of care for the patients, but also ensures the reliability of our obtained data.

4.1 | Pre-transplant assessment

The results of the pre-transplant urological assessment are discussed in the vast majority of the renal transplant centers between the interdisciplinary teams involved in KTx, thereby increasing the quality of patient care and at the same time considering the specific skills and experiences required in pediatric KTx due to differences in medical and anatomical conditions compared to adult transplantation.[6–8]

For the same reasons it is not surprising that 63% of the participating centers have transplant surgeons specialized in pediatric KTx.[8] Interestingly, even though the vast majority of the centers have pediatric urologists with a profound training in ureteral

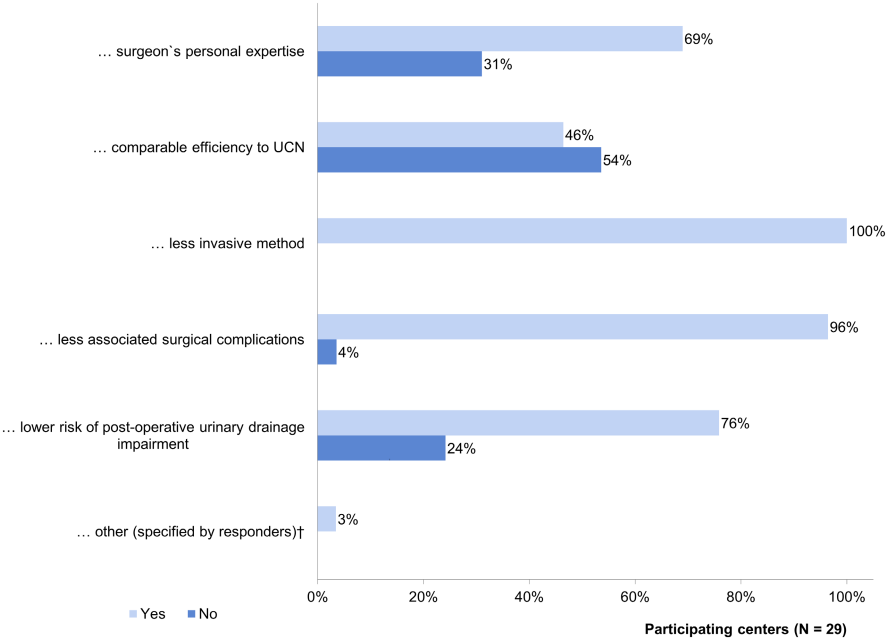


FIGURE 8 Statements about endoscopic treatment of allograft VUR. †Other reasons: no need for hospitalization. *n*, number; UCN, ureterocystoneostomy; VUR, vesico-ureteral reflux

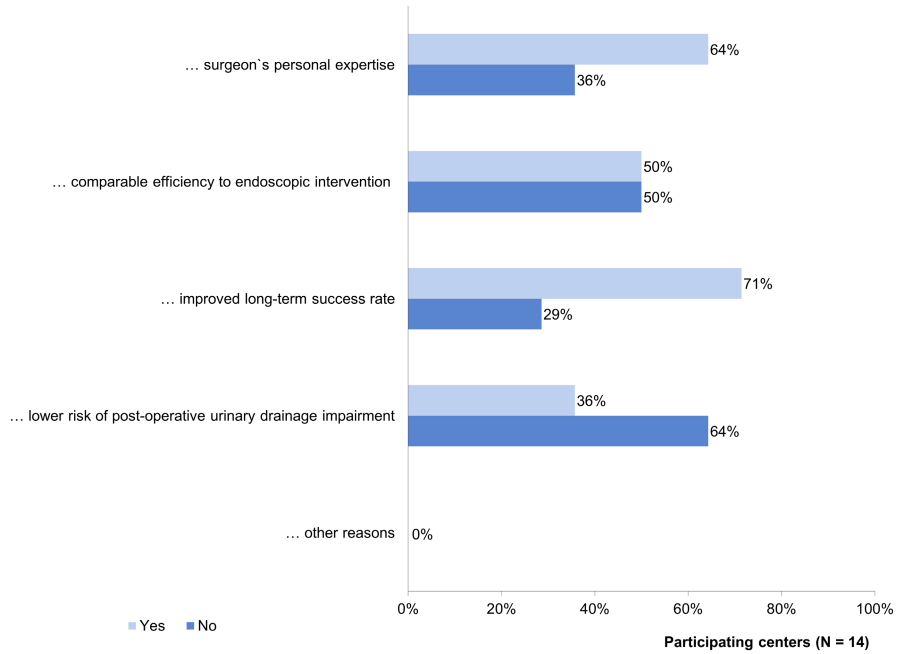


FIGURE 9 Statements about redo ureteral implantation in renal allograft VUR. *n*, number; VUR, vesico-ureteral reflux

implantation, they are consulted to assist for the ureteral implantation procedure in less than one third of pediatric KTx. Considering the high rate of post-transplant VUR, a more frequent and intensive collaboration between transplant surgeons and pediatric urologists for non-refluxing ureteral implantation could be discussed.[3,6,8]

Urological pre-transplant assessment of the kidney and urinary tract is an essential component for a successful pediatric KTx, which is part of the pre-transplant assessment in all renal transplant centers.[7,9,10] Although known to be a risk factor for urinary tract infection, almost one third of the corresponding centers do not routinely exclude postvoid residual urine during routine ultrasonography in renal transplant candidates with residual diuresis.[10,11] Similarly, even though a 24-h urine collection in renal transplant candidates provides valuable information to guide volume monitoring following pediatric KTx, only half of the centers gathered this information.[10,12] Urodynamic studies prior to pediatric KTx play an important role to minimize the risk of bladder-associated allograft failure, particularly in patients with dysfunctional bladder.[13–15] As expected, urodynamic studies and other urological diagnostics including renal scintigraphy and magnetic resonance (MR) urography are reserved for patients with specific urological issues only. This risk-stratified management may improve the renal transplant survival.[15–17]

Although contrast-enhanced VUS is approved as a well-stablished and radiation-free imaging modality for detecting and grading VUR, VCUG still remains the imaging method of choice in almost all participating centers.[18,19]

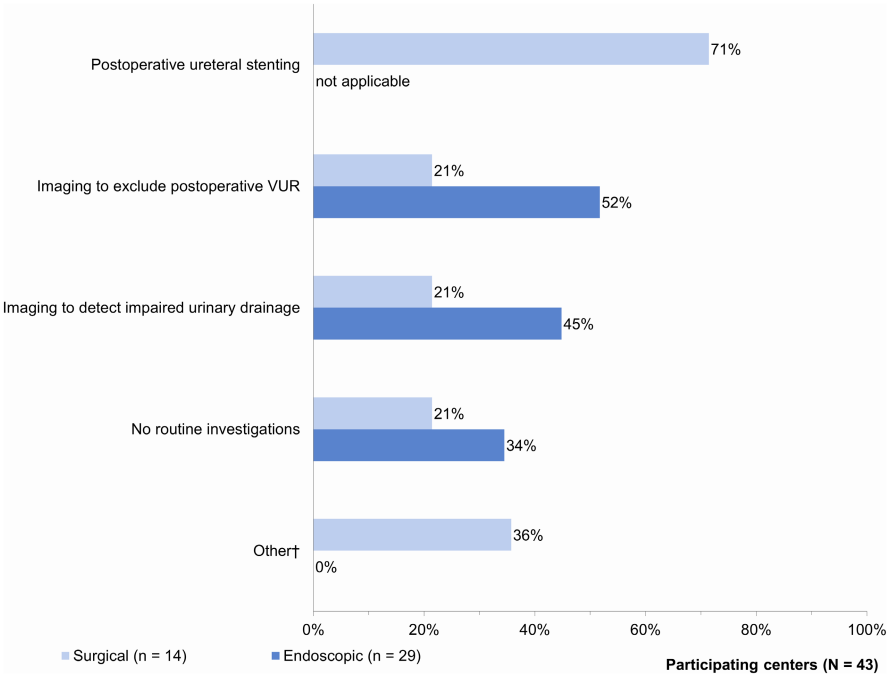


FIGURE 10 Follow-up after endoscopic treatment and redo-UCN. †Other: antibiotic prophylaxis during ureteral stenting, renal and urinary tract ultrasonography ($n = 2$); ureteral stenting selectively; VCUG in selected cases. *n*, number; UCN, ureterocystoneostomy; VCUG, voiding cystourethrography; VUR, vesico-ureteral reflux

The prevalence of VUR is considered to be higher in patients with associated dilatation of the kidney and urinary tract, dysfunctional bladder, and recurrent fUTI.[20] Therefore, these findings represent the most common indications for screening of VUR in the native kidneys of renal transplant candidates and to the renal allograft.[2,20,21] Surprisingly, almost one third of the centers perform routine VUR screening for all renal transplant candidates independent from given clinical risk factors, which is worth questioning with regard to benefit/risk assessment and costs.[22]

The steadily improving body of evidence for treatment of VUR has critically scrutinized the effectiveness of non-surgical and surgical intervention to prevent renal function deterioration following fUTI.[20,23,24] This may explain why the majority of pediatric renal transplant centers mainly prefer surveillance or bladder training in transplant recipients with asymptomatic VUR, and for patients with symptomatic VUR additionally CAP and bladder training.

If the indication for a surgical intervention is made, the intervention is mostly carried out prior to pediatric KTx, very likely to minimize intervention time at KTx.[25] The uncertain probability of spontaneous resolution of the VUR prior to KTx leads to surgical intervention in almost 80% of all renal transplant candidates.[26] The decision to proceed with surgery is nearly twice as high in patients with symptomatic VUR as in patients with asymptomatic VUR. In both cases, the endoscopic method is preferred over other surgical procedures. Interestingly, from a few transplant centers, the effectiveness of endoscopic injection technique is reported to be not only comparable to surgical intervention, but also to be associated with lower risk of urinary drainage impairment. These statements are not consistent with the current evidence, and in disagreement with the more frequent routine imaging methods in patients after endoscopic subureteral injection.[27,28]

4.2 | Transplant procedure

The use of ureteral stenting seems to be associated with less technical adverse events at the junction site of the ureterocystoneostomy, particularly urine leaks and ureteric stenosis.[29] Therefore, almost all transplant surgeons place routinely a ureteral stent during pediatric KTx, with a high preference for double-J-stent, followed by a percutaneous ureteral stent and mono-J-stent among others.[30] Since ureteral stenting may lead to increased risk of fUTI, a few centers follow a policy of stenting anastomoses only in combination with CAP.[31]

Surprisingly, two transplant centers reported to favor a freely refluxing vesico-ureteral anastomosis in order to prevent post-surgical obstruction, even though this procedure may predispose to VUR-associated transplant pyelonephritis.[1,32]

4.3 | Post-transplant management

Even though non-refluxive ureteral implantation is the standard of care in pediatric KTx, fUTI is among the most common complications after kidney transplantation leading to a significant morbidity.[33] Routine screening for transplant VUR is reported in only 7% of the transplant centers, which reflects the current practice in other transplant centers.[2,34] The indications, mode and frequency of urologic investigations performed after pediatric KTx are almost identical to the pre-transplant assessment.[2,35]

Despite the risk of developing resistance to CAP and the uncertain effect of CAP on long-term kidney outcome, almost two third of the pediatric renal transplant centers use CAP routinely in all renal transplant recipients, partially independent from urological abnormalities and recurrent fUTI.[20,36] Discontinuation of CAP varies

considerably with the most often reported criteria removal of the stent, exclusion of VUR by imaging or per transplant protocol in line with other studies.[37,38]

Interestingly, CAP remains the first choice in the case of symptomatic VUR, even though the probability for resolution of VUR without surgical intervention is low.[33,34] Very likely, the decision in favor of antibiotic prophylaxis is driven by the chance of developing fewer fUTI following tapering immunosuppressive therapy.

With regard to the modes of surgical intervention, the less invasive endoscopic subureteral injection technique is the preferred intervention modality for symptomatic and asymptomatic VUR, followed by open surgical options, which still represent the gold standard in terms of success.[27,28,32,39,40] In addition, the success rate of a redo-UCN after a subureteral injection is lower than that of a redo-UCN without prior injection.[28]

This online survey has several limitations. First, not only the diagnostic and therapeutic management of VUR is highly controversial but also many of the clinical definitions, such as grading of VUR and differentiation between asymptomatic and symptomatic VUR used for this survey. Second, the information from this survey cannot be generalized to all pediatric transplant centers because predominantly European countries participated in this survey. Third, although the response rate was quite high compared to other surveys, it remains unclear to what extent the data obtained reflect the overall management strategies because the precise number of pediatric KTx centers within the ESPN is not known, and therefore, a reliable statement about the representativeness and validity of the survey is not possible. In conclusion, this online survey could serve as a good starting point for improving the care of pediatric renal transplant recipients by summarizing the current management of VUR in pediatric KTx centers. Furthermore, this survey is revealing knowledge gaps to be closed through further clinical studies, and highlighting the urgent need for a consensus in order to harmonize the different diagnostic and therapeutic approaches.

AUTHOR CONTRIBUTIONS

MZ and MW designed the study, collected and analyzed the data and wrote the manuscript. KB did statistical analysis, designed the figures and tables, summarized methods and results. TL and BT provided important intellectual input in designing the study and critically revised the manuscript.

DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX A

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