







Current management of symptomatic vesicoureteral reflux in pediatric kidney transplantation—A European survey among surgical transplant professionals

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Abstract

Background: Vesicoureteral reflux (VUR) is common in children and adolescents undergoing kidney transplantation (KTx) and may adversely affect allograft kidney function.

Methods: To explore the current management of symptomatic native and allograft VUR in pediatric KTx recipients, an online survey was distributed to European surgical transplant professionals.

Results: Surgeons from 40 pediatric KTx centers in 18 countries participated in this survey. Symptomatic native kidney VUR was treated before or during KTx by 68% of the centers (all/selected patients: 33%/67%; before/during KTx: 89%/11%), with a preference for endoscopic treatment (59%). At KTx, 90% favored an anti-reflux ureteral reimplantation procedure (extravesical/transvesical approach: 92%/8%; preferred extravesical technique: Lich-Gregoir [85%]). Management strategies for symptomatic allograft VUR included surgical repair (90%), continuous antibiotic prophylaxis (51%), bladder training (49%), or noninterventional surveillance (21%). Redo ureteral implantation and endoscopic intervention for allograft VUR were equally reported (51%/49%).

Conclusions: This survey shows uniformity in some surgical aspects of the pediatric KTx procedure. However, with regard to VUR, there is a significant variation in practice patterns that need to be addressed by future well-designed and prospective studies. In this way, more robust data could be translated into consensus guidelines for a more standardized and evidence-based management of this common condition in pediatric KTx.

KEYWORDS

management strategies, online survey, pediatric kidney transplantation, vesicoureteral reflux

Abbreviations: KTx, kidney transplantation; UCN, ureterocystoneostomy; UTI, urinary tract infection; VUR, vesicoureteral reflux.

Matthias Zirngibl and Marcus Weitz contributed equally to this article.

[†]Collaborators including physicians who completed the survey are listed in [Appendix](#).

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1 | INTRODUCTION

Vesicoureteral reflux (VUR) into native or allograft kidneys is a common condition in children and adolescents undergoing kidney transplantation (KTx).¹⁻⁴ While the body of evidence for VUR in patients without end-stage kidney disease is well established, the available data on the long-term impact of VUR in pediatric KTx recipients for both, native and allograft kidneys, are still conflicting.^{4,5} In particular, the extent to which allograft kidney function may be adversely affected and what management strategies may improve therapeutic outcomes remains unclear.^{4,6-8}

Due to the lack of robust data and consensus guidelines, there is a high variability in the management of pediatric KTx recipients with symptomatic native and allograft VUR.⁸ The involvement of a multidisciplinary team with different perspectives undoubtedly contributes to heterogeneous diagnostic and therapeutic approaches.^{9,10} In this context, a previous online survey specifically investigated the pediatric nephrologist's perspective on the diagnosis and management of VUR in pediatric KTx candidates.¹¹ The current survey was designed to explore different practice patterns among surgeons involved in pediatric KTx in order to fill further knowledge gaps and highlight differences with regard to the transplantation procedure and VUR management, with an additional focus on surgical techniques.

2 | MATERIALS AND METHODS

2.1 | Study design

An electronic, questionnaire-based survey was designed and distributed online to surgical transplant professionals involved in pediatric KTx (68 transplant centers).^{12,13} These contacts were solicited from pediatric nephrologists who had participated in a previous survey on VUR management in pediatric KTx recipients and supplemented by using Eurotransplant database searches.¹¹ The invitation to participate in the survey included study information and a personal link to the survey website (SurveyMonkey Inc., www.surveymonkey.com) (Appendices S1-S3).

The survey was divided into five sections with 57 items (open and multiple-choice questions): (I) demographic and general characteristics of the respective transplant center; (II) management of symptomatic VUR in the native kidneys; (III) intraoperative transplant procedure; (IV) postoperative urologic transplant management; (V) treatment of symptomatic allograft VUR (Appendix S1).

The questionnaire was reviewed in advance by four transplant experts for clarity, usefulness, and redundancy. Ambiguities were then modified and optimized, and the adapted questionnaire was re-tested by another five transplant experts. Because the study did not directly involve patients or require any specific patient data, it was not approved by an ethics committee.

2.2 | Study duration and study population

The survey was conducted between January 17, 2022 and December 28, 2022.

A total of 46 center responses were collected. Multiple data entries were eliminated (double: $n=2$; triple: $n=1$) resulting in 42 corresponding pediatric KTx centers. Participants who did not perform KTx in the pediatric population <18 years ($n=1$) or could not be assigned to a specific institution ($n=1$) were excluded from the analysis. Finally, 40 pediatric KTx centers were included in the data analysis.

2.3 | Definition of symptomatic VUR

In this study, symptomatic VUR was defined as VUR associated with a febrile urinary tract infection (UTI).

2.4 | Statistical analyses

Responses were documented and validated in an electronic database. Double and triple responses from a center were combined into a single response. Statistical analyses were performed based on the total number of responses for each question. The overall completion rate of the questionnaires was 93% (37/40). Details of data completion, including missing and valid data for all items, are presented in Appendix S4. In the case of missing or ambiguous data, participants were contacted for further information.

Data were analyzed using the statistical package SPSS for Windows, version 28 (IBM Corp.). Categorical variables were expressed as frequencies and percentages. Responses to open questions were described narratively.

3 | RESULTS

3.1 | Demographic and institutional characteristics of participating centers

A total of 40 centers from 18 European countries participated in the survey (Figure 1).

3.2 | Management of symptomatic VUR in native kidneys

3.2.1 | Surgical correction of symptomatic native kidney VUR

Symptomatic VUR in the native kidneys was treated surgically by 68% (27/40) of the centers, with 33% (9/27) in all and 67% (18/27) in selected KTx candidates only (Figure 2). Eighty-nine percent (24/27)

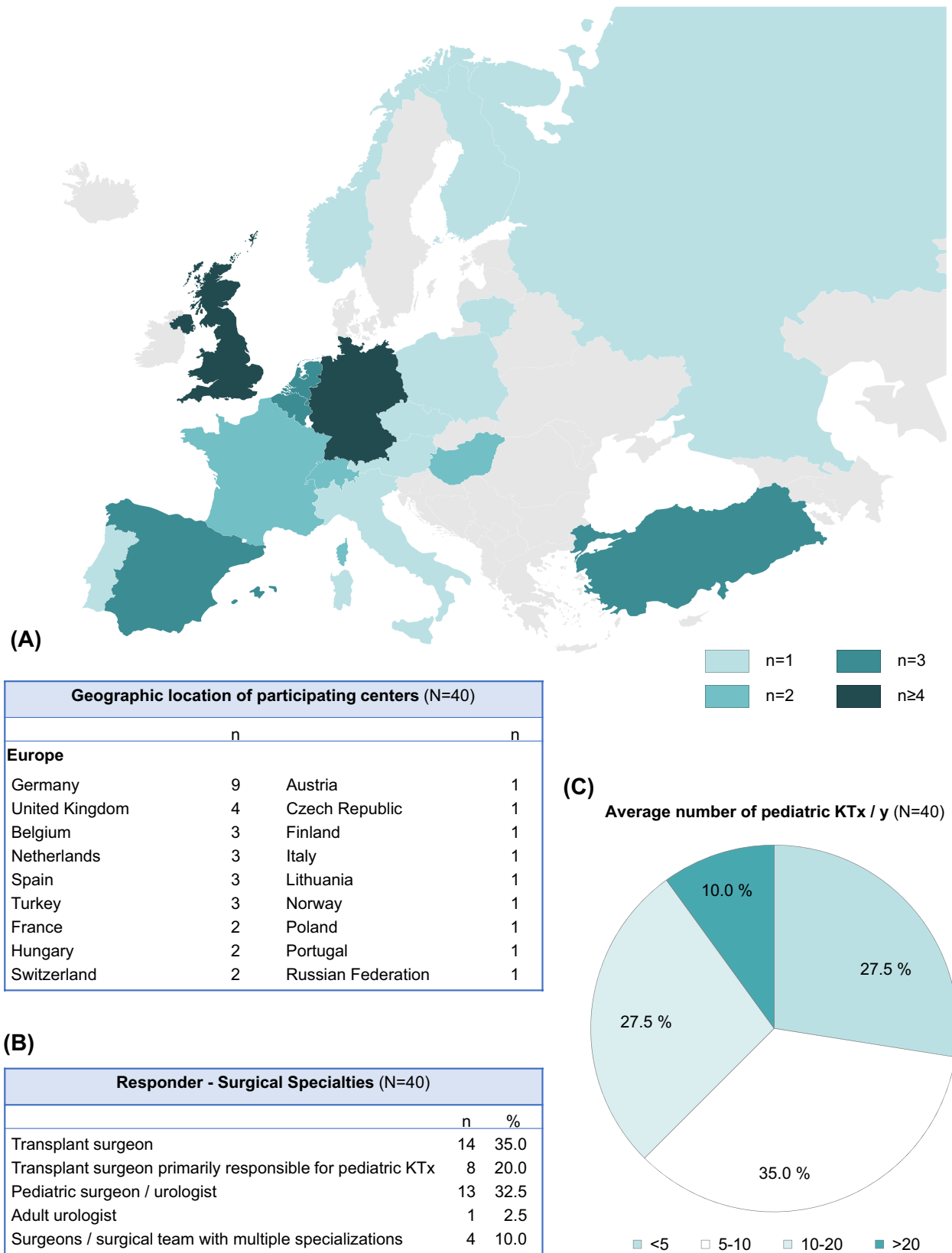


FIGURE 1 Demographic and institutional characteristics of participating centers (N=40). KTx, kidney transplantation; n, number; y, year.

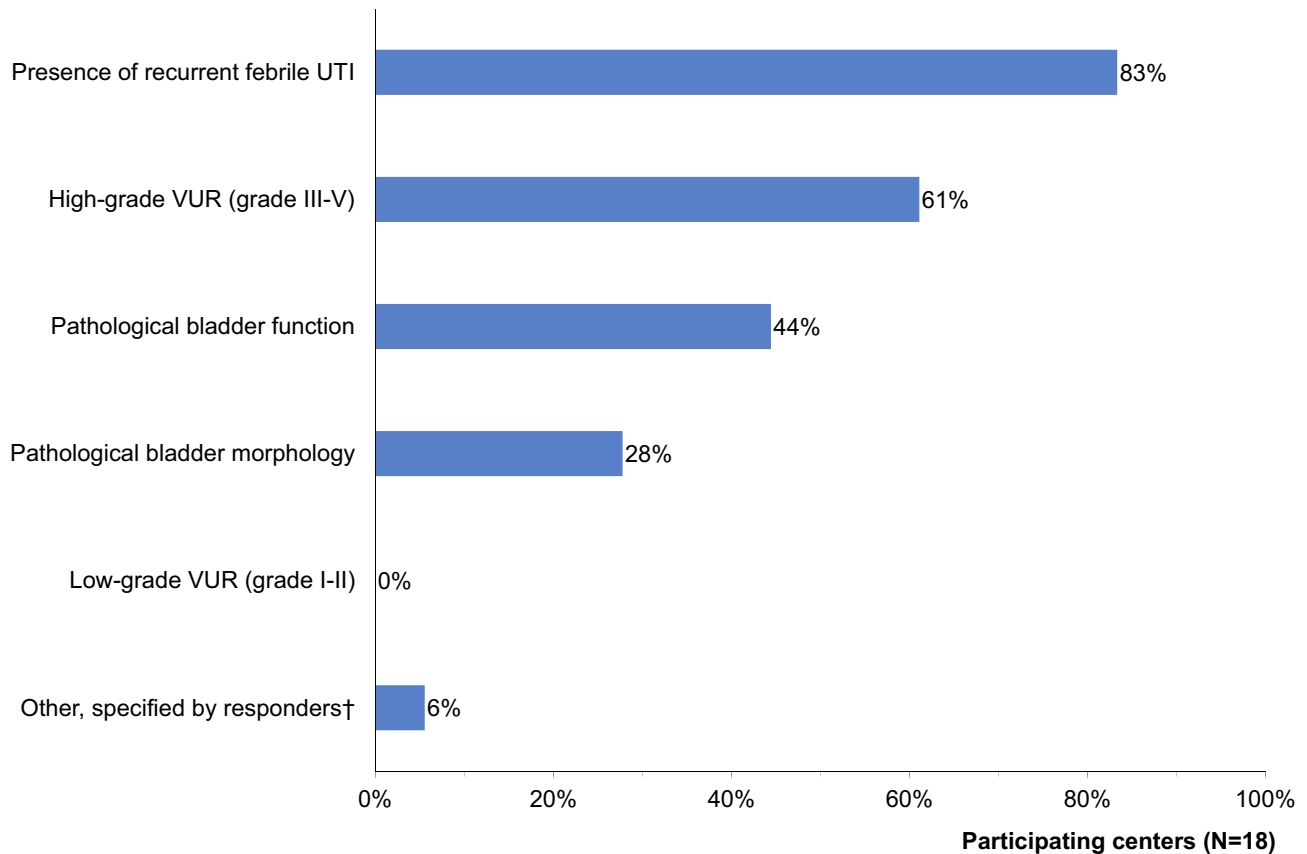


FIGURE 2 Reasons for surgical correction of native kidney VUR including nephroureterectomy in selected KTx recipients. Responses from 18 centers (surgical correction of VUR: $n = 15$; nephroureterectomy: $n = 2$; not specified: $n = 1$). †Other reasons: In case of relevant symptomatic VUR, planning of nephroureterectomy. KTx, kidney transplantation; n, number; UTI, urinary tract infection; VUR, vesicoureteral reflux.

aimed to correct VUR before, and the remainder (11% [3/27]) during KTx (Appendix S5).

The procedure was performed by pediatric surgeons/urologists in 93% (25/27) of centers and by transplant surgeons primarily responsible for pediatric KTx in 7% (2/27) of the centers. Fifty-nine percent (16/27) preferred endoscopic subureteric injection, 30% (8/27) ureterocystoneostomy (UCN), 7% (2/27) nephroureterectomy, one center did not specify. Details regarding surgical techniques are listed in Appendix S6.

3.3 | Intraoperative transplantation procedure

3.3.1 | Surgeons performing transplant ureteral reimplantation

During KTx, ureteral reimplantation was mainly performed by transplant surgeons primarily responsible for pediatric KTx (40% [16/40]), followed by transplant surgeons (33% [13/40]), pediatric surgeons/urologists (25% [10/40]), and vascular surgeons (3% [1/40]). In centers where ureteral reimplantation was not routinely performed by pediatric surgeons/urologists, (pediatric) urologists were involved in selected cases (23% [7/30]) (Appendix S7).

3.3.2 | Transplant ureteral reimplantation techniques

Anti-reflux ureteral reimplantation techniques were preferred by 90% (36/40) of the centers, predominantly by an extravesical approach (92% [33/36], and 85% [28/33] according to Lich-Gregoir) (Figure 3). The reasons for this are shown in Figure 4, and detailed data on surgical techniques can be found in Appendix S8.

The remaining four centers (10%) did not perform anti-reflux surgery at KTx because of prevention of uretero-vesical obstruction ($n = 4$) or because of perceived inferiority of anti-reflux techniques ($n = 1$).

In KTx recipients with dysfunctional or morphologic bladder pathology, 25% (10/40) modified the surgical technique (Figure 3).

3.4 | Ureteral stenting at KTx

In 93% (37/40) of the centers, transplant ureters were routinely stented using a double-J-stent (81% [30/37]), single-J-stent (8% [3/37]), percutaneous stent (5% [2/37]), or other device (5% [2/37]) including single-J-stent with external drainage ($n = 1$) or individual age-related management ($n = 1$) (Figure 5). The remaining 8% (3/40) did not use a ureteral device in order to avoid further intervention ($n = 1$) or did not consider it necessary ($n = 2$). The timing of ureteral stent removal ranged from 1 to 6 weeks, with 73%

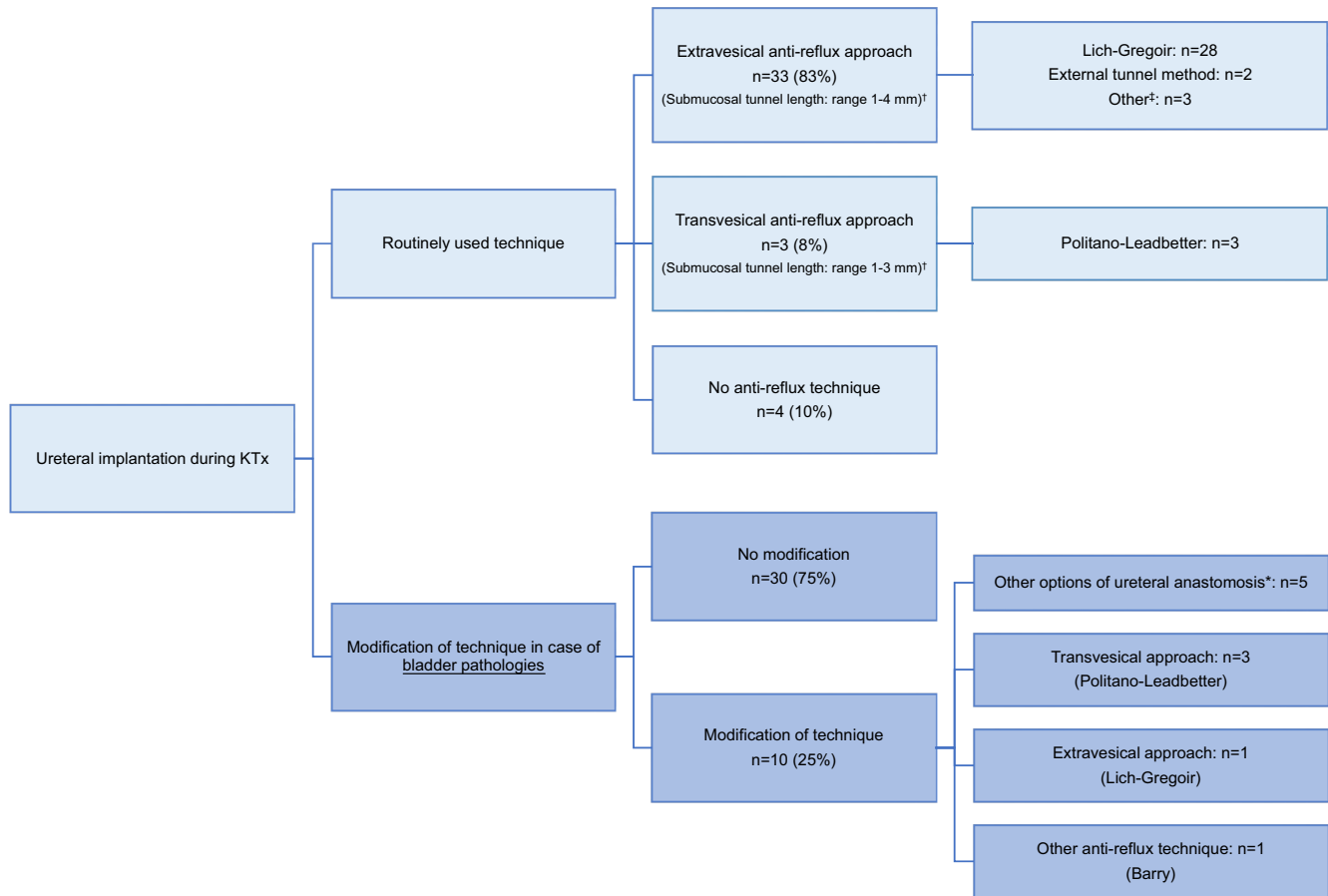


FIGURE 3 Surgical techniques used for ureteral reimplantation at KTx ($N=40$). †Submucosal tunnel length: More detailed data on this aspect can be found in Appendix S7. ‡Other extravesical anti-reflux techniques: Barry technique ($n=1$), modified Lich-Gregoir technique (Woodruff) ($n=1$), technique described as follows: 2 cm muscle incision, distal ureteral anastomosis with separate sutures, closure of the bladder muscle over the ureter ($n=1$). *Other options for ureteral reimplantation in case of bladder pathology: Lich-Gregoir or no anti-reflux ($n=1$), pyeloureterostomy ($n=2$), ureteroureterostomy ($n=1$), ureteroureterostomy/pyeloureterostomy ($n=1$). KTx, kidney transplantation; n, number.

(27/37) retrieved within 4 weeks after KTx. Reasons for and against ureteral stenting and timing of ureteral stent removal are listed in Appendix S9.

3.5 | Bladder drainage by transurethral or suprapubic catheter in KTx

In 93% (37/40) of the centers, KTx recipients routinely received a transurethral or suprapubic bladder catheter, predominantly in combination with a ureteral stent (88% [35/40]) (Figure 5). The catheter was mostly removed (76% [28/37]) within 1 week after KTx. Reasons for the use of a bladder catheter, criteria for its removal and opinions not to use these devices (8% [3/40]) are summarized in Appendix S10.

3.6 | Postoperative management

3.6.1 | Antibiotic prophylaxis

Antibiotic prophylaxis to prevent transplant pyelonephritis was administered in 93% (37/40) of the centers, with 70% (26/37) in

all, and 30% (11/37) in selected patients, mainly because of history of bladder dysfunction (55% [6/11]), with other reasons listed in Appendix S11. Criteria for discontinuation of antibiotic prophylaxis are shown in Figure 6.

Untimely (≤ 36 h) treatment of acute transplant pyelonephritis was considered to be a risk factor for permanent allograft injury by 62% (24/39). The remaining centers did not agree (18% [7/39]) or did not specify (21% [8/39]).

3.7 | Management of allograft VUR

3.7.1 | Management strategies for symptomatic allograft VUR

The following management strategies were considered for symptomatic allograft VUR: surgical repair (90% [35/39]) including redo surgical ureteral implantation (64% [25/39]) and endoscopic intervention (51% [20/39]), continuous antibiotic prophylaxis (51% [20/39]), bladder training (49% [19/39]), noninterventional surveillance only (21% [8/39]) or other individualized strategies (3% [1/39])

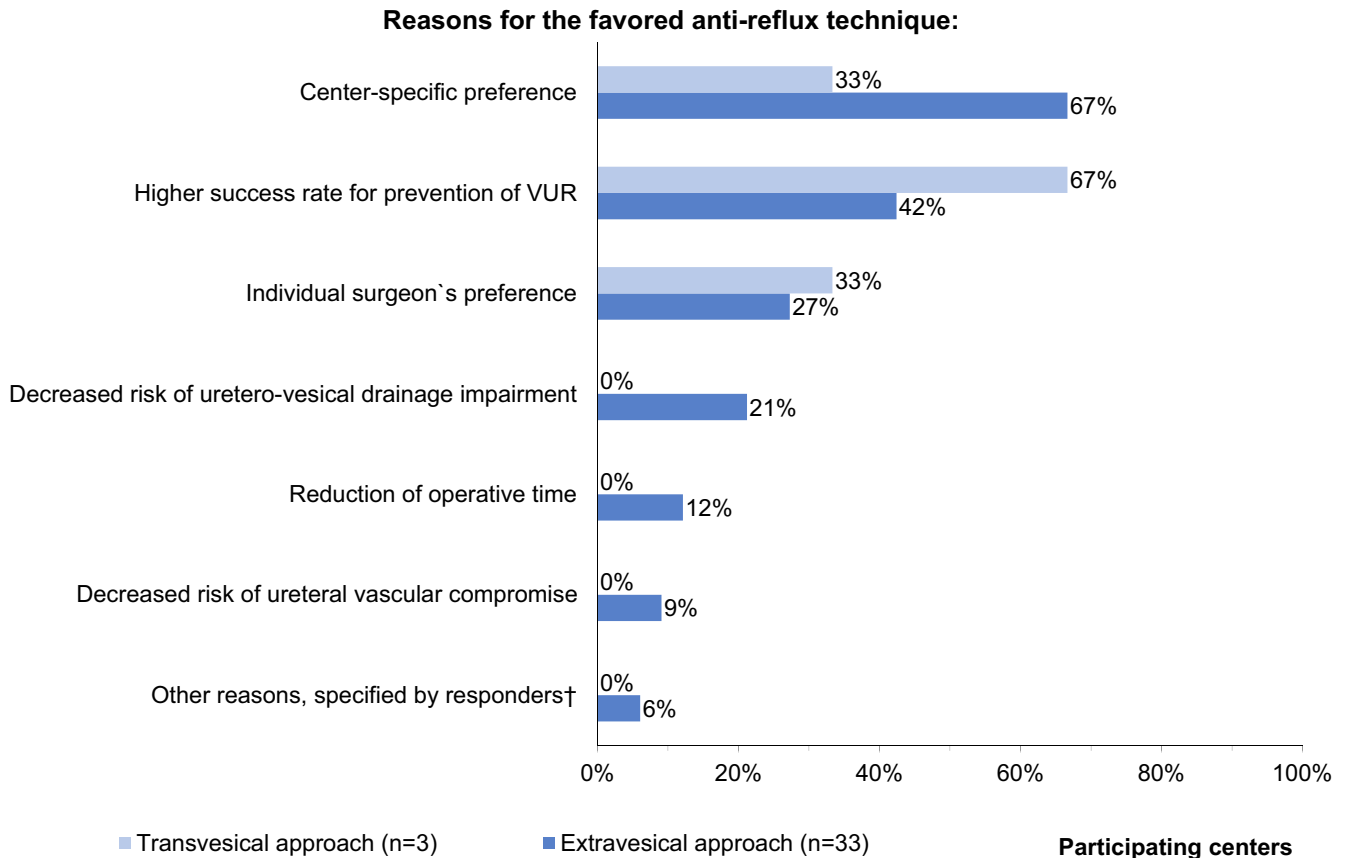


FIGURE 4 Reasons for preferred anti-reflux ureteral reimplantation at KTx. Responses from 36 centers (transvesical approach: $n=3$; extravascular approach: $n=33$). †Other reasons: Reduced risk of hematuria ($n=1$), easy to perform and good long-term results audited in the corresponding institution ($n=1$). KTx, kidney transplantation; n, number; VUR, vesicoureteral reflux.

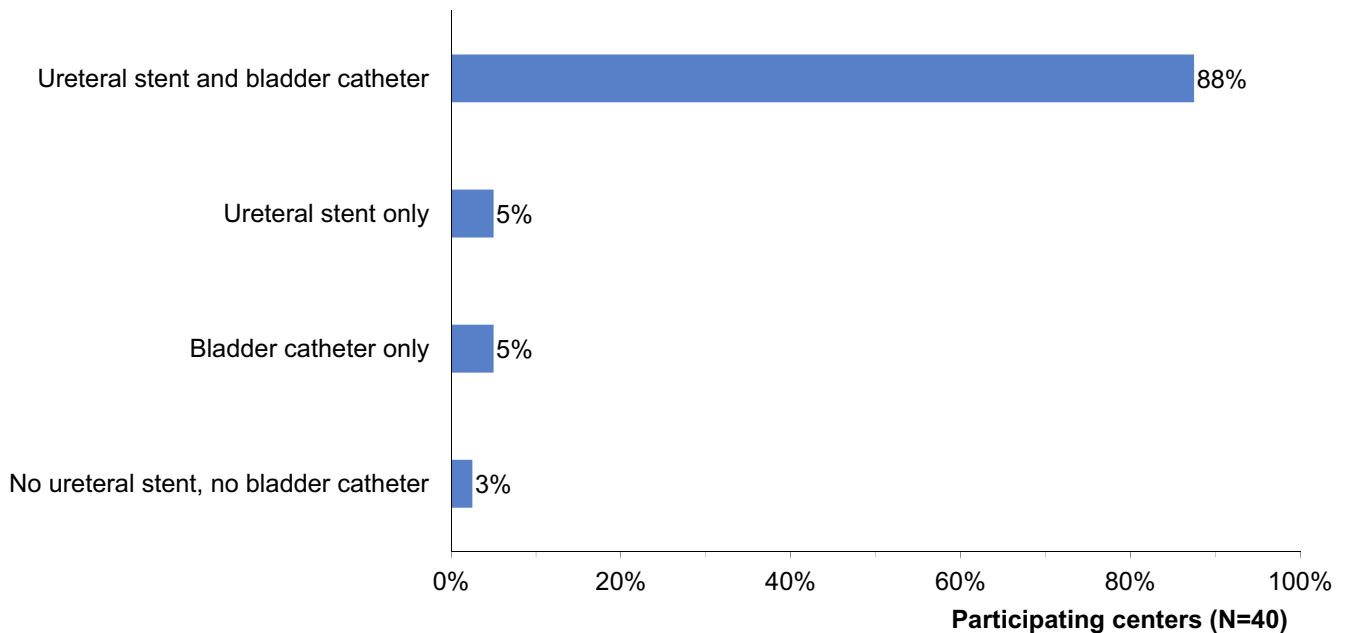


FIGURE 5 Ureteral stenting and bladder drainage at KTx. KTx, kidney transplantation; n, number.

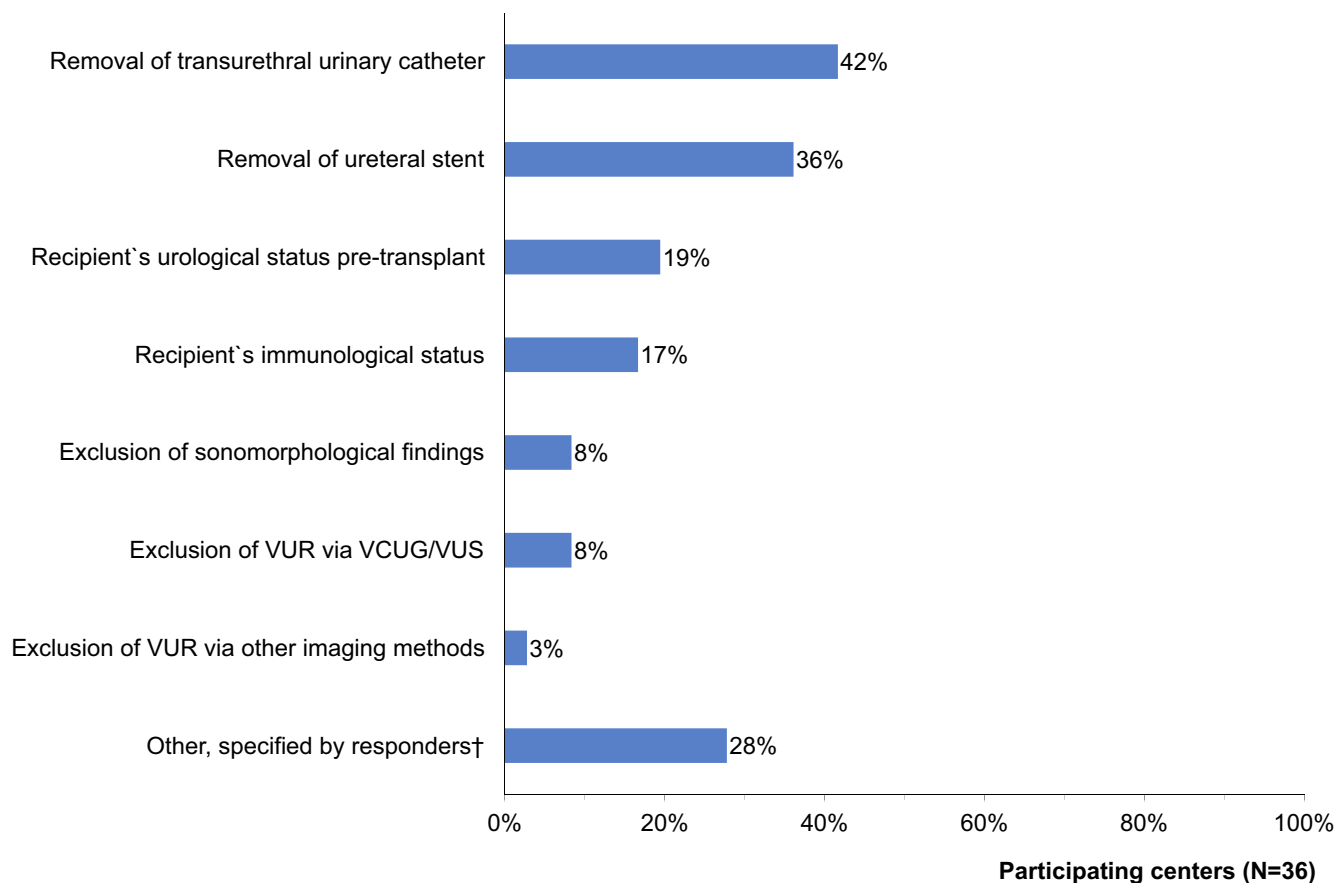


FIGURE 6 Criteria for discontinuation of antibiotic prophylaxis after KTx. †Other criteria: Discontinuation not before 5 days ($n=1$), negative urine culture ($n=1$), only 3 doses given perioperatively ($n=1$), cotrimoxazole administration in order to prevent urinary tract and *Pneumocystis jirovecii* infection ($n=2$), routine procedure ($n=1$), prophylaxis with fixed timing 24 h ($n=1$), single-shot perioperatively ($n=1$), unknown criteria/no specification ($n=1$). KTx, kidney transplantation; n, number; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux; VUS, voiding urosonography.

including bladder rehabilitation based on underlying disease). More detailed information on each strategy is shown in [Figure 7](#), and the determining conditions in [Figure 8](#).

3.8 | Surgical management of symptomatic allograft VUR

The following specialties were commonly involved in the surgical management of symptomatic allograft VUR: pediatric surgeons/urologists (64% [25/39]), transplant surgeons primarily responsible for pediatric KTx (18% [7/39]), transplant surgeons (15% [6/39]), or an interdisciplinary team (consisting of a pediatric urologist and an adult transplant urologist; 3% [1/39]).

Among these 35 centers considering allograft VUR correction, there was a balance between redo surgical (51% [18/35]) and endoscopic intervention (49% [17/35]), with decision criteria listed in [Figure 9](#). Follow-up after surgical treatment is shown in [Figure 10](#).

3.8.1 | Redo surgical ureteral implantation for symptomatic allograft VUR

The extravesical approach was the preferred technique (78% [14/18]) for redo UCN for symptomatic allograft VUR (Lich-Gregoir [$n=12$]; external tunnel method [$n=1$]; not specified [$n=1$]). The remaining centers (22% [4/18]) preferred redo UCN based on a transvesical technique (Politano-Leadbetter [$n=3$]; Cohen transtrigonal technique [$n=1$]).

3.8.2 | Failed endoscopic treatment of symptomatic allograft VUR

For failed endoscopic treatment of symptomatic allograft VUR, the following management strategies were considered: redo surgery (75% [12/16]), redo surgery or redo endoscopic intervention (13% [2/16]), redo endoscopic intervention only (6% [1/16]), continuous antibiotic prophylaxis (25% [4/16]), noninterventional surveillance

Strategies	Redo ureteral implantation	Endoscopic subureteric injection	Bladder training	Continuous antibiotic prophylaxis	Noninterventonal surveillance only	Other strategies, specified by responders [†]	Participating centers	
							n	(% of total)
							4	(10%)
							3	(8%)
							3	(8%)
							3	(8%)
							2	(5%)
							2	(5%)
							2	(5%)
							1	(3%)
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							1	(3%)

FIGURE 7 Management strategies for symptomatic allograft VUR ($N=39$). ■: Surgical strategy/strategies; ■: Non-surgical strategy/strategies; ■: Noninterventional surveillance only. †Other strategies: Bladder rehabilitation based on underlying condition ($n=1$). Overall, the following strategies were reported for symptomatic allograft VUR: Surgical intervention, non-surgical intervention and/or surveillance: 53% (21/39); Surgical intervention only: 36% (14/39); Non-surgical intervention or surveillance only: 8% (3/39); Noninterventional surveillance only: 3% (1/39). n, number; VUR, vesicoureteral reflux.

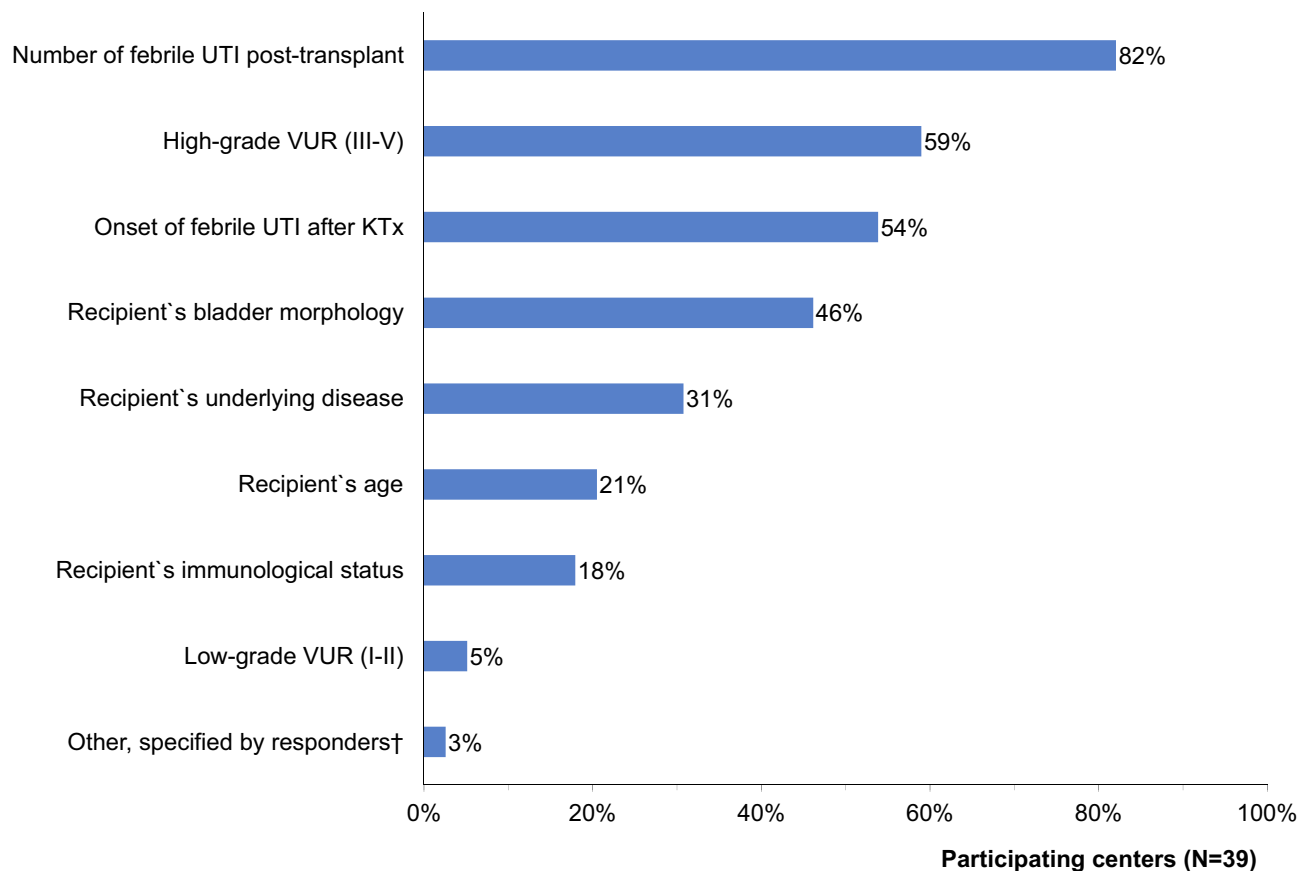


FIGURE 8 Criteria for allograft VUR management. †Other conditions: Statement that no re-operation of a graft ureter except for ureteral stricture ($n=1$). KTx, kidney transplantation; n, number; UTI, urinary tract infection; VUR, vesicoureteral reflux.

only (13% [2/16]) or individualized approaches (surveillance and redo endoscopic intervention for recurrent UTI [$n=1$]). Centers considering redo surgery favored the same surgical technique compared to KTx (86% [12/14]), with the exception of two centers that indicated a different approach (Leadbetter-Politano ureteral reimplantation or pyeloureterostomy [$n=1$]; anti-reflux technique with high native ureteral anastomosis [$n=1$]).

4 | DISCUSSION

The present survey not only shows comparable clinical considerations in many aspects of VUR management strategies but also highlights significant differences. These discrepancies need to be critically evaluated to further improve the care of pediatric KTx recipients with associated VUR.

4.1 | Symptomatic native kidney VUR

Screening for native kidney VUR has become a routine part of the pre-transplant urologic evaluation, particularly in patients with febrile UTI, bladder pathology, and ureteral and/or pelvicalyceal dilatation.^{1-3,11} When symptomatic native kidney VUR is detected, more than two-thirds of the participating centers aim to correct VUR in either all or selected patients, primarily prior to KTx. Interestingly, among pediatric nephrologists asked about VUR management strategies in pediatric KTx recipients previously, the tendency for VUR correction in symptomatic native kidney VUR was even more pronounced.¹¹ These trends are likely driven by concerns that recurrent febrile UTI due to untreated native kidney VUR might proceed native kidney failure, and potentially worsen long-term allograft kidney function. However, conclusive evidence to support these concerns is needed to make informed decisions regarding clinical management.^{4,5,14-16}

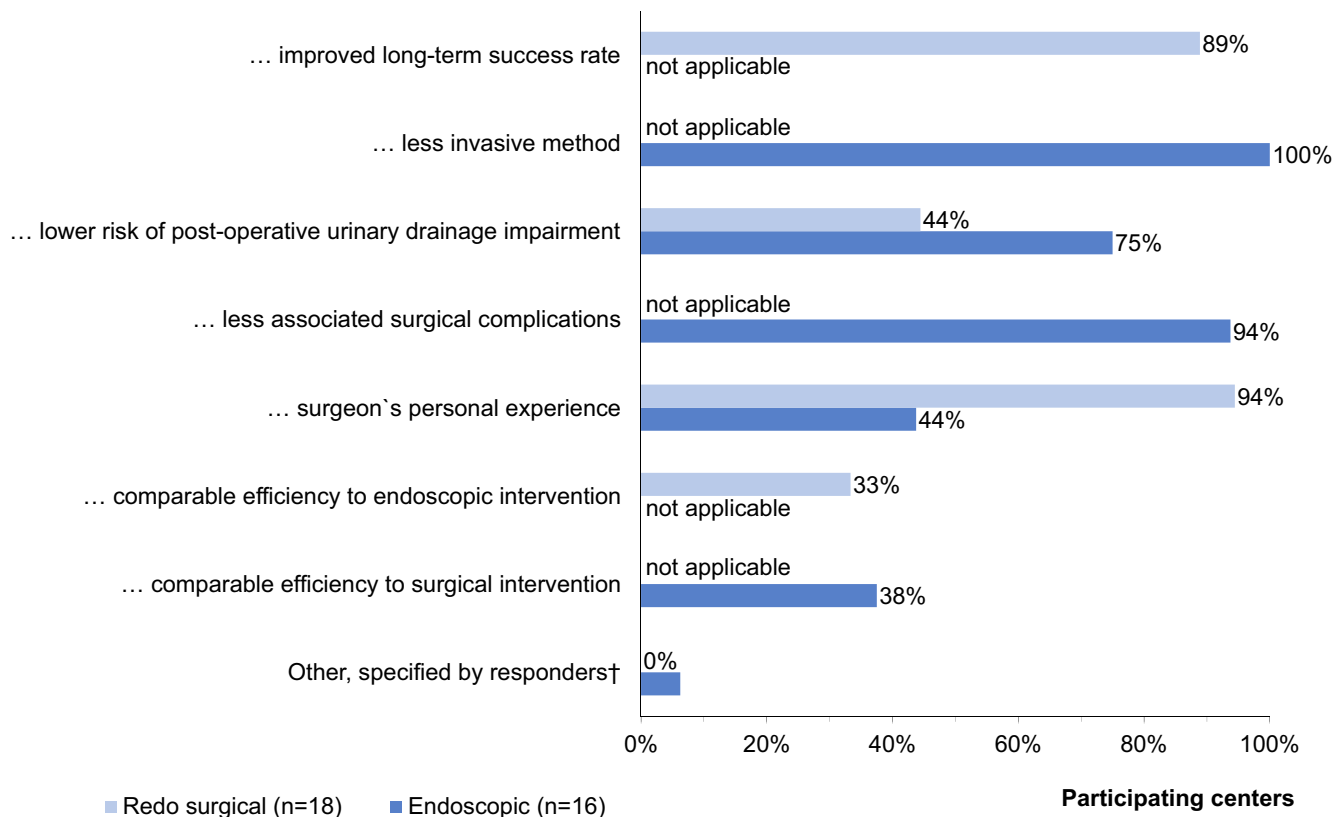


FIGURE 9 Statements regarding the preferred surgical procedure for symptomatic allograft VUR correction. Responses from 34 centers (redo surgical intervention: $n=18$; endoscopic intervention: $n=16$). †Other opinions: Personal experience that endoscopic intervention is sufficient in almost all cases ($n=1$). n, number; VUR, vesicoureteral reflux.

When surgical treatment is chosen for symptomatic native kidney VUR, endoscopic subureteric injection is slightly preferred over surgical ureteral reimplantation in the corresponding centers, although the available evidence indicates higher success rates in terms of VUR resolution, lower need for re-intervention, and lower risk of ureteral obstruction in UCN.^{5,14,17} This practice is in line with the strategy of the previously surveyed pediatric nephrologists.¹¹ Furthermore, this approach reflects the current trend to treat primary pediatric VUR, at least in the younger age groups with the likelihood of maturation over time due to the less invasive procedure.^{5,18}

4.2 | Transplantation procedure and post-transplant management

The vast majority of the reporting centers favor the use of the Lich-Gregoir anti-reflux extravesical approach for UCN in pediatric KTx, presumably due to lower frequency of urinary leakage, shorter operative time, and easy feasibility.^{4,9,19–23} Since no consensus has been reached regarding the transplant ureteral reimplantation, it is not surprising that there are numerous other technical methods including extravesical, transvesical, and other approaches with ongoing modifications.^{6,22,24}

The anti-reflux techniques are characterized by the formation of a submucosal tunnel but if the submucosal tunnel is applied

too short, it has been suggested as a risk factor for post-transplant VUR, especially in patients with urethrovesical anomalies.²⁵ Interestingly, the submucosal tunnel length reported by the participating centers varies considerably, which not only reflects the lack of technical unambiguity but also leaves room for improvement.

Only a minority of the centers does not perform an anti-reflux ureteral reimplantation, possibly to avoid ureteral stricture.²⁶ Of note, the impact of anti-reflux UCN techniques in KTx is controversially debated, given the high prevalence of allograft VUR, presumably regardless of the surgical approach.^{23,27}

In children and adolescents with bladder anomalies, transplant ureteral reimplantation is more challenging and may be associated with a higher incidence of urologic complications, predominantly symptomatic allograft VUR, and less favorable allograft kidney function.^{3,9} Alternative ureteral anastomosis techniques, such as uretero-ureterostomy and pyeloureterostomy have been shown to be feasible options without the risk of allograft VUR.^{28–30} Nevertheless, only one quarter of the centers modify the routine technique in these patients, possibly due to center-specific preferences and surgical training.

Although UCN for correction of native kidney VUR is predominantly performed by pediatric surgeons/urologists, ureteral anastomosis at KTx is performed by transplant surgeons in most centers. Considering the specific pediatric anatomy and the high proportion of patients with urinary tract anomalies, especially bladder anomalies, an increased multidisciplinary collaboration involving trained pediatric

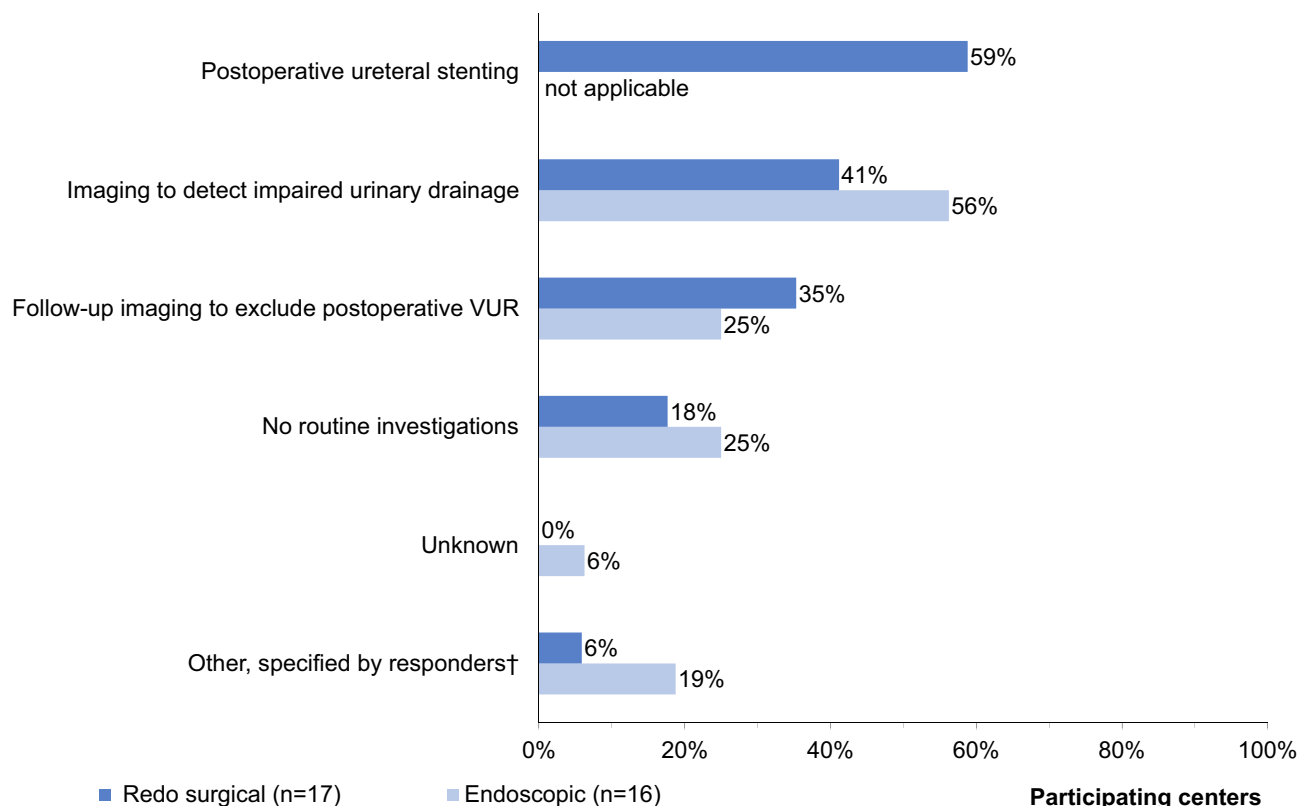


FIGURE 10 Follow-up after surgical treatment of allograft VUR. Responses from 34 centers (redo surgical intervention: $n = 17$; endoscopic intervention: $n = 16$). †Other investigations: Surgical group ($n = 1$): Urine cultures ($n = 1$); endoscopic group ($n = 3$): at urologist's discretion ($n = 1$), ultrasound ($n = 2$). n, number; VUR, vesicoureteral reflux.

surgeons/urologists needs to be discussed to benefit from the presumed higher expertise in this field.^{3,9,11,31}

As expected, almost all transplant centers place a stent in the transplant ureter, preferably a double-J-stent, to prevent major urological complications, especially urinary drainage impairment.^{32,33} The ureteral stent is usually removed within 4 weeks after KTx, a practice supported by data indicating that the benefits of a longer duration (>3 weeks) of indwelling ureteral stents are outweighed by harms, especially increased risk of UTI.^{32,34,35} For the same reasons, urethral or suprapubic bladder catheters are usually removed within the first week after KTx.^{36,37}

Although the benefit is not proven, most centers have adopted a policy of antibiotic prophylaxis in all or selected patients to prevent acute post-transplant pyelonephritis, because febrile UTIs are a common condition in pediatric KTx recipients.^{36,38} This is especially true to the period immediately after KTx with catheters in place.³⁴ For this reason, antibiotic prophylaxis is often discontinued when the indwelling catheters are removed. Of note, early removal of indwelling ureteral stents and bladder catheters appears to prevent UTI rather than prolonged antibiotic prophylaxis.^{34,37} Nevertheless, given the lack of evidence, it is not surprising that the criteria for indication and timing of discontinuation of antibiotic prophylaxis vary widely. It is important to note that the available data, mainly from adult KTx, cannot be fully extrapolated to pediatric KTx candidates with a higher proportion of patients with additional risk factors for UTI, such as urethral valves and a history of recurrent febrile UTI prior to KTx.^{4,36}

4.3 | Symptomatic allograft VUR

The true prevalence of allograft VUR in pediatric KTx recipients is unknown, because the majority of centers limit VUR screening to symptomatic patients only.¹¹ The few pediatric studies that have systematically evaluated allograft VUR have found a prevalence ranging from 36% to 58%.^{15,39,40}

The indications for intervention in symptomatic VUR are similar to those for native kidney VUR prior to KTx; only the onset of UTI after KTx and the recipient's immunologic status play an additional role.

Despite the use of the same highly effective anti-reflux UCN techniques as in the correction of native kidney VUR, the high prevalence of allograft VUR is still surprising.^{5,21,22} In this context, associated congenital anomalies of the urinary tract, lower urinary tract dysfunction, and atrophic bladder appear to contribute more to allograft VUR than surgical expertise or technique.^{3,16} Therefore, especially these patients are recommended to be screened for allograft VUR, if presenting with recurrent febrile UTI.

In the case of symptomatic VUR, redo ureteral implantation or endoscopic subureteric injection is considered equally by almost all corresponding surgeons by using the same surgical methods. This finding is in contrast to our previous survey of pediatric nephrologists who first considered continuous antibiotic prophylaxis despite the unlikely spontaneous resolution.⁸ In addition, among the pediatric nephrologists surveyed previously, endoscopic allograft VUR correction was preferred over other surgical techniques.¹¹ Compared to the correction

of native kidney VUR, surgical treatment of allograft VUR is more challenging due to ureteral scarring and the atypical orifice of the graft ureter, which should inevitably result in a more stringent surgical indication.⁴¹ Of note, although endoscopic treatment has been shown to be effective in some studies, the success rates remain higher with open surgical redo ureteral anastomosis techniques.^{8,41–46} In failed endoscopic treatment of VUR, most centers tend to redo UCN, considering that the latter is less successful after previous endoscopic injection.⁴³ Imaging after surgical repair of allograft VUR is performed by the majority of centers to detect urinary drainage impairment and postoperative persistent VUR.

Additional non-surgical management strategies, including continuous antibiotic prophylaxis and/or bladder management, are considered by only about one half of the centers. Although these strategies are unlikely to resolve VUR, they may reduce the frequency of (febrile) UTIs.^{4,8}

5 | LIMITATIONS AND CONCLUSIONS

This survey has some limitations. First, the clinical definition of symptomatic VUR used is controversial, considering the broader definitions used by some studies, which also include other aspects, such as urinary tract dilatation, renal scarring and/or pathological kidney biopsy findings. Second, although the response rate was relatively high (40/68 centers [60%]), most of the participating centers are classified as medium-volume KTx centers performing ≤ 10 pediatric KTx per year. Therefore, selection bias due to limited enrolment of high-volume KTx centers cannot be excluded. Additionally, there might have also been a selection bias due to different center-specific demographics, such as patient characteristics, which were not obtained in the present survey. Third, the results should be interpreted cautiously, because only European pediatric KTx centers were included. Therefore, the results may not reflect the practice patterns of other geographical regions, limiting the generalizability of the collected data.

In conclusion, although the transplantation procedure is surprisingly standardized, the following critical inconsistencies in certain areas of native and allograft VUR management need to be addressed by further studies: mode and technique of ureteral reimplantation, management strategies for ureteral reimplantation in bladder anomalies, use and timing of antibiotic prophylaxis, criteria for ureteral stent removal, and clinical impact and criteria for the management of native and allograft VUR in pediatric KTx. These data could then be translated into consensus guidelines for a more standardized clinical decision making and better patient care.

AUTHOR CONTRIBUTIONS

MZ, TL, and MW designed the survey. MZ, MW, and KB collected and analyzed the data and drafted the manuscript. KB performed the statistical analysis. MZ and KB designed the figures and tables, and summarized the methods and results. TL, BT, and SN made important intellectual contributions to the design of this study and critically revised the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests.

DATA AVAILABILITY STATEMENT

All data relevant to this study are included in the article or uploaded as Appendices S1–S11.

ETHICS STATEMENT

This survey does not include any studies with human or animal studies performed by any of the authors.

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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

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