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THE NECESSITY OF VOIDING CYSTOURETHROGRAM FOR THE EVALUATION OF RECIPIENT CANDIDATES IN ADULT RENAL TRANSPLANTATION

M. Sarier¹, M. Callioglu², Yu. Yuksel²

¹ Istinye University, Istanbul, Turkey

² Medical Park Hospital, Antalya, Turkey

Objective. While international guidelines necessitate Voiding Cystourethrogram (VCUG) for pediatric patients, it is unnecessary for the evaluation of adult patients without urological disorders as renal transplant candidates. The objective of this study was to evaluate the results of adult candidates who underwent VCUG before transplantation and to demonstrate the necessity for this imaging. **Methods.** A retrospective study of the data of 1265 adult candidates who underwent VCUG before transplantation at our center, was undertaken. VUR, the presence of Post-voiding residual urine (PVR) (>100 ml), Low bladder capacity (LBC) (<100 ml), and urethral pathologies were evaluated with VCUG. **Results.** The mean age was 42.3 ± 1.3 . The mean dialysis period was 27.8 ± 4.2 months. According to the VCUG results, 19.2% of the patients had pathological findings. On the other hand, the rate of urological disorders was only 5.1%, according to end-stage renal disease (ESRD) etiologies. VCUG outcomes indicated bilateral high-grade reflux in native kidneys in 4.4% (n = 56) of the candidates, unilateral high-grade reflux in 4.1% (n = 52), bilateral low grade reflux in 2.1% (n = 26), unilateral low-grade reflux in 2.4% (n = 30), and reflux in rejected transplanted kidney in 2.3% (n = 29). In addition, significant LBC was noted in 4.8% (n = 61), significant PVR in 1.1% (n = 14), and urethral stricture in 0.5% (n = 6) of the candidates. **Conclusion.** VCUG should be considered as a part of routine evaluation in adult renal transplant recipient candidates as well as in pediatric candidates, even if their ESRD etiologies are not due to urological disorders.

Keywords: renal transplantation; transplant candidates; vesicoureteral reflux; voiding cystourethrogram.

НЕОБХОДИМОСТЬ ПРОВЕДЕНИЯ МИКЦИОННОЙ ЦИСТОУРЕТРОГРАФИИ ДЛЯ ОЦЕНКИ ВЗРОСЛЫХ КАНДИДАТОВ НА ТРАНСПЛАНТАЦИЮ ПОЧКИ

M. Сарьер¹, M. Каллиоглу², Ю. Юксел²

¹ Университет Истини, Стамбул, Турция

² Больница Медикал Парк, Анталья, Турция

В то время как во всех международных протоколах при подготовке к трансплантации почки в педиатрической практике потенциальным реципиентам предписано обязательно проводить микционную цистоуретрографию (МЦУГ), нет никаких указаний относительно этого перед проведением трансплантации почки взрослым пациентам без урологических нарушений. **Цель:** оценить результативность МЦУГ, проведенной перед трансплантацией взрослым пациентам, и необходимость использования этого метода визуализации перед операцией. **Материалы и методы.** Было проведено ретроспективное исследование данных 1265 взрослых реципиентов почки, которым выполняли МЦУГ перед трансплантацией в нашем центре. С помощью МЦУГ оценивали наличие и степень пузырно-мочеточникового рефлюкса (ПМР), остаточный объем мочи после мочеиспускания (PVR) (>100 мл), емкость мочевого пузыря (низкая емкость мочевого пузыря <100 мл) и патологию мочеиспускательного канала. **Результаты.** Средний возраст пациентов составил $42,3 \pm 1,3$ года. В среднем пациенты находились на диализе $27,8 \pm 4,2$ месяца. По результатам МЦУГ у 19,2% пациентов были обнаружены патологические изменения. С другой стороны, урологические нарушения были причиной терминальной почечной недостаточности (ТПН) всего в 5,1% случаев. По результатам МЦУГ были выявлены двусторонний ПМР тяжелой степени в нативных почках у 4,4% (n = 56) потенциальных реципиентов, односторонний ПМР тяжелой степени –

For correspondence: Mehmet Sarier. Medical Park Hospital Department of Urology Muratpaşa, Antalya, Turkey. Tel. +905333324960. Fax: +902423143030. E-mail: drsarier@gmail.com

у 4,1% (n = 52), двусторонний ПМП легкой степени – в 2,1% (n = 26), односторонний ПМП легкой степени тяжести – у 2,4% (n = 30) и рефлюкс в трансплантат почки при его отторжении – у 2,3% (n = 29). Кроме того, обнаружено значительное снижение емкости мочевого пузыря у 4,8% (n = 61), значительное снижение PVR – у 1,1% (n = 14) и стриктура уретры – у 0,5% (n = 6) потенциальных реципиентов. **Заключение.** Следует рассмотреть целесообразность включения в повседневную клиническую практику МЦУГ для оценки функционального состояния мочевыводящих путей взрослых потенциальных реципиентов перед трансплантацией почки, а также реципиентов-детей, даже если ТПН не обусловлена урологическими заболеваниями.

Ключевые слова: трансплантация почки, кандидат на трансплантацию; пузырьно-мочеточниковый рефлюкс; цистоуретрография.

ABBREVIATIONS

BOO – Bladder Outlet Obstruction
BPH – Benign Prostate Hyperplasia
ESRD – End Stage Renal Disease
LBC – Low Bladder Capacity
PVR – Post-Void Residual Urine Volume
TURP – Transurethral Resection of the Prostate
VCUG – Voiding Cystourethrogram
VUR – Vesico Ureteral Reflux
UTI – Urinary Tract Infection

INTRODUCTION

Today, renal transplantation is considered the optimal treatment for patients with end-stage renal disease (ESRD), providing favorable physical, socioeconomic, and psychological results [1]. Accurate assessment of recipient candidates is of paramount importance to the success of renal transplantation. Therefore, candidates are subjected to many examinations and evaluations before transplantation. As a part of urologic examinations, voiding cystourethrogram (VCUG) is an important radiologic test that provides information about vesicoureteral reflux (VUR) and anatomical evaluation of the lower urinary system, as well as information about bladder functions. But the use of VCUG in the assessment of candidates is controversial. Urologic disorders account for up to 60% of the etiology of ESRD in pediatric patients [2]. In adult patients, urologic disorders account for 1.4% to 5% of the factors playing a role in the etiology of ESRD [3]. While international guidelines require VCUG in the evaluation of pediatric kidney transplant candidates, VCUG is not necessary in adult patients except for those with a medical history of genitourinary abnormalities [4, 5]. The objective of this study is to evaluate the results of adult candidates who underwent VCUG before transplant and to demonstrate the necessity of this imaging.

MATERIALS & METHODS

In this retrospective study, patients who underwent renal transplantation in Medical Park Hospital Complex Antalya Turkey between November 2008 and October 2011 were evaluated. Pediatric renal transplant patients under 17 were excluded. Of the 1,441 adult patients

who underwent kidney transplant, the completed data of 1,265 patients who had undergone VCUG before transplant were studied. The study analyzed patients' demographic data; the urologic etiology of ESRD, such as the presence of obstructive or reflux uropathy; dialysis duration; and VCUG findings. VUR, the presence of post-void residual urine (PVR), low bladder capacity (LBC), and urethral pathologies were assessed with VCUG. Grading of vesicoureteral reflux is based on the International Reflux Study Committee Scale [6].

In VUR, Grades I and II were considered low-grade reflux; Grades III, IV, and V were considered high-grade reflux. Values less than 100 cc were considered significant in LBC, and values greater than 100 cc were considered significant in PVR.

The study was approved by the local ethics committee and written informed consent was received from all candidates. All statistical analyses were performed using the SPSS statistical software (SPSS for Windows version 16.0 SPSS Inc., Chicago IL, USA). Continuous variables were presented as mean \pm standard deviation.

RESULTS

The data of 1,265 patients who underwent VCUG were examined. The mean age was 42.3 ± 1.3 years and male-to-female ratio was 2.2. The mean dialysis duration was 27.8 ± 4.2 months. According to VCUG outcomes, 19.2% (n = 243) of patients had abnormal pathological findings in the pre-transplantation assessment. Urologic disorders were involved in the etiology of ESRD in 5.1% (n = 65) of the patients. VCUG outcomes indicated bilateral high-grade reflux in native kidneys in 4.4% (n = 56) of the patients, unilateral high-grade reflux in 4.1% (n = 52), bilateral low grade reflux in 2.1% (n = 26), unilateral low-grade reflux in 2.4% (n = 30), and reflux in rejected transplanted kidney in 2.3% (n = 29). In addition, significant LBC was noted in 4.8% (n = 61), significant PVR in 1.1% (n = 14), and urethral stricture in 0.5% (n = 6) of the candidates (Table).

DISCUSSION

Voiding cystourethrogram (VCUG), also called a micturating cystourethrography, is a fluoroscopic study of the lower urinary tract in which contrast is introdu-

Table
**Distribution of abnormal findings determined
 by VCUG**

Type of abnormality	Prevalence
Bilateral High-Grade VUR in Native Kidneys	4.4%
Unilateral High-Grade VUR	4.1%
Bilateral Low-Grade VUR	2.1%
Unilateral Low-Grade VUR	2.4%
VUR in rejected TX Kidney	2.3%
Low Bladder Capacity	4.8%
Post-Void Residual Urine	1.1%
Urethral Stricture	0.5%

ced into the bladder via a catheter. The most important feature distinguishing VCUG from the other imaging modalities is that it is an interactive test. VCUG shows not only the anatomic plane of the low urinary tract and the presence of VUR, but like a urodynamic test, it can demonstrate filling phase and capacity of the bladder as well as the voiding phase and voiding ability of the patient. Thus, it can show whether urodynamic investigation is necessary. VCUG is unnecessary in adult renal transplant candidates unless there is a genitourinary abnormality present, as shown by two studies in the 333 and 517 case series conducted more than two decades ago [7, 8]. Among these studies, Glazier et al. found significant abnormalities of only 2.5% in VCUG performed at pretransplant evaluation [8]. Our study, however, showed abnormalities of 19.2% with VCUG. Similarly, Kabler et al. found 25% abnormalities with VCUG in candidates before transplantation [9]. Ultimately, VCUG is a diagnostic imaging method and 19.2% and 25% abnormalities found in our study and in the mentioned study are significant in showing significance of a test. A solution to these disparities needs to be found to minimize complications that may develop after transplantation.

Low bladder capacity is directly correlated with dialysis duration. It is the most important symptom of a dysfunctioning bladder, which develops due to decreased diuresis. Men are at greater risk of bladder dysfunctions [10]. Storage dysfunction becomes prominent one year after dialysis, especially in male patients over 50 [11]. Fortunately, reduction in bladder capacity is reversible and transplant generally allows restoration of bladder maximal output, normal bladder capacity, and compliance. Studies have shown that low bladder capacity dramatically increases within one year after transplantation [12, 13]. In patients with low bladder capacity, maximum detrusor pressure may require VUR in the transplanted kidney. The risk for VUR in the transplanted kidney within one year was significantly higher in patients with a low bladder capacity than those with a normal capacity [14]. Independent of immunological status, graft survival is significantly lower in patients with a severe bladder

dysfunction such as a decreased maximal detrusor capacity less than 100 mL compared to other patients [15].

In conclusion, it may be risky to merely wait for patients with a low bladder capacity to return to normal. Many patients can be managed with anticholinergic drugs and intermittent self-catheterization, but some patients may require bladder augmentation or urinary diversion before transplant. It should be kept in mind that morbidity is lower and quality of life is better with intermittent self-catheterization compared with surgical approaches [15]. In a study by Song et al. evaluating pre-transplant VCUG outcomes, the rate of less than 100 mL bladder capacity was 14.1% in patients with a mean dialysis duration of 59 months [16] our study found the prevalence of low bladder capacity at 4.8% with a mean dialysis duration of 27 months. We think that the most important factor causing this difference between results of the studies was dialysis duration. It would be reasonable to perform VCUG to determine bladder capacity well before transplant, especially in patients with a dialysis duration longer than one year.

VUR is a prevalent disease, and VCUG is the gold standard in its diagnosis. The prevalence of VUR in the population is higher in younger patients and decreases with age, although VUR is seen in 5% of sexually active women in the non-transplanted population [17]. It is difficult to determine the exact incidence of vesicoureteral reflux in patients undergoing renal transplantation because VCUG is not performed routinely in clinical practice. It should be remembered that these patients may be asymptomatic for VUR. VUR symptoms such as frequently repeating urinary tract infection (UTI) may be suppressed, especially in anuric and oliguric patients who receive dialysis. Immunosuppressive treatments with increased diuresis after transplant may cause persistent infection of the native kidneys due to VUR, leading to morbid or mortal outcomes [9]. International guidelines recommend that consideration be given to the need for native nephrectomy pretransplant or perioperatively in selected patients to reduce the risk of post-transplant complications [18]. In our study, VUR was found in 15% of the candidates, according to VCUG results. Similarly, Song et al. found VUR of 17.5% [16]. Similar results from both studies indicate that, unlike low bladder capacity, the prevalence of VUR is not correlated with dialysis duration in these patients.

PVR is an important pathological finding that can be detected with VCUG. Unlike low bladder capacity, high PVR is not expected during post-transplant recovery. Complications that may develop due to high levels of PVR will persist after transplantation, which may directly affect graft survival. Dysfunction of the bladder that causes long-term high intravesical pressure and significant post-voiding residual volume can cause VUR in the transplanted kidney and can pose a risk to graft function. Consequently, it is advantageous to diagnose these disor-

ders as soon as possible, ideally prior to transplantation [19]. Studies conducted in the non-transplanted patients have reported a direct correlation between high PVR and UTI [20, 21]. UTI is the most common cause of post-transplant mortality and morbidity, affecting the duration of hospitalization [22]. Therefore, it is important to seek and plan treatment for the underlying causes of PVR. It should be remembered that UTI, which results most commonly from neurogenic bladder or bladder outlet obstruction (BOO), may be suppressed in anuric and oliguric patients who receive dialysis. Initiation of intermittent self-catheterization in a neurogenic bladder immediately after transplant is a highly efficient way to protect the transplanted kidney against infection and VUR. Another cause of PVR is BOO, which develops due to benign prostate hyperplasia (BPH). It should be kept in mind that male kidney transplant candidates over 50 are at a higher risk for BOO [23]. However, surgical treatment before transplantation is not recommended in patients undergoing dialysis. Because anuria will persist following the transurethral resection of prostate (TURP), these patients will be at high risk for development of bladder neck contracture in the postoperative period [24]. In addition to the initiation of alpha blockers in patients with severe lower urinary tract symptoms, it was shown that TURP or transurethral incision of the prostate (TUIP) operations can be performed safely in the first month after transplantation [23].

Another remarkable finding of VCUG was a urethral stricture in 0.5% of the patients. Urethral stricture may be seen with LBC in patients who receive dialysis for a long time [25]. As in patients with BOO and ESRD, symptoms may also be masked in these patients; diagnosis can be established during VCUG. In patients considered to have urethral stricture as a result of strain or failure of urethral catheterization at the anterior or bulbar urethra during VCUG the stricture can be restored by performing an internal urethrotomy before transplantation. This will likely prevent a surprise for the transplant team.

VCUG is a minimally invasive imaging method. Complications that may occur with this method should be taken into account. It should be remembered that oliguric and anuric patients are more likely to develop UTI after catheterization of the bladder. A resulting infection can cause postponement of the kidney transplantation, which may result in serious stress to the candidate. There is no sufficient data in the literature regarding a UTI resulting from a VCUG performed in candidates before transplantation. In a study investigating VUR in non-transplanted pediatric patients, UTI was found in 16.9% of children one week after VCUG was performed [26]. Prophylactic antibiotics given before VCUG may reduce this rate to a value as low as 1.7% [27]. Therefore, prophylactic antibiotics should be considered in candidates before VCUG in cases of infection risk.

This study has some limitations. Follow-up outcomes of patients with positive VCUG findings were not mentioned in this study.

CONCLUSION

VCUG should be considered a part of routine evaluation in adult kidney recipient candidates even if the etiology of ESRD is not related to urologic disorders. Candidates who received dialysis for longer than one year and male candidates over 50 should be given a routine assessment with VCUG. Pathologies that may directly affect graft survival after transplant can be diagnosed with VCUG.

The study were approved by Medical Park Hospital Local Ethics Committee (Protocol number: 2019/013).

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The authors declare no conflict of interest.

Авторы заявляют об отсутствии конфликта интересов.

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