



Research Article

Long-Term Pretransplant Dialysis, Bladder Capacity and Vesicoureteral Reflux in Transplanted Kidney

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Abstract

Background: Patients with end-stage renal disease often undergo long-term dialysis before kidney transplantation resulting in severe atrophy of the bladder and decline in its capacity as a result of prolonged disuse and they might still be at risk of developing urinary complications as a result of difficulties in ureteral re-implantation. Aim of this study is to investigate the correlation between bladder capacity, duration of dialysis and vesicoureteral reflux (VUR) in transplanted kidneys.

Materials and Methods From 2017 to 2021, 104 patients were enrolled 8-16 months after kidney transplantation. All patients underwent Voiding Cystourethrography (VCUG), grayscale Ultrasound (US) and Contrast-Enhanced Voiding Urosonography (ceVUS).

Results The 104 patients were divided into three groups based on the duration of pre-transplant hemodialysis: group A had undergone hemodialysis for <5 years, group B for 5-10 years and group C >10 years. In each group, bladder capacity was calculated using grayscale US, ceVUS and VCUG: in group A, mean bladder capacity was 300 ml (range 250-500 ml), in group B 150 ml (range 30-500 ml) and in group C 120 ml (range 30-450). VUR diagnosed with ceVUS was detected more frequently in group B and C (88% and 91% of cases, respectively) than in group A (68 %)

Conclusion Bladder capacity gradually decreased as the pretransplant duration of dialysis increased, and that the incidence of VUR was higher in patients with longer pretransplant dialysis duration and lower bladder capacity.

Keywords: Bladder capacity; CEVUS; Transplanted kidney; Urinary tract; VCUG; Vesicoureteral reflux

Introduction

Patients with end-stage renal disease often undergo long-term dialysis before kidney transplantation resulting in severe atrophy of the bladder and decline in its capacity as a result of prolonged disuse [1-4]. However, after kidney transplantation, the bladder usually undergoes hypertrophy and recovers its normal function. Nevertheless, patients with atrophic bladders might still be at risk of developing urinary complications as a result of difficulties in ureteral reimplantation [1,2,4-7]. Today, ureteroneocystostomy is most commonly carried out using the Lich-Gregoir extravesical tunneling technique. It includes exposure of about 3 cm of the

mucous layer after incision of the muscular layer, anastomosis connecting the ureter to the mucosa and partial closure of the muscular layer in order to create a submucosal tunnel [8,9]. However, reduced bladder size and atrophy of the thin detrusor muscle makes it difficult to create a submucosal tunnel of adequate length to prevent Vesicoureteral Reflux (VUR) or urinary leakage [4-7]. VUR is most frequent in patients with a low residual urinary output and a defunctionalized bladder; another risk factor of VUR is high bladder pressure due to reduced bladder capacity [10,11]. VUR increases the risk of Urinary Tract Infection (UTI) or Pyelonephritis (PNA) leading to reflux nephropathy [12]. Aim of this study was to investigate the correlation between bladder capacity, duration of dialysis and vesicoureteral reflux in transplanted kidneys.

Materials and Methods

Patient population

From 2017 to 2021, 104 patients were enrolled 8-16 months after kidney transplantation (36 females and 69 males); mean age 64 (range: 42-78). Mean duration of pre-transplant hemodialysis was 7 years.

Inclusion criteria were:

- Duration of pretransplant hemodialysis from 1 to 10 years
- Ureteral implantation carried out using the Lich-Gregoir extravesical technique without stenting
- The patient had received antibiotic prophylaxis
- Exclusion criteria were:
- Kidney transplantation combined with other organs (pancreas, liver)
- Previous kidney transplantation

Imaging acquisition and interpretation

All patients underwent retrograde cystourethrography performed with X-ray equipment (Siregraph CF, Siemens); images were saved in the course of fluoroscopy. During filling (using a Foley catheter), multiple spot images in the antero-posterior, oblique, and lateral positions were obtained as well as urethral images during voiding. Contrast agent 100 ml (Iopamiro 370 mg/ml; Bracco, Milan) was administered using a transurethral bladder catheter followed by ≤ 150 ml sterile saline solution. Mean duration of Voiding Cystourethrogram (VCUG) examination was 20 minutes (range: 15-25 minutes). Bladder shape and contours, bladder volume, filling defects or other anomalies, onset of reflux during filling and degree of reflux were evaluated. Maximum bladder volume was calculated using the formula: volume = length \times width \times height $\times 0.52$ (Figure 1).

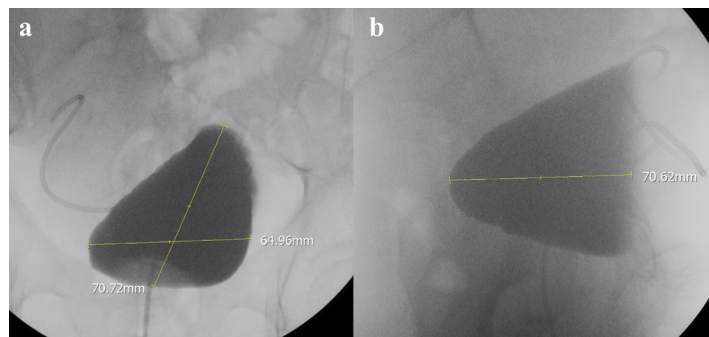


Figure1: Maximum bladder capacity measured at VCUG obtained in antero-posterior (a) and latero-lateral view (b).

In the second stage, the patient initiated voiding. X-rays were taken to evaluate the urethra during urination and to detect the presence of VUR. Radiograms were evaluated by two expert radiologists following a double-blind procedure. All Contrast-Enhanced Voiding Urosonography (ceVUS) examinations were performed by one radiologist with a long-standing expertise in Ultrasonography (US), who was blinded to the VCUG results. US equipment was Samsung RS80A with Prestige using a 3.5-5 MHz curvilinear probe. US was performed after adequate hydration of the patient. Contrast agent, 0.5 ml SonoVue (Bracco, Milan) diluted in 250 ml 0.9 % saline solution, was slowly instilled using a transurethral bladder catheter under US control [10]. Mean duration of ceVUS examination was 15 minutes (range: 10-20 minutes); images were saved both as single images and as video clips. During B-mode US examination, bladder volume (Figure 2), wall thickness, renal size, antero-posterior diameter of the renal pelvis and presence of focal and non-focal pathologies were evaluated. Subsequently, ceVUS was performed after administration of intravesical contrast agent diluted in normal sterile saline with repeated imaging of the bladder and kidneys during and after bladder filling and while voiding. In this phase, maximum bladder volume and the presence of VUR were evaluated (Figure 3). Microbiological and urine culture examinations were carried out to identify and characterize a possible UTI. VCUG and ceVUS were performed after antibiotic therapy (8-10 days after the last UTI). All patients underwent VCUG, and then ceVUS after 3-10 days.

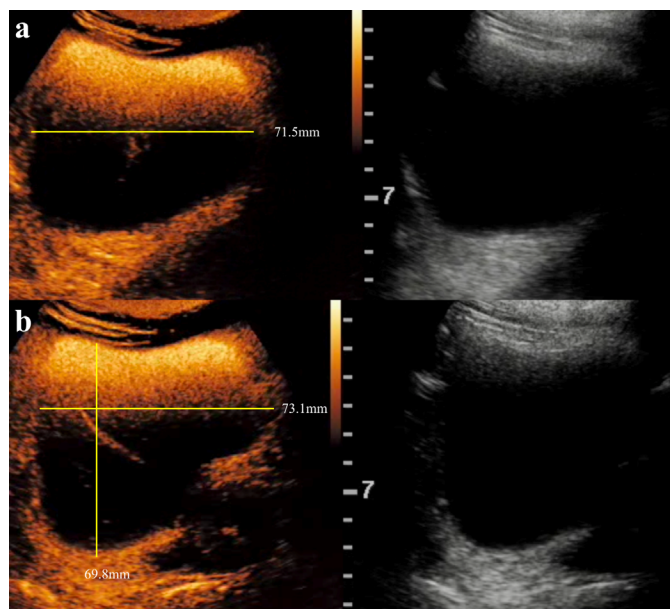


Figure 2: Maximum bladder capacity measured at ceVUS obtained in transverse (a) and longitudinal view (b).

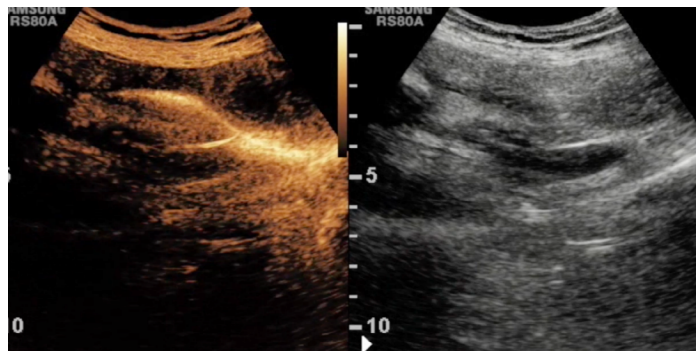


Figure 3: In the course of ceVUS, the passage of contrast agent into the ureter is observed during Voiding Strain (VUR).

Statistical Analysis

Continuous variables were reported as means and ranges. Categorical variables were reported as numbers and percentages. No missing data were reported in the investigated variables. Fisher’s exact test was used for comparisons of categorical variables. Linear regression was used to analyze the correlation between the duration of preoperative dialysis and bladder capacity. Pearson’s r coefficient was estimated with this intent. A value of 1 indicates perfect linear correlation between the two variables. Variables with

a p-value <0.05 were considered statistically significant. We used the SPSS statistical package version 24.0 (SPSS Inc., Chicago, IL, USA). Agreement between grayscale US, VCUG and ceVUS was calculated using the Cohen’s Kappa method. A kappa coefficient value <0 indicates no agreement, 0-0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 substantial, and 0.81-1.00 almost perfect agreement.

Results

No clinically significant contrast agent-related side effects were experienced by the patients. Both examinations and contrast agents were well tolerated. Inter-observer variability in the evaluation of bladder volume occurred in less than 3% of cases. The 104 patients were divided into three groups based on the duration of pre-transplant hemodialysis: group A had undergone hemodialysis for <5 years, group B for 5-10 years and group C >10 years. In each group, bladder capacity was calculated using grayscale US, ceVUS and VCUG revealing a significant difference between the three groups (p <0.001). In group A, mean bladder capacity was 300 ml (range 250-500 ml), in group B 150 ml (range 30-500 ml) and in group C 120 ml (range 30-450). VUR diagnosed with ceVUS was detected more frequently in group B and C (88% and 91% of cases, respectively) than in group A (68 %) (Table 1).

Duration of dialysis (years)	Patients	Mean bladder capacity (ml)	VUR rate
< 5	38	300 ml (250-500 ml)	68 % (25 patients)
5-10	56	150 ml (30-500 ml)	88 % (49 patients)
> 10	10	120 ml (30-450 ml)	91% (9 patients)

Table 1: Duration of pretransplant dialysis, bladder capacity, VUR rate (diagnosed with VCUG).

In 96/104patients there was agreement between grayscale US, ceVUS and VCUG in the measurement of maximum bladder capacity (92 %), whereas there was no agreement in 8 patients (8 %). Agreement between the three methods was considered when the bladder measurement differed by less than 15%. All 8 patients in whom the three methods were in disagreement, presented a maximum bladder capacity greater than 300 ml. UTI was detected in 70/104 patients (63%), in 13/70 (19%) caused by Klesbiella, in 35/70 (50%) by Escherichia coli, in 7/70 (10%) by Enterococcus, in 5/70 (7%) by BK virus (BKV) and in 10/70 (14%) by Candida Albicans. No correlation was found between bladder capacity and the incidence of UTI, and between UTI and the duration of the dialysis. Acute PNA was detected in 7 patients, but none of these presented specific signs at US imaging.

Discussion

In this study, bladder capacity was evaluated and correlation between bladder size, pretransplant dialysis duration and Vesicoureteral Reflux (VUR) was found; bladder capacity

gradually decreased as pretransplant duration of dialysis increased. Incidence of VUR was higher in patients with longer pretransplant duration of dialysis and lower bladder capacity, a fact which could be explained by the difficulty in creating an adequately long submucosal tunnel to prevent VUR in an atrophic and defunctionalized bladder [3]. Our results are in agreement with those of the literature. In their study, Hotta et al found that bladder atrophy in renal transplant recipients after long-term dialysis was associated with a higher risk of urological complications (UCs) and that the rate of bladder atrophy (bladder capacity <50 ml) increased in patients after >10 years of dialysis [1].

Chen et al, [13] found that bladder capacity and bladder compliance decreased with longer duration of dialysis, and that anuria contributed to this reduction. Inoue et al [3] and Drudi et al [7] demonstrated that bladder capacity decreased because of long-term dialysis and that a small bladder may increase the risk of VUR. Martin et al. [5] compared 20 recipients having received long-term dialysis (>15 years) with 20 control recipients (dialysis

<5 years). Pretransplant bladder capacity of long-term dialysis patients was significantly smaller than that of the control group. The incidence of UC in long-term dialysis patients was also higher than in controls. Wu et al. [4] compared the incidence of UC in 41 kidney recipients having received long-term dialysis (>10 years) with 31 recipients who had not received pretransplant dialysis. They found no difference in the incidence of UC between the two groups, but bladder capacity was not evaluated. Other studies report that a pretransplant atrophic bladder did not impair graft function, as bladder capacity improved after transplantation [14,15]. In the present study, the patients (104) were divided into 3 groups based on the duration of dialysis.

Group A had undergone hemodialysis for <5 years, group B for 5-10 years and group C >10 years. In each group, bladder capacity was calculated using grayscale US, ceVUS and VCUG revealing a significant difference between the three groups ($p < 0.001$): in group A mean bladder capacity was 300 ml, in group B 150 ml and in group C 120 ml. In 96 cases (92 %), there was agreement in the measurement of maximum bladder capacity between grayscale US, ceVUS and VCUG, whereas in 8 cases (8 %) there was no agreement. This agreement demonstrated that all three techniques are useful for measuring bladder volume although grayscale US should be preferred being radiation-free as well as inexpensive and widely available. Disagreement was found in all those patients who presented maximum bladder capacity >300 ml. This can be explained by a practical difficulty in measuring a very distended bladder due to two-dimensional projection bias and to the flattening of the walls, so that the bladder does not assume a spherical shape, thus making the calculation less accurate. Another reason for this disagreement is probably the difficulty in obtaining a panoramic view of the entire bladder, especially at US imaging. As to VUR, in a previous study the Authors demonstrated the efficacy of ceVUS in determining the presence and degree of VUR obtaining results comparable with the those obtained using the traditional X-ray technique, VCUG, concluding that ceVUS should be carried out as a first-line examination in transplant patients presenting with reflux symptoms. If ceVUS outcome is negative, VCUG should be performed [7].

Another important aspect is the presence of UTI which is a typical complication occurring in transplanted patients. It is considered the most important risk factor for weak graft function, morbidity and mortality [16-18]. Among the 104 patients included in this study, UTI was found in 70 patients caused by *Klebsiella*, *Escherichia coli*, *Enterococcus*, *BKV* and *Candida Albicans*. All patients were monitored for the presence of Cytomegalovirus, but only those presenting with high concentrations received treatment. The elevated number of UTIs is caused by immunosuppressive therapy [17,18]. No correlation was found between bladder capacity and the incidence of UTI, nor between UTI and pretransplant dialysis duration. VUR damages the urinary tract by causing bacterial infections that may easily spread from the lower to the upper urinary tract also because the ureter of a transplanted kidney

is shorter than that of a native kidney, thus resulting in recurrent parenchymal infections and possibly further complications. The pathogens most frequently encountered in this study were *Klebsiella* and *Escherichia coli*, but acute PNA was detected in 7 patients. Acute PNA is a major infectious complication in graft recipients with a cumulative incidence of 19%-23% reported in the literature [12]. US identified no particularly significant signs of PNA, but only a slight structural alteration of the renal cortex in some patients.

Conclusion

In conclusion, this preliminary experience showed that bladder capacity gradually decreased as the pretransplant duration of dialysis increased, and that the incidence of VUR was higher in patients with longer pretransplant dialysis duration and lower bladder capacity. All techniques used to measure bladder capacity are useful, but grayscale US should be preferred being radiation-free as well as inexpensive and widely available.

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