ORIGINAL RESEARCH

Utilization of Pretransplant Cystography and Hydrodistention Among Anuric Patients on Renal Replacement Therapy and Its Impact on Cost and Timing of Transplantation

Maria Hilda Fe R. Hipolito, MD and Frances Monette P. Bragais, MD, FPUA

Department of Urology, National Kidney and Transplant Institute

Objective: To describe utilization of pretransplant cystography and hydrodistention among anuric end stage renal disease patients (ESRD) on renal replacement therapy (RRT) and its impact on cost and timing of transplantation.
Methods: A chart review was done on all anuric ESRD pretransplant patients on renal replacement therapy who underwent cystography and hydrodistention from 2014 to 2019. The authors analyzed patient demographics, post-transplant outcomes, process indicators and costs incurred due to cystography and hydrodistention.
Results: A total of 151 patients were included in the study. There was female predominance (86, 57%) with a median age of 32 (range 18-61) years. Majority of the patients underwent hemodialysis (144, 95%). Glomerulonephritis was the prevailing etiology of ESRD (119, 79%). Majority had normal bladder capacity (107, 71.5%), while 44 (29%) patients had small bladder capacity who subsequently underwent hydrodistention. There is a moderately negative correlation between bladder capacity and duration of dialysis and anuria. Hydrodistention did not significantly increase duration from diagnosis to kidney transplant (4.2 vs 3.5 months; p = .083). Median cost of cystography was Php 4377 (range 1978 – 5282) and the average total cost incurred per patient due to hydrodistention was Php 643.53.
Conclusion: Longer duration of RRT and anuria yields to lesser bladder capacity. Cystography is recommended in ESRD patients who are anuric for at least three years. Hydrodistention does not significantly prolong duration of diagnosis to kidney transplant.

Keywords: Kidney transplant, bladder capacity, cystography, hydrodistention

Introduction

According to KDIGO, kidney failure is defined as irreversible loss of kidney function defined as glomerular function rate of <15 mL/min/1.73m^2.[1] Renal transplantation is the treatment of choice and is known to provide improved quality of life and better long survival versus dialysis.[2]

Urologic evaluation is necessary prior to kidney transplantation. Successful outcomes require a comprehensive preoperative assessment of the genitourinary tract to identify a continent reservoir and establish a urinary tract free of infection, urolithiasis, malignancy, anatomic malformations and dysfunctional voiding. Effective evaluation will especially benefit patients who would need

pretransplant urologic intervention to decrease overall morbidity or graft loss posttransplant.[3]

Reduction in bladder capacity and compliance are observed in anuric end stage renal disease (ESRD) patients due to loss of the normal physiological distention of the bladder. However, due to unclear mechanism, the defunctionalized bladder regains its capacity and compliance after renal transplantation when urine output returns to normal.[4]

In NKTI, it has been a practice that all service pretransplant patients who are anuric be subjected to cystography for determination of bladder capacity. Those patients with bladder capacity of <150cc are then subjected to hydrodistention until one reaches at least 150cc. However, these practices have been observed to delay transplantation and be a source of additional costs.

This study aimed to describe utilization of pretransplant cystography and hydrodistention among anuric ESRD patients on renal replacement therapy (RRT) and its impact on cost and timing of transplantation.

Specifically, the authors also aimed to describe anuric ESRD patients' demographics (including etiology of ESRD, duration and mode of RRT, cystography findings particularly bladder capacity and presence of abnormalities or defects), determine proportion of patients with small bladder capacity defined as <150cc, determine process indicators such as number of hydrodistention procedures prior to transplant and number of months from anuric ESRD to kidney transplant, determine the direct costs incurred due to hydrodistention and cystography and lastly, to determine transplantation outcomes.

Methods

A retrospective chart review was done on all anuric ESRD pretransplant patients from January 1, 2014 to December 31, 2019. All patients who underwent cystography and hydrodistention were included in the study. Data were collected from a total of 151 consecutive patients. Parameters gathered included the following: patient demographics, etiology of ESRD, mode of RRT, duration of RRT, cystography findings such as bladder capacity and other abnormalities including presence or absence of vesicoureteral reflux, bladder diverticulum, urethral stricture, bladder wall irregularities and residual volume. Process indicators particularly number of hydrodistention procedures prior to transplant and number of months from anuric ESRD to kidney transplant were determined as well as direct cost incurred due to hydrodistention and cystography. Post-transplant outcomes were also described.

Standard Procedure for Cystography

Static cystography was performed with the patient awake and in supine position. A foley catheter (Fr 10) was carefully inserted to avoid trauma. Initially, a plain radiograph was performed then the bladder was passively and slowly filled with diluted contrast until a strong urge to void was perceived. Amount of contrast instilled was determined and another radiographic shot was taken to document full bladder capacity. After voiding, a post-drainage film was performed to complete the study.

Standard Procedure for Hydrodistention

Hydrodistention was performed on an outpatient basis. The patient was awake and positioned supine. A foley catheter (Fr. 10) was then inserted followed by slow instillation of saline into the bladder until patient had a strong urge to void. This procedure was done repeatedly on different occasions approximately two to three times a week until patient reached at least 150cc bladder capacity.

Statistical Analysis

Descriptive statistics was used to summarize the general and clinical characteristics of the participants. Frequency and proportion were used for nominal variables, median and range for ordinal variables, and mean and standard deviation for interval/ratio variables. Independent T-test and Mann-Whitney U test were used to determine the difference of mean and median between groups, respectively. All valid data were included in the analysis. Missing variables were neither replaced nor estimated. Null hypothesis was rejected at 0.05α-level of significance. STATA 15.0 was used for data analysis.

Ethical Considerations

Personal information of patients included in the study were accessible only to the principal investigator, co-author and research assistant. A number or code was assigned to each patient after all pertinent data had been gathered. This study was conducted in accordance with ICH-GCP principles and guidelines and was commenced only upon approval by the NKTI-REC.

Results

A total of 151 patients were included in the study, with a median age of 32 (range 18-61) years. Eighty-six (57%) patients were female and 65 (43%) were male. Majority underwent hemodialysis (144, 95%) prior transplant. Glomerulonephritis (119, 79%) was the prevailing etiology of ESRD followed by hypertensive nephrosclerosis (20, 13.2%), diabetic kidney disease (8, 5.3%), NSAID nephropathy (2, 1.32%) and Uric Acid Nephropathy (2, 1.32%) (Table 1). Majority of patients had normal bladder capacity (107, 70.9%) while 44 patients had small bladder capacity (29.1%) who subsequently underwent hydrodistention. The most common urinary tract abnormalities determined using cystography were vesicoureteral reflux (28, 19%). Other findings are as follows: bladder diverticulum (7, 4.7%), urethral stricture disease (1, 0.66%), irregular bladder wall (1, 0.66%), small outpouchings (1, 0.66%) and cystocoele (1, 0.66%) (Table 1).

Table 2 shows duration of dialysis and anuria in patients with normal bladder capacity compared to those patients with small bladder capacity. Among patients with normal bladder capacity, mean duration of dialysis is 24 months which is shorter compared to those with small bladder capacity with a mean of 42 months. Duration of anuria is also noted to be shorter in patients with normal bladder capacity with a mean of 15 months as opposed to a mean of 29 months in those with small bladder capacity.

Table 3 shows that there is a moderately negative correlation between bladder capacity and duration of dialysis as well as duration of anuria. That is, the lower the duration of dialysis and the lower the duration of anuria, the higher the bladder capacity. As shown in Table 4, among patients who underwent hydrodistention, a median of two procedures (range 1–9) prior to transplant was noted while median interval from cystography to last hydrodistention was 16 days (range 1–301). The waiting time from diagnosis of anuric ESRD to kidney transplant in the same group had a median of 4.2 months (range 1.3–36.8), which was numerically but not statistically greater compared to the corresponding duration in the group who did not undergo hydrodistention with a median of 3.5 months (range 0.3–22.3), p = .083 (Table 4, Figure 1).

Table 1. Demographic and clinical profile of patients (n=151)

	Mean ± SD; Median (Range); Frequency (%)
Age, years	32 (18 – 61)
Sex	
Male	65 (43.05)
Female	86 (56.95)
Etiology of ESRD	
Glomerulonephritis	119 (78.81)
Hypertensive nephrosclerosis	20 (13.25)
Diabetic kidney disease	8 (5.30)
NSAID nephropathy	2 (1.32)
Uric acid nephropathy	2 (1.32)
Mode of RRT	
Hemodialysis	144 (95.36)
Peritoneal dialysis	7 (4.64)
Urinary tract abnormality	
VUR	28 (18.54)
Bladder diverticulum	7 (4.64)
Urethral stricture disease	1 (0.66)
Irregular lateral wall	1 (0.66)
Small outpouchings	1 (0.66)
Cystocoele	1 (0.66)
Initial bladder capacity, cc	
<150	44 (29.1)
≥150	107 (70.9)
Underwent hydrodistention	44 (29.1)

ESRD, end-stage renal disease; VUR, vesicoureteral reflux; RRT, renal replacement therapy

Table 2. Duration of dialysis and anuria in patients with normal bladder capacity versus patients with small bladder capacity

	Normal Bladder Capacity (≥150cc) Mean (Range)	Small Bladder Capacity (<150cc) Mean (Range)
Duration of dialysis (months)	24 (4-96)	42 (10-120)
Duration of anuria (months)	15 (1-96)	29 (4-96)

Table 3. Correlation of bladder capacity with durations of dialysis and anuria

	Correlation coefficient, r	Interpretation	p-value
Duration of dialysis	-0.436	Moderate negative relationship	<.001
Duration of anuria	-0.479	Moderate negative relationship	<.001

Statistical test used: Spearman's Correlation
Correlation coefficient interpretation: 0, no relationship; 0-0.2, very weak; 0.2-0.4, weak; 0.4-0.6, moderate; 0.6-0.8, strong; 0.8-0.99, very strong; 1, perfect

Table 4. Process indicators from diagnosis, hydrodistention and transplant (n=151)

	All (n=151)	Hydrodistention		p
		Yes (n=44)	No (n=107)	
No. of hydrodistention procedures prior to KT	2 (1–9)	2 (1–9)	-	-
Time from cystography to last hydrodistention (days)	16 (1–301)	16 (1–301)	-	-
Time from anuric ESRD diagnosis to KT (months)	3.8 (2.7–36.8)	4.2 (1.3-36.8)	3.5 (0.3–22.3)	.083

Values are in median (range)

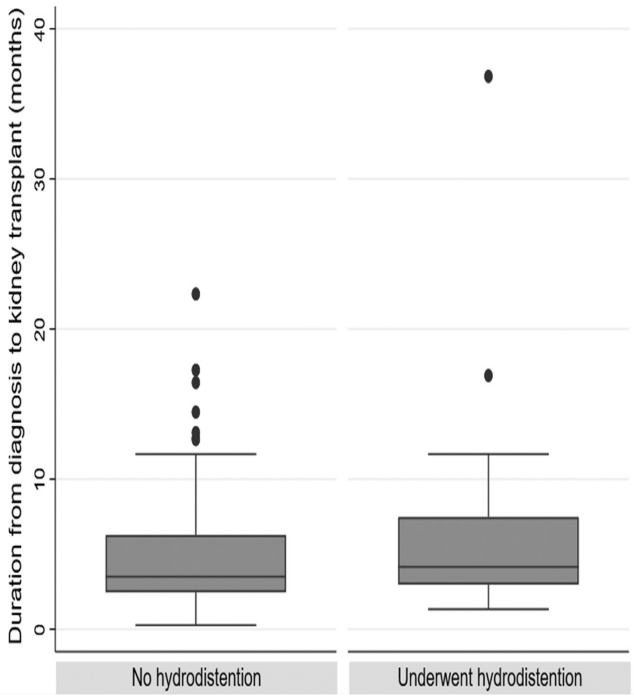

Figure 1. Interval (months) from anuric ESRD diagnosis to kidney transplant.

The median discharge serum creatinine of patients was 1 mg/dL (range 0.4–4.8) which was not significantly different between patients with and without hydrodistention. The only complication noted was recurrent UTI observed in three (9%) patients in the hydrodistention group and five (5%) in the non-hydrodistention group (Table 5).

As shown in Table 6, during the period covered, there were a total of 127 hydrodistention procedures performed on 43 pretransplant patients. At a unit cost of Php 224 per procedure, this costs a total of more than Php 28,000 in all. The median cost of cystography was Php 3,473 and the total cost incurred by 44 patients for this procedure was approximately Php 457,000.

Patients in this cohort who were required to undergo hydrodistention had a median total of two sessions, hence, an additional cost of Php 447.20 was incurred per patient. Adding to the median cost of cystography, these procedures cost a total of Php 3,920 for patients with small bladder capacity (Table 7).

Table 5. Post-kidney transplant outcomes (n = 151).

	All (n=151)	Hydrodistention		p-value
		Yes (n=44)	No (n=107)	
	Median (Range); Frequency (%)			
Creatinine, mg/dl	1 (0.4–4.8)	1 (0.5–4.3)	1 (0.4–4.8)	.831
Re-operation	0	0	0	-
Graft rejection	0	0	0	-
Recurrent UTI	8 (5.30)	3 (6.82)	5 (4.67)	.692
Frequency	0	0	0	-
Urgency	0	0	0	-
Nocturia	0	0	0	-
Weak stream	0	0	0	-
Intermittency	0	0	0	-
Straining	0	0	0	-
Incomplete emptying	0	0	0	-

Table 6. Total costs incurred by cystography and hydrodistention

	Total No. Performed	Unit Cost (Php)	Total Cost (Php)
Procedure			
Cystography	151	3473.00	456,954.38
Hydrodistention	127	223.60	28,397.20

Table 7. Direct costs of different management options, per patient.

	Expenditure	Cost	Total Cost (Php)
Hydrodistention	Hydrodistention, Cystography	= (3473.0 + 447.2)	3920.2
No hydrodistention	Cystography	= (3473.0)	3473.0

Discussion

Successful transplantation requires extensive work up which includes a comprehensive urologic evaluation. This is to ensure a sterile, continent, compliant urinary tract which is able to store an adequate amount of urine. Bladder outlet needs to be carefully assessed and malignancies should be ruled out. Identification and proper management of urologic problems decreases the risk of posttransplant graft loss.[5]

In NKTI, cystography has been routinely performed for anuric ESRD patients to determine bladder capacity. Those with small bladder capacity defined as <150cc undergo subsequent hydrodistention or bladder cycling until the patient reaches the normal volume of ≥150cc. However, it has been observed that these procedures delay transplantation and incur additional costs.

There are different schools of thought regarding utilization of cystography in work up of pretransplant patients. Several studies claimed that invasive diagnostic procedures such as cystography, urodynamics and cystoscopy should only be done in patients with history or abnormal basic work up results suggestive of bladder dysfunction[5-7], while other authors recommend thorough and proper examination of the lower urinary tract prior transplant.[8]

Reduction in bladder capacity results due to loss of normal physiological distention, which is seen in ESRD patients. According to Chen, et.

al., bladder capacity in ESRD patients shrinks with the time of ESRD (300 cc in five years and 150 cc in fifteen years), hence patients with ESRD for more than fifteen years showed more diffuse atrophic bladder (60%) than patients with ESRD of less than four years. Although after transplantation, once patient has normal urine output, the bladder achieves its normal capacity due to an unclear mechanism.[9] In the present study, it has been shown that there is a moderately negative correlation between bladder capacity and duration of dialysis and anuria. That is, the lower the duration of dialysis and anuria, the higher the bladder capacity. The mean duration of dialysis in patients with small bladder capacity is 42 months while mean duration of anuria is 29 months. Both were noted to be longer compared to those patients who had normal bladder capacity.

Hydrodistention or bladder cycling has been widely used to increase bladder compliance and eventually achieve normal bladder capacity. However, its use in the pretransplant setting is still controversial. Several studies reported favorable posttransplant results in abnormal bladders given that dysfunctions have been detected and corrected either surgically (e.g. bladder augmentation and urinary diversion) or through hydrodistention avoiding urologic complications and graft loss.[10] In this study, patients who underwent hydrodistention achieved normal bladder capacity with a median of two procedures prior transplant.

Post-transplant outcomes noted in the present study was favorable. However, given that this is a retrospective study, analysis of post-transplant outcomes is very limited. In a study by Hotta, et al., one of the complications related to long term dialysis is atrophic bladder. Among these patients, there is a risk of developing urological complications post-transplant as a result of difficulties in ureteral reimplantation.[11] Other studies also reported that debilitating lower urinary tract symptoms may result post-transplant due to low bladder capacity.[12] The authors reported that the median discharge serum creatinine of patients was 1.0 mg/dl (range 0.4–4.8) which was not significantly different between patients with and without hydrodistention. The only complication noted was recurrent UTI, observed in three patients (9%) in the hydrodistention group and five (5%) in the non-hydrodistention group.

Delay in transplantation and additional costs have been associated with cystography and hydrodistention however, there is lack of literature supporting this claim and results may vary per institution. In this study, it was found that the waiting time from diagnosis of anuric ESRD to kidney transplant was not statistically significant between the two groups. The median cost of cystography was Php 3473 while patients required to undergo hydrodistention had an additional cost of Php 447.20 incurred per patient adding up to Php 3,920.20.

The study conducted is retrospective hence, data collection and analyses on outcomes are very limited and inconclusive. The authors recommend a prospective study to be performed more specifically on bladder capacity and lower urinary tract symptoms post -transplant. Intraoperative parameters such as technical difficulties in reimplantation and need for a JJ stent are also suggested as well as post-operative urinary leakage and anastomotic stenosis. A follow up posttransplant cystography is also recommended to assess posttransplant bladder capacity and presence of graft vesicoureteral reflux. Lastly, a questionnaire can be used to thoroughly assess lower urinary tract symptoms pre- and post-transplant.

Conclusion

The authors therefore conclude that bladder capacity is diminished in patients with longer duration of dialysis and anuria, which can be detected by cystography and corrected by hydrodistention pretransplant. They recommended cystography in patients who are anuric for at least three years and those with medical history suggesting bladder dysfunction. Hydrodistention can be done to achieve normal bladder capacity and does not significantly prolong duration of diagnosis to kidney transplant however additional costs incurred may be a burden for some of these patients.

Disclosure

There are no conflicts of interests, financial sources nil.

References

1. Wein, et al. Campbell-Walsh Urology 11th edition. Philadelphia, PA: Elsevier Inc. Chapter 2016; 46: 1053-5.
2. Salman B, Hassan A, Sultan S, Tophill P, Halawa A. Renal transplant in the abnormal bladder: long-term follow-up. Experimental and Clinical Transplantation 2017; 1: 10-5. DOI: 10.6002/ect.2016.0193
3. Rude T, Nassiri N, Naser-Tavakolia A, Ginsberg D. The role of urodynamics in the pre-transplant evaluation of renal transplant. Curr Urol Rep 2019; 20: 6. DOI: 10.1007/s11934-019-0887-3
4. Song M, Park J, Hoon Kim Y, Jong Han D, Hoon Song S, Choo MS, Hong B. Bladder capacity in kidney transplant patients with end-stage renal disease. Int Urol Nephrol 2015; 47: 101–6. DOI:10.1007/s11255-014-0848-1
5. Antoniewicz AA, Zapala A, Bogucki A, Malecki R. The standard of urological consultation of patients qualified for renal transplant – a review. Cent European J Urol 2015; 68(3): 376–82. DOI: 10.5173/ceju.2015.551
6. Power RE, Hickey DP, Little DM. Urological evaluation prior to renal transplantation. Transplantation Proceedings 2004; 36(10): 2962-7. DOI: 10.1016/j.transproceed.2004.11.006
7. Cabello BR, et al. The candidate for renal transplantation work up: medical, urological and oncological evaluation. Arch Esp Urol 2011; 64(5): 441-60.
8. Chmura A, Borkowski A, Radziszewski P, Kwiatkowski A, Rowinski W. Significance of urodynamic assessment of lower urinary tract in dialysis patients before renal transplantation. Transplant Proceedings 2007; 39: 2733–5. https://doi.org/10.1016/j.transproceed.2007.09.020
9. Chen JL, Lee MC, Kuo HC. Reduction of cystometric bladder capacity and bladder compliance with time in patients with end-stage renal disease. J Formosan Med Ass 2010; 111: 209-13. DOI: 10.1016/j.jfma.2011.09.023
10. Errando C, Batista JE, Caparros J, Araño P, Villavicencio H. Is bladder cycling useful in the urodynamic evaluation previous to renal transplantation? Urol Int 2005; 74: 341–5. DOI: 10.1159/000084435
11. Hotta K, Miura M, Wada Y, Fukuzawa N, Iwami D, Sasaki H, Seki T and Harada H. Atrophic bladder in long-term dialysis patients increases the risk for urological complications after kidney transplantation. Int J Urol 2017; 24(4): 314-9. DOI: 10.1111/iju.132
12. Dion M, Cristea O, Langford S, Luke PPW and Sener A. Debilitating lower urinary tract symptoms in the post-renal transplant population can be predicted pretransplantation. Transplantation 2013; 95: 589594. DOI: 10.1097/TP.0b013e3182782f7e