PREVALENCE OF LOWER URINARY TRACT SYMPTOMS POST KIDNEY TRANSPLANTATION AND ITS URODYNAMIC PROFILE

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ABSTRACT

Objective: *This study aimed to describe the urodynamic characteristics of post-transplant kidney patients with LUTS who were indicated for urodynamics.* ***Material & Methods:*** *This research is a cross-sectional study conducted at Cipto Mangunkusumo General Hospital between 2011-2017. Data were collected from patients who had undergone urodynamic examination after kidney transplantation due to LUTS/urinary retention. Data were collected from the patient's medical record.* ***Results:*** *A total of 536 patients underwent kidney transplants at Cipto Mangunkusumo General Hospital from 2011-2017. Eleven patients (2%) developed LUTS and then underwent urodynamic examination with an average age of 41.4 (30.1 ± 52.6) years. Six patients (55%) had type 2 diabetes mellitus (DM) and 5 patients (45%) had hypertension (HT). A total of 6 out of 11 patients (54%) experienced urinary retention of which 4 subjects (67%) had decreased bladder compliance, 4 (67%) patients experienced detrusor overactivity (DO), 3 patients (50%) had bladder outlet obstruction (BOO), while 2 patients (33%) experienced detrusor underactivity (DU) respectively. Of 5 patients without urinary retention, decreased bladder compliance was found in 1 patient (20%), DO in 2 patients (40%), BOO in 1 patient (20%), and no subject experienced DU. In both groups, no subject was discovered to experience any urinary incontinence.* ***Conclusion:*** *Small number of post renal transplantation patients developed LUTS and half of which accompanied by urinary retention. Among these patients, urodynamic examination revealed detrusor overactivity as the most common underlying problem followed by decreased bladder compliance, BOO, and detrusor underactivity.*

Keywords: *Urinary retention, kidney transplant, urodynamic.*

ABSTRAK

Tujuan: *Penelitian ini bertujuan menggambarkan karakteristik urodinamik pada pasien pasca transplantasi ginjal dengan gejala saluran kemih bawah.* ***Bahan & Cara:*** *Penelitian ini merupakan sebuah studi potong lintang yang dilaksanakan di RSUPN Dr. Cipto Mangunkusumo pada tahun 2011-2017. Data dikumpulkan dari pasien yang telah menjalani transplantasi ginjal diikuti dengan pemeriksaan urodinamik dengan indikasi LUTS atau retensi urin. Seluruh data didapatkan melalui rekam medis.* ***Hasil:*** *Sebanyak 536 pasien menjalani transplantasi ginjal di RSCM dari tahun 2011-2017. Sebelas pasien (2%) dari seluruh pasien mengalami LUTS dan menjalani pemeriksaan urodinamik. Rata-rata umur pasien yang mengalami LUTS adalah 41.4 (30.11 ± 52.6) tahun. Enam pasien (55%) menderita diabetes mellitus tipe 2 dan 5 (45%) pasien menderita hipertensi. Sebanyak 6 dari 11 pasien (54%) mengalami retensi urin dimana 4 subjek (67%) mengalami decreased bladder compliance, 4 pasien (67%) mengalami bladder overactivity (BO), 3 pasien (50%) mengalami bladder outlet obstruction (BOO), dan 2 pasien (33%) mengalami detrusor underactivity (DU). Dari 5 pasien yang tidak mengalami retensi urin, decreased bladder compliance ditemukan pada 1 pasien (20%), DO pada 2 pasien (40%), BOO ditemukan pada 1 pasien (20%), dan tidak terdapat pasien dengan detrusor underactivity pada kelompok ini. Melalui pemeriksaan urodinamik, tidak ada gambaran inkontinensia yang ditemukan pada kedua kelompok.* ***Simpulan:*** *Sebagian kecil pasien yang menjalani transplantasi ginjal akan mengalami LUTS dimana setengahnya mengalami retensi urin. Pada pasien-pasien ini, pemeriksaan urodinamik menunjukkan bahwa BO merupakan salah satu temuan tersering diikuti oleh, decreased bladder compliance, BOO, dan DU.*

Kata Kunci: *Retensi urine, transplantasi ginjal, urodinamik.*

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INTRODUCTION

Kidney transplantation has been established as the main therapy for end-stage renal disease (ESRD). Kidney transplantation has been shown to improve the health-related quality of life and overall survival of patients affected by end-stage kidney disease.[1] From January 2011 to January 2018, Cipto Mangunkusumo General Hospital has done up to 563 kidney transplants with satisfying results. Long-term outcomes of recipient survival also continue to improve due to developments in immuno-suppressive therapy.[1-3]

However, as a complex procedure, several changes occur in patients following renal transplantation. The main change after transplantation is the adaptation of storage and voiding functions in the lower urinary tract (LUT) in the first six months post-transplantation where urine retention can occur. The amount of urine produced in ESRD is very different, varying from normal volume to anuria. As the consequence, many patients cannot utilize their lower urinary tract during the long waiting period for kidney transplants.

Disuse of the lower urinary tract may impact the bladder smooth muscle tissue constituent that tends to go atrophied if not used regularly or trained. Although there has been no specific research regarding this subject, it is generally assumed that long-term bladder disuse may result in degenerative processes in the bladder wall that can occur during ESRD.[4] Kidney transplantation is a routine procedure performed at RSCM from 2011 until now, however, there are no available data regarding the prevalence of LUTS after renal transplantation, hence the evaluation of LUT before and after transplantation in our center has not been standardized.

After a successful kidney transplant, urine production will start immediately within the first few days. The bladder is initially drained by a catheter that is inside to protect the anastomosis between the ureter and the bladder. After the removal of the urethral catheter, the bladder begins to store and evacuate the urine which may alleviate storage and voiding problems. Acute problems can arise immediately after the removal of the catheter, including irritation and urinary tract infections, which result in urgency and frequency. Several studies have shown that chronic lower urinary tract problems can occur in post-transplant patients, such as frequency, nocturia, low bladder volume, and decreased bladder wall compliance.[5]

The lower urinary tract will immediately adjust its storage and emptying functions to varying urine volume following kidney transplantation. In non-neurogenic patients, LUT adaptation usually occurs within six months after a kidney transplant.[6] However, some patients experienced voiding dysfunction and LUT symptoms, which can have an impact on quality of life.[7-9]

More than half of patients with kidney transplants will often experience micturition and nocturia that can last for years.[10-11] Patients who had undergone kidney transplantation are also instructed to take lots of fluids to maintain kidney function. However, this can alleviate the LUTS.[9] This condition can worsen the patient's quality of life and the general post-transplant condition.

OBJECTIVE

This study was conducted to evaluate the prevalence of post-transplant urine retention and to describe the urodynamic characteristics of patients with renal post-transplant urine retention. No data regarding the prevalence of LUTS in patients undergone renal transplantation and its urodynamic profile despite the ever-increasing number of kidney transplantation surgeries in various centers in Indonesia.

MATERIAL & METHODS

This study was conducted in a retrospective cross-sectional manner evaluating all patients with LUTS that occurred after kidney transplantation at Cipto Mangunkusumo General Hospital from 2011-2017. Patient data were taken from the medical records six months following a successful kidney transplantation surgery. A urodynamic study was performed based on clinical assessment.

Study subjects were gathered in total sampling manner, in which 563 post-transplant kidney patients from January 2011 to January 2017 were gathered. All patients who undergone urodynamic examinations were based on the indication of voiding dysfunction such as LUTS and urinary retention were included as study subjects. Patient demographic data and urodynamic profiles were recorded from direct examination and patient medical records. A urodynamic examination is performed using a urodynamic Helix Laborie which is calibrated annually. Urodynamic studies were

carried out by experienced urologists specialized in functional urology.

Descriptive statistical analysis was performed using SPSS version 21.0. Data normality test was performed using Kolmogorov-Smirnov normality test. Data regarding filling phase profile on urodynamic examination included first sensation, bladder compliance, detrusor overactivity, and bladder capacity were presented as categorical descriptive data. Measurement of opening detrusor pressure (Pdet), maximum detrusor pressure (maximum Pdet), voided volume, maximum flow rate (Qmax), post voiding residual volume, bladder outlet obstruction index (BOOI), bladder contractility index, and the presence of urinary retention were also recorded as voiding phase data. The frequency and occurrence of decreased bladder compliance, incontinence, detrusor overactivity (DO), bladder outlet obstruction (BOO), and detrusor underactivity (DU) among patients with and without urinary retention were also regarded as the main outcome of this study.

RESULTS

Of the 563 patients who undergone kidney transplantation, LUTS were discovered among 11 patients (2%) and were indicated for urodynamic

Table 1. Subjects' characteristics.

Variable	n (%)	Mean ± SD / Median (range)
Gender		
Male	9 (82)	-
Female	2 (18)	-
Age (year)	-	41.4 ± 16.8
Cause of ESRD		
Type 2 Diabetes Mellitus	4 (36.4)	-
Hypertension	5 (45.5)	-
Diabetes Mellitus + Hypertension	2 (18.1)	-
Dialysis duration before transplantation (months)	-	7 (0 - 120)
History of previous transplantation	0 (0)	-
Urinary retention		
Yes	6 (54.5)	-
No	5 (45.5)	-
Pre transplantation ureum level	-	75.0 ± 22.2
Pre transplantation creatinine level	-	6.6 ± 3.2
48-hour post-transplantation ureum level	-	84.5 ± 24.7
48-hour post-transplantation creatinine level	-	5.5 ± 2.5
Lowest ureum level	-	37.9 ± 20.9
Lowest creatinine level	-	1.7 ± 0.9
Decrease of creatinine (%)	-	72.5 ± 13.5
Delayed graft function (DGF)		
Yes	1 (9.1)	-
No	10 (90.9)	-
Filling Phase		
First sensation (ml)	-	99.2 ± 68.0
Qmax (cmH_2O)	-	11 (4.2 - 116)
Bladder capacity (ml)	-	232.7 ± 47.6
Voiding Phase		
Opening Pdet (cmH_2O)	-	25.9 ± 25.8
Pdet Maximum (cmH_2O)	-	85.3 ± 46.6
Voiding volume (ml)	-	139.2 (20 - 463)
Post voiding residual volume (ml)	-	0 (0 - 345)
Bladder outlet obstructive Index (BOOI)		
Obstruction	1 (9.1)	-
Not Obstructed	4 (36.4)	-
Equivocal	2 (18.2)	-
Undetermined	4 (36.4)	-
Bladder Contractility Index (BCI)		
Normal	5 (45.5)	-
Weak	2 (18.2)	-
Not available	4 (36.4)	-

*Kolmogorov-smirnov normality test.

Table 2. Urodynamic profile of subject post kidney transplantation.

Patient	First sensation (ml)	Bladder Compliance	Bladder Capacity (ml)	BOOI	Detrusor Overactivity	BCI	Qmax (cmH_2O)	Voiding Volume (ml)	PVR (ml)	Urinary Retention
1	89.0	↓	191	O	+	N	7.6	20	100.0	+
2	107.0	↓	153	N/A	+	N/A	-	-	-	+
3	46.0	N	63	O	+	↓	4.2	67.0	0	+
4	47.0	N	136	E	+	↓	4.9	221.0	0	+
5	54.0	↓	99	O	-	N	6.8	75.0	0	+
6	-	↓	44	N/A	-	N/A	-	-	-	+
7	141.0	↓	208	N/A	+	N/A	14.0	45.0	143.0	-
8	177.0	N	436	O	+	N	16.0	463.0	0	-
9	118.0	N	142	NO	-	N	116.0	139.2	2.0	-
10	8.0	N	501	E	+	N	11.0	156.0	345.0	-
11	212 5	N	318	N/A		N/A	30 7	461 6	0	

N= normal, = decreased, O= obstruction, N/A= data not available, E= equivocal, NO= not obstructed

examination. The mean study subject's age was 41.4 (30.1 ± 52.6) years, with 9:2 female to male ratio respectively. All subjects had never undergone any kidney transplantation prior to the study. Among all study subjects, diabetes mellitus type 2 was discovered in 6 patients (55%) and hypertension was found in 5 patients (45%).

Of 6 patients indicated for urodynamics due to urinary retention, type 2 diabetes mellitus and hypertension were discovered in 4 patients (67%) and 2 patients (33%) respectively. In this particular group, 4 subjects (67%) had decreased bladder compliance, 4 patients (67%) had DO, 3 patients (50%) had BOO, and 2 patients (33%) experienced DU.

Of 5 patients indicated for urodynamics without urinary retention, two subjects (40%) had history of type 2 diabetes mellitus while 3 subjects (60%) among this group had history of hypertension. Further, decreased bladder compliance was found in 1 patient (20%), DO in 2 patients (40%), BOO in 1 patient (20%), and no subject experienced DU. Incontinence incidence was also recorded as the intended outcome of this study. However, no subject experienced any urinary incontinence in both (with urinary retention and without urinary retention) groups.

In all study subjects, we found urinary retention as the most reported complaints (6 patients; 54%) followed by frequency (4 patients; 36%), and difficulty urinating with the feeling of incomplete voiding (1 patient; 10%). Further information regarding subjects' characteristics was listed in Table 1.

DISCUSSION

Kidney transplantation is currently the recommended treatment for patients with ESRD, while improvements in surgical techniques and immunosuppressive therapy are beneficial for better outcomes following kidney transplantation. Regarding this issue, several patients experience voiding dysfunction after kidney transplantation.

From January 2011 to January 2018, 11 patients suffered from voiding dysfunction (LUTS) after kidney transplantation surgery who underwent urodynamic examination. Of the 11 patients, six patients (54%) complained of urinary retention, four patients (36%) complained of frequency, and one patient (10%) had difficulty urinating and incomplete bladder emptying.

A total of 6 out of 11 subjects (54%) reported urinary retention. Among these patients, the age of patients who experienced urinary retention was 14 years, 43 years, 50 years, 54 years, 55 years, and 50 years respectively. Patients started having LUTS after a median of 2 months, although direct comparison and correlation analysis cannot be conducted due to the limited number of subjects, several studies have indicated that there was a correlation between older age and type 2 DM with the occurrence of urinary dysfunction after kidney transplantation.

Van der Weide et al. have examined 63 patients following kidney transplantation reporting that 50% of subjects are complaining about frequency and 62% of nocturia. In this study, 36% of patients reported frequency and none reported

nocturia.[10] However, a similar study in the same center comparing the voiding profile of patients after renal transplantation using uroflowmetry examination in 71 subjects resulted in frequency (85%) and nocturia (97%) as the most frequently reported LUTS complaint. OABSS was also found to correlate with factors such as DM, history of pre-transplantation anuria, and age. The IPSS storage assessment component also confirms these findings where a history of pre-transplantation anuria affects higher post-transplant IPSS scores (unpublished data). Findings of frequency symptom following post-transplant kidney can be associated with high fluid intake and bladder disuse before kidney transplant.[11] Several studies reported decreased bladder capacity, bladder compliance, and excessive detrusor activity in patients were aligned with dialysis duration before undergoing kidney transplantation.[12-13] This is consistent with the findings of this study, where 50% of patients experienced a decrease in bladder compliance with detrusor overactivity found in four patients out of the total sample (36%).

Of 6 patients who experienced urinary retention, 4 (66%) also have a history of diabetes mellitus. The high incidence of diabetes mellitus in the incidence of urinary retention can be explained by the occurrence of autonomic nerve function disorders and nephropathy. Autonomic disorders associated with diabetes mellitus are involved in urinary dysfunction in some diabetic patients.[14] Glucose-regulating pathways that affect prostate growth, in particular, insulin growth factor binding protein-3[15-16] and insulin[17-18] have been reported to correlate with an increased risk of LUTS. However, in other studies, no correlation was found between diabetes and LUTS, as shown in Italian and Korean men.[19-20]

The study conducted by Errando C et al. reported that there were 3 indications for conducting urodynamic investigations before they were performed: (1) clinical history of LUT abnormalities (neurogenic bladder, urethral valve) because it is dangerous to carry out kidney transplants where abnormal bladder might play an important role in kidney failure and hence can reproduce the same problem in the transplanted kidney; (2) the presence of LUTS in non-anuric patients so it is advisable to know whether there is BOO before a kidney transplant is performed, and (3) when cytometry shows a very small bladder capacity, so it is feared that the bladder becomes retracted and nonfunctional kidney transplantation.[21]

Examining based on the subject's diabetes history, 6 out of the 11 patients (54%) studied in this study had a history of diabetes mellitus all of whom are male with the median age of 50 years. Through the urodynamic results, 2 out of 6 patients (33%) with a history of diabetes mellitus had decreased bladder compliance, 4 patients (66%) experienced DO, 2 subjects (33%) had BOO, and 2 subjects (33%) with DU. In patients without any history of diabetes mellitus, we obtained 3:2 female to male ratio, the median age was 31 years (14-54 years). Three out of 5 subjects (60%) had related finding regarding decreased bladder compliance, 2 of them (40%) experienced DO, 2 subjects (40%) experienced BOO, and no subject had DU on the urodynamics study. This finding shows that a higher proportion of DO and urinary retention were found in patient with history of diabetes mellitus while the proportion of decreased bladder compliance was found to be higher in the group without a history of diabetes mellitus.

To date, there has been no established standard for the evaluation of post-transplant kidney patients with LUTS at our hospital. Referring to this study, patients with kidney disorders and diabetes mellitus are at risk of post-transplantation voiding dysfunction. For this reason, we strongly recommend routine urodynamic examinations for patients before the kidney transplant procedure and other risk factors for urinary dysfunction to determine the risk of further urinary dysfunction after a kidney transplant.

CONCLUSION

This study demonstrates the possibility of LUTS with or without urinary retention after kidney transplantation. This study also found that majority of patients with urinary retention after renal transplantation had type 2 Diabetes Mellitus, BOO, and DO. Routine urodynamic examinations in patients before a kidney transplant are recommended in selected patients.

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