

Urodynamic assessment of bladder and urethral function among men with lower urinary tract symptoms after radical prostatectomy: A comparison between men with and without urinary incontinence

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Purpose: We compared bladder and urethral functions following radical prostatectomy (RP) between men with and without urinary incontinence (UI), using a large-scale database from SNU-experts-of-urodynamics-leading (SEOUL) Study Group.

Materials and Methods: Since July 2004, we have prospectively collected data on urodynamics from 303 patients with lower urinary tract symptoms (LUTS) following RP at three affiliated hospitals of SEOUL Study Group. After excluding 35 patients with neurogenic abnormality, pelvic irradiation after surgery, or a history of surgery on the lower urinary tract, 268 men were evaluated. We compared the urodynamic findings between men who had LUTS with UI (postprostatectomy incontinence [PPI] group) and those who had LUTS without UI (non-PPI group).

Results: The mean age at an urodynamic study was 68.2 years. Overall, a reduced bladder compliance (≤ 20 mL/cmH₂O) was shown in 27.2% of patients; and 31.3% patients had idiopathic detrusor overactivity. The patients in the PPI group were older ($p=0.001$) at an urodynamic study and had a lower maximum urethral closure pressure (MUCP) ($p<0.001$), as compared with those in the non-PPI group. Bladder capacity and detrusor pressure during voiding were also significantly lower in the PPI group. In the logistic regression, only MUCP and maximum cystometric capacity were identified as the related factor with the presence of PPI.

Conclusions: In our study, significant number of patients with LUTS following RP showed a reduced bladder compliance and detrusor overactivity. PPI is associated with both impairment of the urethral closing mechanism and bladder storage dysfunction.

Keywords: Prostate; Prostatectomy; Urodynamics

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INTRODUCTION

Urinary incontinence (UI) after radical prostatectomy (RP) is not uncommon and one of a major postoperative complication, which has been reported in 2% to 87% of patients, depending on the definitions, types of surgery, and diagnostic methods [1-5]. The cause of persistent postprostatectomy incontinence (PPI) is multifactorial, but can be sphincteric deficiency, bladder abnormalities such as detrusor overactivity (DO), reduced bladder compliance, and impaired detrusor contractility. The past paradigm held that DO was the main cause of PPI [6-8]. But recent studies revealed that PPI is mainly caused by sphincteric deficiency [9-11].

An urodynamic study is considered as the best method that can definitively ascertain the cause of UI and has been used by many previous studies on the cause of PPI. In clinical practice, urodynamic study may be performed only when patients have unresolved UI or new-onset lower urinary tract symptoms (LUTS) after RP, hence it is not easy to obtain large-scale data on the of bladder and urethral function following RP through performing an urodynamic study. Therefore, functional alteration of bladder and urethra after surgery has not been extensively studied.

Although the various studies reported the urodynamic findings on the bladder and urethral function following RP, most of them performed an urodynamic study only aimed at incontinent patients. In the present study, using a large-scale database from SNU-experts-of-urodynamics-leading (SEOUL) Study group, we analyzed the urodynamic parameters to compare bladder and urethral function following RP between men who had LUTS with UI and those who had LUTS without UI.

MATERIALS AND METHODS

Between July 2004 and June 2013, we have prospectively collected data on the urodynamics of 555 patients who had undergone RP or other prostatic surgery at three affiliated hospitals of the SEOUL Study Group. Of these, 303 patients with LUTS determined by the subjective reports following RP were evaluated for this study. We excluded the patients with neurogenic abnormalities before RP (14 patients), with pelvic irradiation (11 patients), or who had a history of surgery due to bladder neck contracture or urethral stricture (10 patients) after RP. Finally, 268 patients were enrolled in this study. The Institutional Review Board (IRB) of the Seoul National University Bundang Hospital (IRB

No: B-1506/304-107) approved the study protocol based on the Declaration of Helsinki and the acquisition of the informed consent was waived due to the retrospective analysis of the database. All personal identifiers were removed from the database and all data were anonymously analyzed.

The methods for RP were open retropubic, pure-laparoscopic or robot-assisted approach based on a decision by the surgeon and the patient. Before the introduction of robotic surgery, most surgeries had been performed by open approach in three affiliated hospitals and laparoscopic approach had accounted for less than 5% of the whole cases. After the introduction of robotic surgery, most surgeries have been performed by robot approach. Regular follow-up after surgery consisted of physical examination, urinalysis, prostate-specific antigen, digital rectal examination, and relevant questionnaires assessing the status of urinary or erectile function, and were performed every 3 months for the first 1 or 2 years, every 6 months in the next 3 or 4 years, and yearly thereafter. The status of UI and the number of pads per day required for urinary control were assessed serially at the follow-up by a physician or a research assistant. Usually, all patients with PPI were advised to conduct Kegel exercises without participation in a specific rehabilitation program.

The evaluation of LUTS including UI after surgery included a complete history taking of clinical symptoms, physical examination, questionnaires evaluating status of urinary function and symptom bother, noninvasive uroflowmetry, cystoscopic inspection, and urodynamic study. Cystoscopy and urodynamic study were performed when LUTS or UI was persistent beyond 1 year after surgery. UI was defined as regularly wearing one pad or more per day due to any involuntary leakage of urine in daily living, based on the patient interview.

All terms and procedures for urodynamic evaluation were based on the guidelines of the International Continence Society [12,13]. Also, as SEOUL Study Group urodynamic database has been obtained from three affiliated hospitals, we have tried to maintain the consistency of data by standardizing the urodynamic procedure and interpretation of the results between the hospitals through the periodic audit and quality control. Conventional multichannel urodynamic study (UD-2000, Medical Measures System, Enschede, The Netherlands), including a pressure-flow study, was performed after discontinuation of all drugs possibly affecting micturition function for at least 3–7 days, based on the predetermined protocol. First, urethral pressure profiles were measured at rest while the catheter was withdrawn at a speed of 2 mm/s with saline perfused

at 2 mL/min. An aseptic 6-Fr double-lumen catheter and a 9-Fr balloon catheter were used to assess the intravesical and abdominal pressures during a filling cystometry. Pelvic floor electromyography was performed with surface electrodes attached at 3 and 9 o'clock positions near the anus. Intravesical pressure was measured under conditions of room-temperature saline infusion at 50 mL/min. However, in individuals with severe storage symptoms or lower functional bladder capacity in bladder diary, the filling rate was decreased to 20 mL/min.

Abdominal leak point pressure (ALPP) was assessed in the sitting or standing position at the amount of half maximum cystometric capacity (MCC). For patients who failed to demonstrate urine leakage on intubated urodynamic ALPP test, the urethral catheter was removed and ALPP was rechecked via the rectal catheter.

Patients were instructed to void in a standing or sitting position under quiet and relaxed circumstances during a pressure-flow study. Considering the possibility of cortical inhibition, an additional voiding trial was performed if the first voiding trial failed. In cases of severe leakage in the sitting or standing position before the command for voiding, manual compression was applied on the penile urethra to identify the MCC and the presence of detrusor pressure during voiding trial.

Reduced bladder sensation was defined as a diminished bladder sensation or not having a strong desire to void during filling cystometry [12]. Bladder compliance was considered reduced when the $\Delta V/\Delta p_{det}$ was ≤ 20 mL/cmH₂O. DO was regarded as positive if spontaneous or provoked involuntary detrusor contraction (IDC) was observed [13]. Detrusor underactivity (DU) was considered as present if the bladder contractility index (BCI) was less than 100 [14]

and bladder outlet obstruction (BOO) was defined as an Abrams-Griffith number of 40 or greater [15].

Patients were divided into individuals with UI (PPI group) and those without UI. The type of UI, such as stress or urgency, was not concerned in the statistical analyses because UI, itself, may be more relevant to patients regardless of the type of UI after surgery. Comparisons between groups were assessed by a Student t-test or a Chi-square test depending on the types of variables. Logistic regression analysis was performed to identify the possible factors related with PPI among the variables from patient demographics, uroflowmetry, urethral pressure profilometry, and filling cystometry. The significance level of two-tailed p-value<0.05 in the univariate analyses was a screening criterion for entrance into the multivariate logistic regression analyses. The IBM SPSS Statistics ver. 19.0 (IBM Co., Armonk, NY, USA) was used, and a two-tailed p-value<0.05 was determined to demonstrate statistical significance.

RESULTS

The mean age of 268 patients included in the analysis was 66.8 years at the surgery and 68.2 years when receiving an urodynamic study. Of all the patients, UI was reported in 150 individuals (56.0%). Patients with UI were significantly older; however, other demographics were not different between patients with and without UI (Table 1). As for other LUTS except for UI, frequency, nocturia, and urgency were the most common.

Fourteen patients (9.3%) among the PPI group did not demonstrate urine leakage on urodynamic ALPP test, despite the presence of subjective symptoms of UI in daily

Table 1. Comparison of patient demographics between men with and without urinary incontinence among patients with lower urinary tract symptoms after radical prostatectomy

Variable	Total (n=268)	PPI group (n=150)	Non-PPI group (n=118)	p-value
Age (y)				
At RP	66.8±6.5	67.5±5.6	65.9±7.4	0.047
At urodynamic study	68.2±6.8	69.4±6.0	66.7±7.4	0.001
Body mass index (kg/m ²) ^a	25.3±8.5	24.7±2.8	25.9±11.6	0.282
Diabetes mellitus (%) ^a	22 (8.2)	12 (8.0)	10 (8.5)	0.888
Surgery type (%)				0.690
Open (retropubic) RP	128 (47.8)	69 (46.0)	59 (50.0)	
Laparoscopic RP	7 (2.6)	6 (4.0)	1 (0.8)	
Robot-assisted RP	133 (49.6)	75 (50.0)	58 (49.2)	

Values are presented as mean±standard deviation or number (%).

PPI, postprostatectomy incontinence; RP, radical prostatectomy.

^a:Data on body mass index and the presence of diabetes mellitus were available for statistical analysis in 217 and 174 subjects of 268 men at urodynamic study.

living. Also, 33.9% in the non-PPI group showed a positive result on the test, though they did not report the subjective symptoms on UI. Actual value of ALPP among the patients with a positive test was lower in the PPI group (Table 2).

Urodynamic findings are listed in Table 3. Overall, reduced bladder compliance was found in 27.2% of the patients; and 31.3% had IDC. During voiding phase, 63.1% and 7.8% had DU and BOO by the urodynamic definition.

Compared to patients of the non-PPI group, those in the PPI group had a lower maximum urethral closure pressure (MUCP) and lower MCC (Table 3). As for voiding parameters, maximum flow rate during a pressure-flow study was higher and the detrusor pressures recorded at the onset of urine flow and at maximum measured flow rate were lower in the PPI group. Concerning DU, incidences between both groups were not different, while the occurrence of BOO was higher in the non-PPI group (Table 3).

In the multivariate logistic regression models with

variables from patient demographics, uroflowmetry, urethral pressure profilometry, and filling cystometry, only MUCP and MCC were identified as the related factors with the presence of PPI (Table 4).

DISCUSSION

To date, various studies reported the urodynamic findings on the bladder and urethral function following RP [6,7,9-11,16-18]. However, these studies only considered small patient number less than 100 cases and some had a heterogenic cohort of both RP for prostate cancer and transurethral resection for benign prostatic hyperplasia. Furthermore, most of them performed an urodynamic study only aimed at incontinent patients.

In the present study, we analyzed urodynamic parameters to evaluate the bladder and urethral function following RP, not only in the PPI group, but also in the patients with

Table 2. The results of the abdominal leak point pressure (ALPP) test during urodynamic study between men with and without urinary incontinence

ALPP test	Total (n=268)	PPI group (n=150)	Non-PPI group (n=118)
Positive, n (%)	176 (65.7)	136 (90.7)	40 (33.9)
Mean±SD (cmH ₂ O) ^a	127.9±50.4	122.1±54.3	147.8±35.1

PPI, postprostatectomy incontinence; SD, standard deviation.

^a:Data on ALPP value were evaluated only for patients with the positive ALPP test.

Table 3. Comparison of urodynamic findings between men with and without urinary incontinence among patients with lower urinary tract symptoms after radical prostatectomy

Variable	Total (n=268)	PPI group (n=150)	Non-PPI group (n=118)	p-value
Uroflowmetry				
Qmax (mL/s)	15.1±8.6	15.8±9.0	14.3±8.0	0.159
PVR (mL)	21.6±33.5	21.2±38.1	22.1±26.7	0.843
Urethral pressure profilometry				
MUCP (cmH ₂ O)	64.9±23.6	60.2±25.5	70.8±19.5	<0.001
FUL (mm)	43.1±11.2	42.9±11.3	43.5±11.0	0.679
Filling cystometry				
MCC (mL)	373.9±112.5	352.1±109.6	401.8±110.3	<0.001
IDC (%)	84 (31.3)	49 (32.7)	35 (29.7)	0.599
Reduced sensation (%)	12 (4.5)	5 (3.3)	7 (5.9)	0.307
Compliance≤20 mL/cmH ₂ O (%)	73 (27.2)	43 (28.7)	30 (25.4)	0.554
Pressure-flow study				
Qmax (mL/s)	12.8±8.1	13.7±8.5	11.6±7.5	0.036
Pdet open (cmH ₂ O)	29.2±14.2	25.5±13.2	33.5±14.1	<0.001
PdetQmax (cmH ₂ O)	29.8±15.8	24.7±14.7	36.0±14.9	<0.001
DU (%)	169 (63.1)	94 (62.7)	75 (63.6)	0.795
BOO (%)	21 (7.8)	6 (4.0)	15 (12.7)	0.010

Values are presented as mean±standard deviation or number (%).

PPI, postprostatectomy incontinence; Qmax, maximum flow rate; PVR, postvoid residual volume; MUCP, maximum urethral closing pressure; FUL, functional urethral length; MCC, maximum cystometric capacity; IDC, involuntary detrusor contraction; Pdet open, opening detrusor pressure; PdetQmax, detrusor pressure at maximum flow rate; DU, detrusor underactivity; BOO, bladder outlet obstruction.

Table 4. Multivariate logistic regression analyses of the possible variables related with postprostatectomy incontinence in patients with lower urinary tract symptoms after radical prostatectomy

Variable	OR (95% CI)	p-value
Age at urodynamic study (y)	1.037 (0.996–1.081)	0.081
MUCP (cmH ₂ O)	0.984 (0.972–0.995)	0.006
FUL (mm) ^a	0.995 (0.972–1.020)	0.711
MCC (mL)	0.996 (0.994–0.999)	0.009
IDC ^a	0.980 (0.558–1.720)	0.943
Reduced sensation ^a	1.391 (0.357–5.426)	0.635
Compliance ≤20 mL/cmH ₂ O ^a	0.967 (0.537–1.740)	0.911

The significance level of two-tailed p-value < 0.05 in the univariate logistic regression analyses with variables of patient demographics, uroflowmetry, urethral pressure profilometry, and filling cystometry was a screening criterion for entrance into the multivariate analyses.

OR, odds ratio; CI, confidence interval; MUCP, maximum urethral closing pressure; FUL, functional urethral length; MCC, maximum cystometric capacity; IDC, involuntary detrusor contraction.

^aFUL, IDC, reduced sensation, and compliance 20 mL/cmH₂O or less were entered into the multivariate analysis regardless of significance in the univariate model because they might be the possible variables for postprostatectomy incontinence.

LUTS other than UI using a large-scale database. A reduced bladder compliance and IDC were shown in 27.2% and 31.3% of the patients enrolled. Two thirds of patients had DU by the urodynamic definition. The PPI group patients were older when receiving surgery and urodynamic study, had lower levels of MUCP, MCC, and detrusor pressure during voiding, as compared with those in the non-PPI group. Finally, only MUCP and MCC were identified as the related factors with the presence of PPI in the logistic regression models. Therefore, we assume that both impairment of the urethral closure pressure and lower bladder capacity during the storage phase are deeply associated with the presence of PPI.

In the previous studies with urodynamic assessment, sphincteric deficiency has been investigated as the main cause of PPI [9-11]. In our study, MUCP in the PPI group was about 10 cmH₂O lower than in the non-PPI group and was identified as the related factor with the presence of PPI, supporting the findings of previous researches on the relationship between sphincteric deficiency and PPI. However, there have been controversial results on this issue [19]. Furthermore, Cameron et al. [20] reported no differences in MUCP at rest, rather, did observe a large difference in the ability to increase closure pressure during a Kegel maneuver between men with and without PPI. Therefore, the clinical significance of MUCP at rest would require further large study. As for functional urethral length, no statistical difference was found between men with and without PPI in our study, similar to the study by Cameron et al. [20]. One systematic review revealed that functional urethral length did not show any significant difference between men with and without PPI in three of five studies, whereas MUCP was significantly different between these men in five out of

seven studies [19].

Sphincteric deficiency is a predominant factor associated with PPI, but the bladder components may also contribute to this problem. In the present study, lower MCC was another related factor with the presence of PPI. The actual difference was about 50 mL between both groups. Similar to our findings, Cameron et al. [20] found MCC was 95 mL smaller in men with PPI. The clinical significance of MCC, however, has not been clearly determined in men with PPI until now, and may be difficult to interpret. In women with overactive bladder, it has been reported that MCC is smaller in women with DO than in those without DO [21]. Considering this relation, our findings could be explained by the assumption that lower MCC in the PPI group may be related with higher frequency of IDC in this group, albeit not statistically significant (32.7% vs. 29.7%) or is perhaps a new finding needing further study. Similar to our findings, Kadono et al. [10] also reported the significant relation of postoperative MCC with the status of UI, measured by urine loss ratio, in men with RP. More well-designed studies will clarify the clinical evidence to support MCC as a relevant factor of PPI.

Another parameter of bladder dysfunction that can be related with PPI may be a reduced bladder compliance and IDC. *De novo* reduced compliance has been observed in up to 32% of men receiving RP, with persistence in 28% after 36 months [22] and IDC has been found in 30%–40% among patients with PPI [9,16,22]. However, as previously reported, these parameters are rarely the sole cause of PPI and less than 10%–15% of patients with PPI have only bladder dysfunction without sphincteric deficiency [8,9,16]. In our study, the percent of patients with these parameters was not statistically different between both groups though

the actual rates were relatively higher in the PPI group. Therefore, its clinical significance for the development of PPI deserves more study.

In contrast to men with a prostate, those receiving RP may more readily initiate and maintain urinary flow with relatively less use of detrusor power, and this can particularly apply to the patient with PPI who has a weak sphincteric function. Kleinhans et al. [18] have reported significant decreases in detrusor pressure at the maximum flow, opening urethral pressure, and an increase in the maximum flow rate after RP. Therefore, it is not surprising that the PPI patients had the higher maximum flow rate and lower detrusor pressures during the voiding phase in the present study.

Although we defined DU as the BCI less than 100 [14], the specific method of assessment for detrusor contractility has not been standardized and there are no acceptable normal levels of contractility for men receiving RP [23]. Unlike men with an intact prostate, men receiving RP may have the lower outflow resistance. Therefore, the simple use of the BCI derived from men with benign prostatic hyperplasia can be inappropriate for patients receiving RP. Previous study insisted that the best method for the assessment of contraction strength was the isometric detrusor contraction pressure independent of urinary flow in men receiving RP and, also, found that the use of common methods, such as the BCI, was the imprecise way for the diagnosis of DU in this population [24]. Therefore, further studies on more proper measures of DU independent of outlet resistance are needed in men devoid of a prostate.

About 10% (14 patients) of the PPI group did not demonstrate urine leakage during the ALPP test, despite their clinical symptoms. In these patients, DO, DU with increased postvoid residual volume, and lower detrusor compliance were identified in 3, 4, and 2 patients, respectively. The remaining five patients showed no definite bladder dysfunctions. For these five patients, we're not sure whether UI in daily living arose from the bladder or sphincteric dysfunction. One possible assumption is that the urodynamic test could not replicate the clinical symptoms in these patients with possible sphincteric dysfunction. Approximately 10%–15% of men with PPI demonstrate only bladder dysfunction without sphincteric deficiency [8,9,16]. In contrast, 33.9% of the non-PPI group showed a positive ALPP result during the test. As the mean value of ALPP in this population did reach nearly 150 cmH₂O, it is possible that UI may be insignificant and ignored in daily living in this population.

Several limitations of the present study deserve mention.

First, we did not determine the type of incontinence, such as stress or urgency, in the statistical analyses and medications such as anticholinergics were not concerned when defining the presence of PPI. However, published data have shown that only 2% of patients with PPI complain of urgency incontinence alone [25] and over 90% of our PPI group showed the positive result during the ALPP test. Therefore, UI symptoms might be ascribed to the impairment of the urinary sphincter in most of our PPI group. Second, we only analyzed the status of UI, but did not assess the qualitative status of various urinary symptoms. We used validated questionnaires, but they could not be unified, in part, for the three affiliated hospitals of the Study Group and the response rate was not high for a statistical analysis. This might affect the clinical characteristics of our study cohort. Third, we did not have urodynamic measurements before RP. In some previous studies, DO, bladder compliance, and low MUCP evaluated preoperatively have been shown to adversely affect continence status after RP [26,27]. However, there are some evidences on the contrary [28,29]. To assess the urodynamic change between pre and postoperative period will be essential to identify the predictor for the development of PPI. However, to date, such studies [18,22,27] have only involved a small sample size, around 50 patients. Our main objective was to identify the urodynamical differences of bladder and urethral function, in other words, the possible cause of PPI among men with LUTS including UI after RP. Therefore, the lack of preoperative urodynamic study would have little impact on our results. Fourth, because of retrospective nature of the study, we could not analyze the detailed data about the modification of the operative procedure, prostate size, and tumor extent. Last, interval between the surgery and an urodynamic study varied (around 18 months), even though the bladder and urethral function following RP could change with time.

Nevertheless, our findings confirm the urodynamical differences of bladder and urethral function among men with LUTS including UI after RP and should improve understanding about the pathophysiology of PPI which is one of major postoperative complications experienced by patients undergoing RP.

CONCLUSIONS

In our study, significant number of patients with LUTS following RP showed a reduced bladder compliance and DO. PPI is associated with both impairment of the urethral closing mechanism and bladder storage dysfunction. Both urethral and bladder factors should be considered

in the evaluation and management of the patients with PPI. Some effort not to attenuate MUCP such as precise identification of the sphincter complex and meticulous dissection to prevent tissue damage would be beneficial to prevent the development of PPI. Further studies including symptom assessment using unified form of questionnaire are necessary to elucidate the influence of other bladder abnormalities on the PPI.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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