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Use of preoperative factors including urodynamic evaluations and nerve-sparing status for predicting urinary continence recovery after robot-assisted radical prostatectomy: nerve-sparing technique contributes to the reduction of postprostatectomy incontinence

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Running head: Prediction of Postprostatectomy Incontinence

Key words: Urodynamic; prostatectomy; urinary incontinence; nerve sparing

ABSTRACT

Aims: To examine which preoperative factors including urodynamic evaluations and operative procedure could predict the incontinence status after robot-assisted radical prostatectomy (RARP) in this study.

Materials and Methods: Univariate and multivariate logistic regression analyses of preoperative such as age, body mass index, prostate-specific antigen level before biopsy, prostate size before surgery, membranous urethral length measured using magnetic resonance imaging (MRI), bladder compliance and maximum urethral closure pressure (MUCP) measured by the urodynamic study (UDS), and nerve-sparing (NS) status predicting 24-h pad test > 2 g/day at 1 year after RARP were examined in 111 patients enrolled in this study.

Results: The number of patients with incontinence at 1 year after RARP was 39 (35.1%). The only predictive factor for urinary continence was NS grades. To investigate the contribution of NS to urinary continence, the UDS was conducted in 84 patients who had undergone the procedure three times, before, immediately after, and 1 year after RARP. Chronological UDS revealed that recovery patterns of storage and voiding functions were the same among non-NS, unilateral-NS, and bilateral-NS groups, and the higher degree of NS

contributed to a lesser decreases in MUCP and longer functional urethral length (FUL) after RARP

Conclusion: Preoperative factors, including the results of UDS, could not predict continence 1 year after RARP. The NS procedure contributed to the continence status. NS favorably affected MUCP and FUL; however, it did not affect the bladder function after RARP.

INTRODUCTION

Radical prostatectomy (RP) is a standard treatment for localized prostate cancer. One of the most inconvenient complications influencing the quality of life after RP is urinary incontinence.¹ Robot-assisted radical prostatectomy (RARP) is reported to offer a better outcome with regard to post-prostatectomy incontinence (PPI) than the conventional methods.² However, not all patients achieved the continence status after RARP.

Predictive factors such as patient age,^{3,4} body mass index (BMI)⁵ and prostate size,^{6,7} have been reported to date. In addition, the membranous urethral length (MUL) measured using magnetic resonance imaging (MRI) is reported to be a predictive factor for PPI.⁸ In some report, detrusor overactivity⁹ and low maximum urethral closure pressure (MUCP)^{9,10} evaluated by the urodynamic study (UDS) before surgery have been shown to adversely affect the continence status after RP. In terms of the operative technique, a nerve-sparing (NS) procedure has been reported to contribute not only to the recovery of urinary continence immediately after RP, but also to the continence status for a long time after RP.^{11,12}

To evaluate the continence status, some validated questionnaires had

been invented. The International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) is one of these and has been used for the evaluation of PPI.¹³ Many reports have adopted pad use as a definition of the continence status because of its simplicity. However, this definition offers subjective evaluation and possibly little objectivity, therefore, its evaluation is possibly ambiguous.¹⁴ The International Continence Society (ICS) has recommended the pad weight test for the evaluation of PPI¹⁵, and a 24-hr pad test seems to be the most accurate.^{14,16}

In this study, using the data of RARP performed in our institution, PPI was evaluated using the 24-hr pad test. We examined which preoperative factors including urodynamic evaluations, and operative procedures, could predict the PPI status. Using chronological urodynamic data, we also examined how predictive factors could contribute to the continence status.

MATERIALS AND METHODS

Following institutional ethics committee approval, patients with clinically localized prostatic cancer undergoing RARP by a surgeon who had performed RARP in more than 100 cases at the Kanazawa University Hospital between

November 2011 and July 2013 were included in this study. All patients provided written informed consent. They were taught pelvic floor muscle exercises; patients began these exercises 1 month preoperatively and continued them postoperatively until urinary continence was recovered. The estimated prostate size was measured using transrectal ultrasound few days before surgery. MUL was measured on the coronal images of MRI as the distance from prostatic apex to the entry of the urethra into the penile bulb.⁸

RARP was performed via a transperitoneal approach. Transection of the prostate began from the anterior surface of the bladder neck; thereafter, an incision was made between the bladder and the prostate toward the retrotrigonal layer.¹⁷ NS procedures, such as inter- or intrafascial dissection, were performed depending on the cancer status.¹² When a non-NS procedure was performed, the neurovascular bundle was resected. The dorsal venous complex was athermally divided without ligation and sutured for hemostasis after division. Double-layered posterior reconstruction was performed before urethrovesical anastomosis. Urethrovesical anastomosis was performed using a running suture with a double-armed 3-0 monocryl. The urethral catheter was removed 6–7 days postoperatively by cystographic evaluation. Cystometry (CM), pressure-flow

study (PFS), urethral pressure profilometry (UPP), and abdominal leak point pressure (ALPP) were performed 1–2 days preoperatively (pre), 3–4 days after catheter removal (post), and approximately 1 year postoperatively considered as the stable continence period (stable). To obtain the information of the incontinence status, 24-h pad tests were performed. A platform scale was provided to the patients, and they were asked to weigh the pad before and after use. The increase in weight of the pad over 24 h was measured for 3 consecutive days approximately 1 year after RARP. The continence status was defined as not exceeding 2 g/day pad weight gain at mean weight of 3 consecutive days. A questionnaire for daily pad use and the ICIQ-SF were administered at the same time.¹⁸

UDSs were performed according to the Good Urodynamic Practice Guidelines of the ICS.¹⁹ CM was performed using a 6-F double-lumen Nelaton transurethral catheter with normal saline solution (37°C) at a filling rate of 50 ml/min and abdominal pressure was monitored using a 10-F intrarectal balloon catheter. The maximum cystometric capacity (MCC), and bladder compliance (BC) were measured by the filling CM. After the patients were asked to void at capacity, the maximum flow rate (Qmax) and detrusor pressure at the maximum

flow rate (PdetQmax) were measured. The transurethral catheter was removed at 60 mm/min using an electronic puller with a perfusion rate of 2 mL/min to measure static UPP. MUCP and functional urethral length (FUL) were measured by UPP. ALPP was measured at a volume of 150 mL (or half bladder capacity if the capacity was \geq 300 mL) using a rectal monitor with urethral catheter removal. The cough or valsalva maneuver was performed at least 5 times, and ALPP was defined as the lowest pressure inducing visible incontinence. If no incontinence was observed with an abdominal pressure of >100 cmH₂O, ALPP was defined as “negative.” In this analysis, the maximum abdominal pressure in all cases without urine leakage in the ALPP test was measured over 100 cmH₂O.²⁰ These measured values were used in calculations as ALPP. UDSs and analyses were performed using the Solar Silver digital urodynamic apparatus (Medical Measurement Systems, Enschede, The Netherlands).

Categorical variables used to calculate the incidence and percentage of each factor and continuous variables were summarized by mean \pm standard deviation (SD). Unpaired *t* test was used for categorical variables of 2 levels, and analysis of variance (ANOVA) was used for categorical variables of more than 2 levels. Tukey’s honest significant difference test was used for multiple

comparisons/post hoc tests. Univariate and multivariate logistic regression analyses were used to evaluate the variables significantly related to urinary continence after RARP. All data analyses were performed using SPSS for Windows (SPSS Inc, Chicago, IL). In all analyses, $P < 0.05$ was considered statistically significant.

RESULTS

In total, 111 patients who underwent preoperative MRI and UDS preoperatively and a 24-hr pad test at the stable period after RARP were enrolled. No patient used pads or collecting devices before RARP. No patients had complications >grade III of RARP according to Clavian Classification. Univariate and multivariate logistic regression analyses of preoperative factors such as age, BMI, prostate-specific antigen (PSA) level before biopsy, prostate size before surgery, MUL measured using MRI, BC measured by CM, MUCP measured by UPP, and the NS status predicting 24-h pad test > 2 g/day at 1 year after RARP were examined (TABLE I). All patients with a 24-h pad test ≤ 2 g/day were those with no daily pad use or security pad use per day. The number of patients with a 24-h pad test > 2 g/day at the stable period was 39

(35.1%). Univariate analysis showed that the NS procedure was the only predictive factor for urinary continence at the stable period. Multivariate analysis with the NS status and bladder compliance, as representatives of bladder functions, and MUCP, as a representative of urethral function, also showed that the NS procedure was the only predictive factor for urinary continence at the stable period. To investigate chronological changes in lower urinary functions with or without NS, the results of UDS of 84 patients who had previously undergone UDS three times at the pre, post, and stable periods were examined. Non-NS procedures were performed in 33 patients (39.3%), unilateral NS in 36 (42.8%), and bilateral NS in 15 (17.9%). The demographics are shown in TABLE II. The D'Amico risk group and urinary continence status were statistically different among the groups. The results of CM and UDS are shown in Fig 1. There was no statistical difference among the groups. The results of UPP and ALPP are shown in Fig. 2. MUCP of non-NS at post-RARP decreased to 39.2% compared with MUCP at pre-RARP, MUCP of unilateral-NS at post-RARP decreased to 42.0%, and MUCP of bilateral-NS at post-RARP decreased to 53.6%. Subsequently, MUCP of non-NS at stable-RARP recovered to 72.3% compared with MUCP at pre-RARP, MUCP of

unilateral-NS recovered to 79.7%, and MUCP of bilateral-NS recovered to 93.3%. The decline in MUCP after RARP became mild with high-grade NS (Fig. 2 A). FULs with higher NS grades tended to be longer, and there was a statistical difference between non-NS and bilateral-NS at post-RARP (Fig. 2B). ALPPs with higher NS grades tended to be higher; however, there was no statistical difference among the groups (Fig. 2C).

DISCUSSION

Daily pad use, interviews or questionnaires for the incontinence status, and a pad test were usually used to evaluate PPI. However, there is no consensus on how to appropriately evaluate PPI. Little correlation between the number of pads used and the severity of urinary incontinence has been reported¹⁴, and older patients have a higher volume of urine leakage per pad than the younger generation.¹⁶ Therefore, the 24-h pad test which strongly correlates with subjective urinary incontinence¹⁸ and seems to be the most reliable test was used for evaluating PPI in this study.¹⁵ There is no consensus on the definition of pad weight gain as urinary continence in the 24-h pad test. All patients with a 24-h pad test ≤ 2 g/day answered “no urine leakage” by questionnaires

simultaneously completed in this study, therefore, the definition of urinary continence as a 24-h pad test ≤ 2 g/day was adopted.²¹ In the present study of the preoperative factors predicting PPI as reported previously, such as age^{3,4}, BMI⁵, prostate size^{6,7}, MUL measured by MRI⁸, BC evaluated by CM, MUCP evaluated by UPP^{9,10}, and PSA, preoperative MUCP tended to affect urinary continence at the stable period. However, there were no statistically significant predictive factors in this study. The results indicated that there were no preoperative predictive factors for PPI (TABLE I), as reported previously.²² In the previous reports, evaluations of PPI were mostly determined by subjective answers through interviews or questionnaires^{3,5,7} or daily pad use.^{4,6,8-10} There are few reports using a 24-h pad test for evaluating PPI.²² One of the reasons for the difference in results from previous studies may be the definition of PPI. Some reports have shown that the NS procedure favorably affected RP both immediately after and a long time after RP.^{11,12} In agreement with that reported previously,¹² in the present study, the degree of preservation of neurovascular bundles affected urinary continence at the stable period after RARP.

Chronological UDS were performed to evaluate each lower urinary tract elements affected by the NS procedure. Among the non-NS, unilateral-NS and

bilateral-NS groups, there were no statistical differences in preoperative factors such as age, BMI, PSA before biopsy, neoadjuvant androgen deprivation therapy (NADT), prostate size before surgery, and MUL measured by MRI; however, there was a statistical difference in the D'Amino risk group criteria because the indications of NS were determined by the cancer status (TABLE II). From the results of UDS, bladder storage function evaluated by MCC and BC deteriorated immediately after RARP; however, it recovered to the preoperative level at the stable period after RARP, and there was no statistical difference by the NS status (Fig. 1A, B). The results of PdetQmax showed low-pressure urination immediately after RARP because of the removal of the prostate. However, the maximum flow rate did not improve immediately after RARP but at the stable period after RARP. This shows the possibility that the detrusor functions need time to recover. Recovery patterns of voiding functions were the same among different NS groups (Fig. 1C, D). MUCP evaluated by UPP decreased immediately after RARP and recovered at the stable period; however, it did not reach preoperative levels. The higher degree of NS contributed to a lesser decrease in MUCP (Fig. 2A). FUL decreased after RP because of the removal of the prostate, and FUL after RP was only measured by the length of

membranous urethra. MULs measured by MRI before RP were not statistically different among different NS groups (TABLE II). The higher degree of NS contributed to significantly longer FUL immediately after RARP, and FULs tended to be longer. However, these levels were statistically insignificant among different NS groups at the stable period (Fig.2B). ALPP showed no urine leakage in the test before RARP, and no significant difference in the number of patients with a urine leak in the test after RARP among different NS groups (Fig. 2C). The measured values of ALPP decreased immediately after RARP, and recovered almost to the same preoperative level at stable period after RARP. The results evaluated by UDS in this study showed that the NS procedure possibly contributed to maintain static urethral closure pressure after RP by preventing a decrease in MUCP and FUL. Even if the NS procedure is conducted, the nerves are impaired by the operative procedure and require several months to recover their function. Anatomically, multiple connective tissue layers, including nerves and vessels, surround the prostatic capsule. In the nerve-sparing procedure, we performed prostatectomy, ensuring least disturbance to the surrounding tissues. Therefore, the structures near the urethral sphincter are thought to be well-preserved more in NS than in non-NS. These preserved structures may

contribute to sphincter function immediately after surgery. ALPP was used to investigate stress urinary incontinence (SUI) and did not show significant differences among the different NS groups; therefore, NS may not contribute to prevent SUI, such as bladder neck hypermobility, after RP. Bladder functions recovered to preoperative levels at the stable period after RARP in this study. A previous report on open RP series evaluating changing bladder function after RP using UDS showed the deterioration in bladder function at the early period after RP, and little recovery of bladder function was observed after a long period following RP.²³ The anterior approach performed in RARP, for transection between bladder and prostate contributes to minimize the invasiveness of the bladder neck. Therefore, compared with open RP, the lesser invasiveness of this procedure seems to affect the improvement of bladder function at the stable period after RARP.²⁴

This study had several limitations. The sample size of patients in this study was not large enough to draw definitive conclusions. Pathological examinations to evaluate resected periprostatic nerves were not performed; therefore, pathological evidences of NS are not shown in this study. The urinary continence definition in this study was considered to be a 24-h pad test ≤ 2 g/day

on the based of our data from questionnaires and a previous study.²¹ The 24-h pad test is possibly more objective and accurate than the subjective questionnaires and a daily pad use; however, there is no consensus on the cut-off levels for pad weight gain after 24-h pad use to define the continence status. If no incontinence was observed with an abdominal pressure >100 cmH₂O, the ALPP was defined as “negative.” In this analysis, the maximum abdominal pressure in all cases without urine leakage in the ALPP test was measured over 100 cmH₂O.²⁰ These measured values were used in calculations as ALPP. However, there is no standard method for evaluating method of ALPP which we used in this study. In this study, the period of 1year after RARP was defined as stable period; however, changes in the function of the lower urinary tract lasted longer than 1 year after RARP and the evaluations for longer time period were not performed.

CONCLUSIONS

Preoperative factors including the results of UDS could not predict the continence status at the stable period after RARP in this study. The NS procedure contributed to the continence status at the stable period after RARP.

UDS revealed that NS favorably affected MUCP and FUL after RARP and this is thought to be one of the mechanisms of NS contribution to the continence status. Chronological UDS in this study revealed that the storage functions recovered to the preoperative level at 1 year after RARP. In addition, the voiding function improved at 1 year after RARP compared with that before RARP, whereas NS did not affect the bladder functions after RARP.

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FIGURE LEGENDS

Fig 1. Urodynamic evaluation at each time point in filling cystometry and pressure-flow study: (A) maximum cystometric capacity, (B) bladder compliance, (C) maximum flow rate, (D) detrusor pressure at maximum flow rate (PdetQmax).

The numbers in the figure show mean \pm SD of the urodynamic results at each time point. pre: before robot-assisted radical prostatectomy (RARP); post: immediately after RARP; stable: 1 year after RARP.

Fig 2. Urodynamic evaluation at each time point in urethral pressure profile and abdominal leak point pressure test: (A) maximum urethral closure pressure, (B) functional urethral length, (C) abdominal leak point pressure. The numbers in the figure show mean \pm SD of the urodynamic results at each time point. pre: before robot-assisted radical prostatectomy (RARP); post: immediately after RARP; stable: 1 year after RARP. (C) The numbers above the figure show the number (%) of positive abdominal leak point pressure.

TABLE I. Univariate and multivariate logistic regression analyses of preoperative factors and nerve sparing status predicting 24-hr pad test > 2gr/day at stable period (n = 111)

	Univariate		Multivariate	
	OR (95%CI)	<i>p</i> value	OR (95%CI)	<i>p</i> value
Age	1.008 (0.936-1.085)	0.834		
Body mass index	0.922 (0.799-1.064)	0.265		
PSA	0.997 (0.907-1.095)	0.942		
Prostate size	1.001 (0.961-1.042)	0.973		
MUL by MRI	0.972 (0.831-1.138)	0.725		
Bladder compliance	1.002 (0.975-1.030)	0.971	1.003 (0.975-1.033)	0.816
MUCP	0.990 (0.974-1.006)	0.115	0.988 (0.972-1.004)	0.144
NS non (n = 39)	Ref.		Ref.	
unilateral (n = 53)	0.375 (0.158-0.892)	0.027	0.364 (0.151-0.878)	0.024
bilateral (n = 19)	0.253 (0.071-0.901)	0.034	0.228 (0.063-0.827)	0.025

Number of patients with 24 h pad test > 2gr./day at stable period = 39 (35.1%)

OR, odds ratio; CI, confidence interval; PSA, prostate specific antigen; MUL, membranous urethral length; MUCP, Maximum urethral closure pressure; MRI, magnetic resonance imaging; NS, nerve sparing

TABLE II. Demographics of the study population receiving chronological UDS

	Mean (\pm SD) or n (%)				p-value
	ALL n = 84	non NS n = 33	unilateral NS n = 36	bilateral NS n = 15	
Age, y	65.0 (\pm 5.4)	65.8 (\pm 5.0)	64.8 (\pm 6.0)	63.8 (\pm 5.1)	0.518
Body mass index, kg/m ²	23.8 (\pm 2.6)	23.7 (\pm 2.2)	23.8 (\pm 3.1)	23.9 (\pm 2.1)	0.958
PSA, ng/ml	8.2 (\pm 4.4)	8.1 (\pm 3.6)	8.8 (\pm 5.5)	7.0 (\pm 3.1)	0.38
Biopsy Gleason score					0.068
6	31 (37%)	12 (36%)	9 (25%)	10 (67%)	
7	43 (51%)	17 (52%)	21 (58%)	5 (33%)	
8-10	10 (12%)	4 (12%)	6 (17%)	0 (0%)	
Clinical T stage					0.068
1	28 (33%)	12 (36%)	10 (28%)	6 (40%)	
2	49 (59%)	15 (46%)	25 (70%)	9 (60%)	
3	7 (8%)	6 (18%)	1 (3%)	0 (0%)	
D'Amico risk group					0.021
Low	26 (31%)	9 (27%)	8 (22%)	9 (60%)	
Intermediate	33 (39%)	10 (30%)	18 (50%)	5 (33%)	
High	25 (30%)	14 (42%)	10 (28%)	1 (7%)	
NADT					0.385
No	67 (80%)	24 (73%)	31 (86%)	12 (80%)	
Yes	17 (20%)	9 (27%)	5 (29%)	3 (20%)	
Prostate size, ml	40.4 (\pm 9.0)	39.9 (\pm 8.9)	39.4 (\pm 9.6)	43.8 (\pm 7.2)	0.267
MUL, mm	13.6 (\pm 2.4)	13.9 (\pm 2.4)	13.9 (\pm 2.2)	14.7 (\pm 3.1)	0.382
24-h pad test > 2g/day					0.023
No	53 (63%)	15 (46%)	26 (72%)	12 (80%)	
Yes	31 (37%)	18 (55%)	10 (28%)	3 (18%)	
24-h pad weight, g					
≤ 2	53 (63%)	15 (46%)	26 (72%)	12 (80%)	
2 < ≤ 10	17 (20%)	8 (24%)	7 (19%)	2 (13%)	
10 < ≤ 50	11 (13%)	7 (21%)	3 (9%)	1 (7%)	
50 <	3 (4%)	3 (9%)	0 (0%)	0 (0%)	

SD, standard deviation; NS, nerve sparing; PSA, prostate-specific antigen; NADT, neoadjuvant androgen deprivation therapy; MUL, membranous urethral length



