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ORIGINAL ARTICLE

Prostate Cancer

Significance of preoperatively observed detrusor overactivity as a predictor of continence status early after robot-assisted radical prostatectomy

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Several recent studies have reported the involvement of bladder dysfunction in the delayed recovery of urinary continence following radical prostatectomy (RP). The objective of this study was to investigate the significance of detrusor overactivity (DO) as a predictor of the early continence status following robot-assisted RP (RARP). This study included 84 consecutive patients with prostate cancer undergoing RARP. Urodynamic studies, including filling cystometry, pressure flow study, electromyogram of the external urethral sphincter and urethral pressure profile, were performed in these patients before surgery. Urinary continence was defined as the use of either no or one pad per day as a precaution only. DO was preoperatively observed in 30 patients (35.7%), and 55 (65.5%) and 34 (40.5%) were judged to be incontinent 1 and 3 months after RARP, respectively. At both 1 and 3 months after RARP, the incidences of incontinence in patients with DO were significantly higher than in those without DO. Of several demographic and urodynamic parameters, univariate analyses identified DO and maximal urethral closure pressure (MUCP) as significant predictors of the continence status at both 1 and 3 months after RARP. Furthermore, DO and MUCP appeared to be independently associated with the continence at both 1 and 3 months after RARP on multivariate analysis. These findings suggest that preoperatively observed DO could be a significant predictor of urinary incontinence early after RARP; therefore, it is recommended to perform urodynamic studies for patients who are scheduled to undergo RARP in order to comprehensively evaluate their preoperative vesicourethral functions.

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INTRODUCTION

Radical prostatectomy (RP) is the most widely performed curative therapy for patients with organ-confined prostate cancer, and could offer life expectancy >10 years to such patients.[1] Since the introduction of the prostate-specific antigen test into clinical practice, the diagnosis of prostate cancer is currently possible in significantly earlier stages and at younger ages, resulting in a marked increase in the number of patients, who could be optimal candidates for RP.[1] These findings suggest the prevalence of adverse events associated with RP, which negatively influence the postoperative quality-of-life.

Of several adverse events following RP, urinary incontinence remains one of the most distressful complications,[2] despite recent advances in knowledge of the pelvic anatomy and refinement of surgical techniques.[3] Urinary incontinence after RP has been mainly attributed to the deficiency of the external urethral sphincter;[4,5] however, several recent studies have reported the involvement of parameters associated with bladder dysfunction, which could be detected by preoperative urodynamic tests, in the delayed recovery of postoperative urinary continence. Of these, detrusor overactivity (DO), characterized by the occurrence of involuntary detrusor contractions during filling cystometry, has been regarded as one of the potential factors negatively affecting the recovery of urinary continence following open RP.[6–8] Accordingly, it is strongly recommended to perform urodynamic studies in order to accurately assess the cause of incontinence and other urinary dysfunctions in patients undergoing RP.

Robot-assisted RP (RARP) has become markedly favored over open or pure laparoscopic approach, since robotic technologies allow surgeons to perform precise and accurate movements that help preserve key anatomic structures to achieve favorable postoperative functional outcomes, including urinary continence.[9] Although there is still debate concerning the superiority of RARP over other surgical procedures with respect to urinary continence recovery, a previous systematic review of the literature reported comparatively favorable continence outcomes following RARP; that is, continence recovery 12 months after RARP in referral centers ranged from 84% to 97%.[10] However, it remains difficult to achieve a satisfactory continence status in the early postoperative period.

Considering these findings, this study included a total of 84 consecutive patients with clinically localized prostate cancer who underwent urodynamic studies prior to surgery, and were subsequently treated with RARP in order to analyze the significance of several urodynamic parameters, particularly that of preoperatively detectable DO, as predictors of the postoperative urinary continence status in these patients, focusing on the early postoperative period.

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MATERIALS AND METHODS

Patients

This study included a total of 84 consecutive patients with clinically localized prostate cancer who preoperatively received urodynamic examinations and subsequently underwent RARP between January 2011 and December 2012. Informed consent for this study was obtained from all patients, and the study design was approved by the Research Ethics Committee of our Institution. In this series, postoperative urinary continence was defined as the use of either no or one pad per day as a precaution only, and the continence status was evaluated by interviews before and 1 and 3 months after RARP.

Surgical procedure of robot-assisted radical prostatectomy

Robot-assisted radical prostatectomy was performed employing a four-arm da Vinci® robot system (Intuitive Surgical Inc., Sunnyvale, California, USA) with a transperitoneal approach, as previously described.[11] Briefly, an anterior approach was adopted by initially isolating and ligating the dorsal venous complex, followed by bladder neck dissection and mobilization of the seminal vesicles before ligating the prostatic vascular pedicles and removing the prostate. If possible, preservation of the neurovascular bundles was conducted through interfascial dissection into the avascular plane between the prostatic capsule and Denonvilliers' fascia. Posterior reconstruction of the rhabdomyosphincter, but not anterior suspension, was routinely conducted, and vesicourethral anastomosis was performed as described by Van Velthoven *et al*.[12]

Urodynamic studies

Urodynamic studies, including filling cystometry, pressure flow study, electromyogram of the external urethral sphincter and urethral pressure profile, were performed in these patients 2–4 days prior to RARP by a single urologist, as previously described.[13] Briefly, after filling cystometry with normal saline at a filling rate of 50 ml min^{-1} through a 6-Fr two-channel transurethral catheter, a voiding cystometrogram was recorded. The abdominal pressure was measured through a 10-Fr transrectal balloon catheter. After voiding cystometry, the transurethral catheter was withdrawn at 0.5 cm s^{-1}, while being perfused at 2 ml min^{-1} with normal saline, to measure the urethral pressure profile. We assessed the first sensation, maximum cystometric capacity (MCC), bladder compliance, DO, voided volume, postvoid residual urine, maximum flow rate (Q_{max}), watt factor maximum (WF_{max}), maximum urethral closure pressure (MUCP) and functional length of the urethra according to the standard criteria described in a previous study.[14]

Statistical analyses

All statistical analyses were performed using StatView 5.0 software (Abacus Concepts, Inc., Berkley, CA, USA). Differences in several parameters according to the presence of baseline DO were compared using the chi-square test or Student's *t*-test. Forward stepwise logistic regression analysis was conducted to determine the association between several parameters and postoperative urinary continence status. $P < 0.05$ was considered as significant.

RESULTS

Prior to RARP, all patients were judged to show urinary continence, and DO, which was defined as the involuntary detrusor contractions during the filling phase at any time prior to "permission to void" being given, was detected in 30 (35.7%) of the 84 patients by urodynamic studies. **Table 1** summarizes several demographic and urodynamic parameters in the 84 patients according to the presence of preoperative DO. The proportion of patients with DO was significantly higher in elderly patients or those with a large prostate. Despite the lack of a significant difference in the first sensation between patients with and without baseline DO, the MCC and bladder compliance in patients without DO were significantly greater than in those with DO. In addition, the voided volume in patients without DO was significantly greater than that in those with DO, and WF_{max} in patients without DO was significantly smaller compared to that in those with DO; however, there were no significant differences in the postvoid residual urine and Q_{max} between these two groups. As for the parameters reflecting the urethral pressure profile, including MUCP and functional length, there were no significant differences between the two groups.

Table 1: Comparison of demographic and urodynamic factors according to the presence of preoperatively detectable detrusor overactivity

Variables	*Detrusor overactivity*		
	Negative (n=54)	*Positive (n=30)*	*P*
Age (year)*	64.4±5.8	67.1±6.1	0.016
Prostate volume (ml)*	26.4±12.6	35.1±24.6	0.029
Prostate-specific antigen (ng ml^{-1})	8.4±4.2	10.7±7.5	0.31
Nerve-sparing procedure			
Negative	29	14	0.54
Positive**	25	16	
First sensation (ml)*	196.2±67.2	170.6±53.3	0.16
Maximum cystometric capacity (ml)*	391.1±114.8	292.7±92.0	<0.001
Bladder compliance (ml per cm H_2O)	49.8±30.1	33.4±18.0	0.012
Voided volume (ml)*	330.8±160.7	251.4±103.0	0.035
Postvoid residual urine (ml)*	87.4±112.4	57.8±81.1	0.24
Maximum flow rate (ml s^{-1})*	8.6±4.6	9.1±4.2	0.59
Watt factor maximum (μw m^{-2})*	15.3±10.5	20.6±11.6	0.016
Maximum urethral closure pressure (cm H_2O)*	89.2±32.1	82.5±19.8	0.41
Functional length of urethra (cm)*	5.7±1.3	5.7±1.1	0.70
Urinary continence status 1 month after surgery			
Continence	24	5	0.010
Incontinence	30	25	
Urinary continence status 3 months after surgery			
Continence	37	13	0.024
Incontinence	17	17	

*Mean±standard deviation; **Including 7 and 34 patients undergoing unilateral and bilateral nerve-sparing procedures, respectively

Of the 84 patients included in this study, 55 (65.5%) and 34 (40.5%) were judged to be incontinent 1 and 3 months after RARP, respectively. As shown in **Table 1**, the incidences of incontinence in patients with preoperative DO were significantly greater than in those without preoperative DO at both 1 and 3 months after RARP.

We then assessed the significance of several preoperatively available parameters as predictors of the postoperative continence status using uni- and multi-variate analyses. At both 1 and 3 months after RARP, univariate analysis identified DO and MUCP as significant predictors of the continence status (**Table 2**). Furthermore, these two significant factors appeared to be independently associated with the continence status at both 1 and 3 months after RARP on multivariate analysis (**Table 2**). As shown in **Table 3**, when the 84 patients were classified into three groups according to the positive numbers of two independent risk factors of postoperative urinary incontinence (i.e., negative for risk factor *vs* positive for a single risk factor *vs* positive for two risk factors), there were significant differences in the continence status at both 1 and 3 months after RARP among these three groups.

Table 2: Uni- and multi-variate analyses of several factors predicting postoperative recovery of urinary continence status

Variables	*1 month after surgery*				*3 months after surgery*			
	Univariate analysis		*Multivariate analysis*		*Univariate analysis*		*Multivariate analysis*	
	OR	*P*	*OR*	*P*	*OR*	*P*	*OR*	*P*
Age*	0.84	0.40	-	-	0.69	0.49	-	-
Prostate volume*	1.26	0.21	-	-	0.99	0.32	-	-
Prostate-specific antigen*	0.10	0.92	-	-	0.89	0.37	-	-
Nerve-sparing procedure	1.14	0.26	-	-	0.70	0.48	-	-
First sensation*	1.60	0.11	-	-	1.28	0.21	-	-
Maximum cystometric capacity*	1.40	0.17	-	-	0.37	0.72	-	-
Bladder compliance*	0.82	0.42	-	-	1.83	0.070	-	-
Detrusor overactivity*	3.04	0.0029	2.95	0.0042	2.30	0.024	2.09	0.040
Voided volume*	0.86	0.39	-	-	0.52	0.61	-	-
Postvoid residual urine*	0.31	0.76	-	-	0.46	0.65	-	-
Maximum flow rate*	0.15	0.88	-	-	0.68	0.50	-	-
Watt factor maximum*	0.52	0.60	-	-	0.44	0.66	-	-
Maximum urethral closure pressure*	2.67	0.0091	2.57	0.012	2.31	0.023	2.11	0.038
Functional length of urethra*	1.21	0.23	-	-	0.99	0.33	-	-

*Cut-off level of each variable was determined based on its median value in 84 patients included in this study. OR: odds ratio

Table 3: Impact of positive numbers of independent risk factors for urinary incontinence on postoperative continence status

Positive independent risk factors (%)	*1 month after surgery*			*3 months after surgery*		
	Continence	*Incontinence*	*P*	*Continence*	*Incontinence*	*P*
0	17 (56.7)	13 (43.3)	0.0035	24 (80.0)	6 (20.0)	0.013
1	10 (27.0)	27 (73.0)		19 (51.4)	18 (48.6)	
2	2 (11.8)	15 (88.2)		7 (41.2)	10 (58.8)	

DISCUSSION

Radical prostatectomy has been widely regarded as a standard treatment for patients with clinically localized prostate cancer;[1] however, despite the excellent oncological outcomes, RP results in the induction of marked changes in the urinary function, including the urinary continence status, particularly during the early postoperative period.[2] It is currently recognized that multiple factors are involved in the early recovery of the continence status following RP; however, the significance of lower urinary tract symptoms as risk factors of postoperative incontinence has not been fully elucidated.[15] Furthermore, to the best of our knowledge, no study has assessed the significance of urodynamic parameters in the recovery of urinary continence in patients undergoing RARP. In this study, therefore, urodynamic studies were preoperatively performed in a total of 84 consecutive patients with clinically localized prostate cancer who were treated with RARP, and the association between these outcomes and the continence status early after RARP was investigated.

In this study, we focused on DO, which is characterized by the occurrence of involuntary detrusor contractions of variable amplitude and duration during filling cystometry, among several urodynamic parameters, since there have been several studies suggesting the negative impact of preoperatively detectable DO on the recovery of urinary continence following open RP.[6–8] For example, Dubbelman *et al*.[8] have reported that DO was preoperatively present in 34.0% and 5.3% of patients who were still incontinent and those who regained continence 6 months after open RP, respectively.[8] In this series consisting of patients undergoing RARP, the presence of baseline DO was also shown to be significantly associated with the impaired recovery of the continence status early after surgery, despite the lack of significant association between the degrees of DO and incontinence at both 1 and 3 months (data not shown). Furthermore, patients with baseline DO appeared to have additional urodynamic factors, including low bladder compliance and high WF_{max}, which could adversely affect the continence status after RP. Collectively, these findings suggest that patients without preoperatively observed DO may have less bladder outlet obstruction as well as bladder damage, and therefore, a better regenerative bladder capacity after RP, regardless of the surgical approach.

It is of interest to identify useful urodynamic factors for predicting the continence status following RARP. In this series, the association between several urodynamic factors and the postoperative recovery of urinary continence was analyzed, and preoperative DO and MUCP were identified as independent predictors of the continence status after RARP on multivariate analysis. As described above, the significance of DO as a predictor of urinary continence after open RP has been recognized,[6–8] while there have also been several studies showing that the preoperative MUCP in patients who regained continence after open RP was significantly higher than in those who remained incontinent after surgery.[7,8,15] To the best of our knowledge, however, this is the first study to identify urodynamic parameters independently associated with the recovery of the continence status in patients undergoing RARP.

It is difficult to obtain precise information on the recovery of continence in patients undergoing RP using preoperatively available parameters, since the postoperative continence status is markedly affected by factors associated with the surgical technique as well.[16] However, on simultaneously considering DO and low MUCP, two independent urodynamic risk factors identified in this series, it becomes possible to make a relatively accurate prediction of the continence status during the period early after RARP; that is, 88.2% of patients positive for both risk factors remained incontinent 1 month after RARP, while 80.0% of patients without both risk factors regained continence 3 months after RARP. Furthermore, the significance of simultaneous consideration of these two factors could be suggested by the almost similar distribution of patients positive for a single risk factor to continence status at both 1 and 3 months after RARP (data not shown). Accordingly, it is recommended to routinely perform urodynamic investigation in patients who are scheduled to be treated with RP to obtain comprehensive information on postoperative lower urinary tract symptoms, including the urinary continence status, despite the invasiveness of urodynamic examinations.

Here, I would like to emphasize several limitations of this study. Firstly, this was a retrospective study, and a sample size of 84 patients for such a common disease like prostate cancer is not large enough to draw definitive conclusions on the issues described in this study. In particular, the usefulness of simultaneous assessment of DO and MUCP in the prediction of continence recovery should be prospectively validated. Secondly, the definition of postoperative urinary continence varies among several studies. If no pad use would be defined as continence in this series, it becomes difficult to perform a suitable statistical analysis due to the small number of continent patients, especially that 1 month after RARP. In addition, we assessed the effects of urodynamic parameters on the continence status early after surgery

alone. Therefore, it might be difficult to apply the present findings to the entire cohort of patients undergoing RARP with a long-term follow-up period. Finally, the 84 patients included in this study received RARP immediately after the introduction of the da Vinci® robot system into our institution; hence, despite diverse outcomes of urinary continence recovery after RARP even in high volume centers,[9] it can be expected that the current outcomes, including postoperative continence recovery, would be improved after the accumulation of experience with robotic surgery.

CONCLUSIONS

These findings suggest that DO observed by preoperatively performed urodynamic studies was closely associated with several factors negatively involved in the recovery of the urinary continence status in patients undergoing RARP in the early postoperative period, and that there was a significantly negative impact of the presence of baseline DO on the continence status early after RARP. Moreover, further refinement of the system predicting the postoperative continence status could be achieved by the combined assessment of DO and MUCP, identified as an independent risk factors of urinary incontinence following RARP.

AUTHOR CONTRIBUTIONS

AY designed the study, analyzed the data and wrote the paper. HM supervised the project and wrote the paper. KT analyzed the data and performed the statistical study. MF supervised the project.

COMPETING INTEREST

The authors have no competing interests.

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