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Impact of bladder neck angle measured by postoperative magnetic resonance imaging on mid-term recovery of urinary continence in prostate cancer patients undergoing robot-assisted radical prostatectomy

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Running Title: bladder neck angle and incontinence after RARP

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Abstract

Introduction: Magnetic resonance imaging (MRI) has helped clarify the relationship between pelvic anatomical structures and functional outcomes after robot-assisted radical prostatectomy (RARP). The objective of this study was to assess the impact of the bladder neck angle (BNA) measured by postoperative MRI on mid-term recovery of urinary continence (UC) in patients undergoing RARP.

Methods: This study retrospectively included 200 consecutive patients with prostate cancer who were treated by RARP and received MRI 3 months after RARP. Based on postoperative MRI, the BNA was measured as the angle between the anterior and posterior bladder walls. The mid-term recovery of UC was defined as the use of either no pad or an occasional security pad at 6 months after RARP.

Results: 144 of the 200 patients (72.0%) achieved mid-term recovery of UC and the median BNA was 70°. The were no significant differences in several parameters, including age, body mass index, total prostate volume, preservation of the neurovascular bundle, and postoperative membranous urethral length (MUL), between patients with BNA ≥70° and <70°. Of these parameters, only the BNA and postoperative MUL were independently associated with the mid-term recovery of UC. The optimal cutoff points of the BNA and MUL (65° and 9 mm, respectively) were calculated by the receiver operating characteristics curve, and a scoring model for the prediction of mid-term recovery of UC was developed according to the logistic regression analysis. This scoring model was demonstrated to be satisfactorily calibrated (p for Hosmer-Lemeshow test = 0.49) and provide good discrimination (area under the curve: 0.723; p <0.001).

Conclusions: These findings suggest that mid-term recovery of UC after RARP is favorably affected by the large BNA and long postoperative MUL, and our scoring model can be used as a reliable tool for predicting the mid-term continence status after RARP.

Introduction

The introduction of prostate-specific antigen testing into routine clinical practice has enabled the diagnosis of prostate cancer at younger ages and earlier stages, resulting in a significant increase in potential candidates for radical prostatectomy (RP), the most prevalent curative therapy for clinically organ-confined prostate cancer.[1] Accordingly, it has become important to provide optimal management for adverse events (AEs) caused by RP, particularly those with negative impacts on postoperative functional outcomes.[2]

Of several AEs after RP, urinary incontinence is one of the most distressful complications, which usually has a markedly negative effect on the postoperative quality of life.[3] This remains true even after the wide spread of robot assisted RP (RARP), which enables surgeons to perform precise operations that preserve key anatomic structures affecting the achievement of favorable postoperative functional outcomes, including urinary continence (UC).[4] This may be explained, at least in part, by the involvement of multiple factors in postoperative continence status; that is, urinary incontinence after RP is mainly due to injury of the external urethral sphincter during surgery, but demographic factors, such as the age, body mass index, prostate size, and membranous urethral length, are also closely associated with the recovery of postoperative UC.[5-8]

In this study, we therefore focused on the bladder neck angle (BNA), measured by postoperative magnetic resonance imaging (MRI) as the angle between the anterior and posterior bladder walls, and retrospectively analyzed the impact of the BNA and other parameters on mid-term recovery of UC in 200 consecutive prostate cancer patients undergoing RARP in order to develop a reliable model for predicting the mid-term continence status after RARP.

Patients and Methods

Patients

A total of 220 patients with prostate cancer underwent RARP at out institution between November 2016 and July 2019. Of these, 200 who underwent pelvic MRI 3 months after RARP and did not receive salvage radiotherapy or androgen deprivation therapy during the period of postoperative evaluation for UC were retrospectively enrolled in this study. All data used in this study were obtained from the medical records of each patient, including recovery of UC, defined as the use of either no pad or an occasional security pad at 6 months after RARP, which was evaluated based on findings on the Expanded Prostate Cancer Index Composite (EPIC) survey questionnaire as well as detailed interview to each patient. The design of the study was approved by the research ethics committee of our institution, and the need to obtain informed consent from the patients was waived because of its retrospective design.

Surgical technique

At our institution, RARP is performed employing a four-arm da Vinci Xi™ surgical system (Intuitive Surgical Inc., Sunnyvale, CA, USA) via a transperitoneal approach, as previously described,[9] by a total of five surgeons, consisting of one with the experience of RARP for >500 patients and the remaining four with that <100 patients. Briefly, an anterior approach was adopted by initially dissecting the bladder neck. After mobilization of the seminal vesicles, the prostatic vascular pedicles were ligated, followed by removal of the prostate. As a rule, preservation of the neurovascular bundle on the negative side on needle biopsy was performed by interfascial dissection into the avascular plane between the prostatic capsule and Denonvilliers' fascia. Posterior reconstruction of the rhabdomyosphincter was routinely conducted and vesicourethral anastomosis was carried out as reported by Van Velthoven et al.[10] Approximately 5 days after RARP, the indwelling urethral catheter was removed when cystography confirmed the absence of urinary leakage from the vesicourethral anastomosis.

Postoperative assessment by MRI

In this series, pelvic MRI examinations were performed 3 months after RARP for all included patients approximately 2 hours after urination using a 3.0-Tesla whole-body magnetic resonance scanner (Discovery MR750w 3.0T, GE Healthcare, Hino, Japan). Based on MRI findings, two anatomic parameters were independently evaluated by two urologists who were blinded to all other clinicopathological findings. The values of each parameter were measured as follows: BNA, the angle between two lines originating from the bladder-urethral anastomosis along the anterior and posterior bladder walls; and membranous urethral length (MUL), the mean distance from the bladder neck to entry of the urethra at the penile bulb between the sagittal and coronal MRI planes. Representative images of these two parameters are shown in Fig. 1.

Statistical analysis

Differences between the two groups divided by the median value of the BNA were compared by the Mann-Whitney U test. Logistic regression analysis was carried out to determine the predictors of mid-term recovery of UC by the multivariate analysis of parameters judged to be P <0.15 based on univariate analyses of all extracted parameters. To develop a predictive model of the mid-term recovery of UC, independent factors identified by logistic regression analysis were dichotomized based on the optimal cutoff value on the receiver operating characteristics (ROC) curves, and point values of these factors were generated according to the regression coefficients for each factor. To validate the performance of the predictive model involving their point values, the Hosmer-Lemeshow test was used for calibration and the discrimination was assessed using area under the curve (AUC), as previously described.[11, 12] In this study, MedCalc® (version 13.0.2.0) was used for all statistical analyses, which were two-sided, and P-values < 0.05 were considered significant.

Results

Initially, the BNA was measured based on postoperative MRI and its median value was 70° (range, 40-103°). Several patient characteristics expected to affect the postoperative recovery of UC, including age, body mass index (BMI), total prostate volume, preservation of the neurovascular bundle, and postoperative MUL, according to median value of the BNA are presented in Table 1. There were no significant differences in all factors between patients with a BNA ≥70° and those with a BNA <70°.

Of the 200 included patients, 144 were judged to be continent 6 months after RARP; thus, the mid-term recovery rate of UC in this series was 72.0%. We then analyzed the impact of several potential predictors, including the BNA, on the mid-term recovery of UC. As shown in Table 2, age, BMI, postoperative MUL, and BNA had P-values <0.15 by univariate analyses, and multivariate analyses of these four parameters identified only postoperative MUL and BNA as independent predictors of mid-term recovery of UC after RARP.

The optimal cutoff points of the postoperative MUL and BNA were assessed using ROC curves. The AUCs were 0.747 (95% confidence interval, 0.68-0.80; cutoff value, 9 mm; P <0.001) and 0.672 (95% confidence interval, 0.60-0.74; cutoff value, 65°; P <0.001) for the postoperative MUL and BNA, respectively. Based on the cutoff points, point values of the postoperative MUL and BNA as predictors of mid-term recovery of UC after RARP were generated from the regression coefficients for these two parameters. As shown in Table 3, optimal scores for the postoperative MUL (≥9 mm) and BNA (≥65°) were 2 and 1, respectively.

The usefulness of the developed scoring model was finally investigated by calculating the total points in each patient. The calibration plot of observed and predicted rates of mid-term recovery of UC is shown in Fig. 2A, and the P-value by the Hosmer-Lemeshow test was 0.49. Furthermore, the ROC curve of this scoring model revealed an AUC of 0.723 (95% confidence interval, 0.66-0.78; cutoff value, ≥2; P <0.001) (Fig. 2B), with a sensitivity and specificity of 72.2 and 64.3%, respectively.

Discussion

Recovery of UC after RP was reported to be affected by numerous anatomical and demographic factors, and modifications of surgical techniques, although there is a lack of established predictive factors.[5-8] Among these, morphological changes in the lower urinary tract after RP may have a significant impact on the postoperative continence status due to the induction of substantial anatomical changes caused by removal of the prostate, and subsequent anastomosis of the urethra and bladder neck. Recent progresses in anatomical studies of pelvic structure have led to increased understanding of the urinary continence mechanism with the widespread use of MRI. It seems to be commonly acceptable that longer pre- and postoperative MUL is significantly and positively associated with recovery of UC[13-15], since the report by Myers et al initially describing MUL after RP to assess postoperative urinary continence.[16, 17] Furthermore, considering well controlled preoperative urinary continence in the majority of patients regardless of the length of

MUL, it could be assumed that postoperative dramatic changes in the bladder shape have a significant effect on urinary continence. During daily clinical practice regarding RARP, we noted a wide distribution in the postoperative BNA among patients undergoing RARP; therefore, we assessed the impact of this newly introduced anatomical parameter, in addition to several conventional factors, on the mid-term recovery of UC in 200 patients undergoing RARP.

In this series, all included patients underwent a detailed interview survey regarding the continence status to provide accurate data. As a result, the proportion of patients who were mid-term continent 6 months after RARP was 72.0%, which is comparatively lower than that in previous studies.[18] This may be explained by many reasons in addition to the strict survey in this series, such as the involvement of multiple surgeons, including those without sufficient experience in robotic surgery.

In this series, we focused on a novel anatomical parameter, BNA, defined as the angle between the anterior and posterior bladder walls, and it was easily measured based on postoperative MRI in each patient. The median value of the BNA among the 200 included patients was 70°; however, there were no significant differences in several parameters expected to affect the postoperative recovery of UC between patients with a BNA ≥70° and those with a BNA <70°, suggesting that BNA may be unlikely to be influenced by other factors. Furthermore, a BNA was identified as one of the independent parameters predicting the mid-term recovery of UC after RARP. To date, there have been several studies showing close correlation between urinary continence and the location of vasicourethral anastomosis, which can be easily assessed by cystography findings [19, 20]. Although the position of vesicourethral anastomosis may be affected by the MUL rather than BNA considering pelvic anatomical features after RP, it will be of interest to analyze the association among various anatomical parameters in order to objectively select candidate factors for predicting postoperative UC status.

In recent years, with widespread understanding of the anatomical structures in the pelvis, several surgical techniques have been reported. For example, Rocco et al demonstrated that posterior reconstruction dramatically shortens the recovery period of UC,[21] while Tewari et al reported the importance of total reconstruction of the vesicourethral junction.[22] However, the BNA measured in this study seems to be a patient-specific factor that strongly depends on the shape of the pelvic cavity; therefore, it remains unknown whether BNA could be changed by surgical techniques. However, Kojima et al. reported that a bladder neck sling during RARP improved the return of UC by reducing the posterior urethrovesical angle,[23] which may result in the increase in BNA.

Although the structural changes in the pelvis seem to be fixed at least 3 months after RARP, urinary incontinence can be further improved within 6 months after RARP, and stabilize between 6 and 12 months after RARP; therefore, we evaluated UC status 6 months after RARP, and identified the BNA and postoperative MUL as independent predictors of mid-term recovery of UC. In also the assessments of early recovery of UC, the BNA and postoperative MUL in addition to age were shown to be independently associated with UC status 3 months after RARP (data not shown). Collectively, these findings suggest that despite significant advantage of younger age in early recovery of UC, BNA and postoperative MUL may have potential impacts of UC status in patients undergoing RARP throughout postoperative period. However, the remaining potential factors, including, BMI, total prostate volume, and preservation of the neurovascular bundle, had no independent effects on the recovery of UC. Indeed, the controversial effects of these factors on postoperative continence status were reported in previous studies.[20, 24]

A model system to predict whether patients undergoing RARP can achieve the mid-term recovery of UC using the two independent parameters identified in this study was designed. Accordingly, optimal cutoff points of the postoperative MUL and BNA were calculated using ROC, and point values were determined based on the regression coefficients for these two parameters, resulting in the development of a new scoring model, which was satisfactorily calibrated and provided good discrimination. As these two objective parameters can be easily measured, further evaluation of the usefulness of this model in a prospective setting is warranted.

Several limitations of this study must be mentioned. First, this was a retrospective study with an insufficient sample size at a single institution, thus our findings should be supported using data from other cohorts. Secondly, although the status of continence was evaluated using a self-reported questionnaire, it might be suitable to conduct 24-hour pad weight test to more accurately assess the degree of urinary incontinence. Lastly, although representative parameters were evaluated in this study, the usefulness of many other potential parameters as predictors of the recovery of UC has been reported.[19,20,25] Therefore, more parameters should be included to further improve the ability of the present system to predict the postoperative continence status.

Conclusions

This study assessed the outcomes of 200 prostate cancer patients undergoing RARP, and found that mid-term recovery of UC after RARP was independently associated with the large BNA and long postoperative MUL. Furthermore, we developed a scoring model for the prediction of continence status mid-term after RARP using these two anatomical parameters, which will help to estimate the postoperative outcomes of UC recovery and relieve emotional stress concerning the continence status after RARP.

Disclosure Statement

No competing financial interests exist.

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Abbreviations Used

MRI = Magnetic resonance imaging

RARP = robot-assisted radical prostatectomy

BNA = bladder neck angle

UC = urinary continence

MUL = membranous urethral length

RP = radical prostatectomy

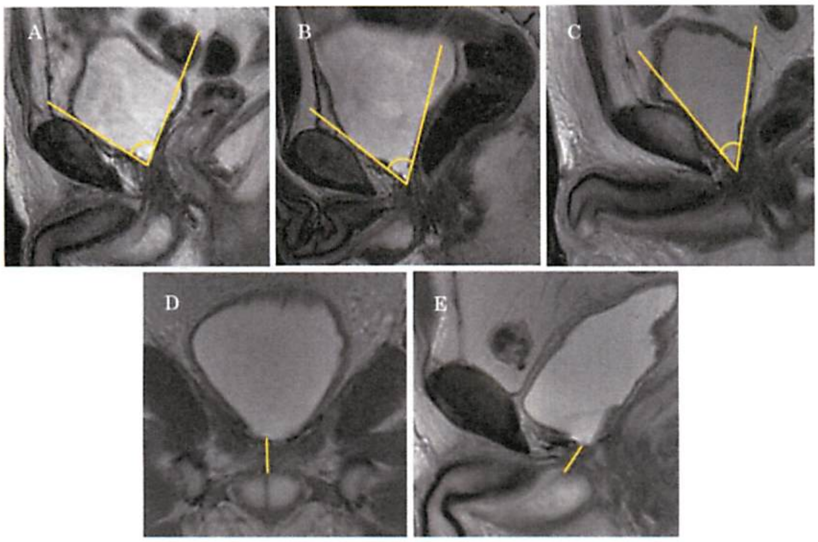
AEs = adverse events

ROC = receiver operating characteristics

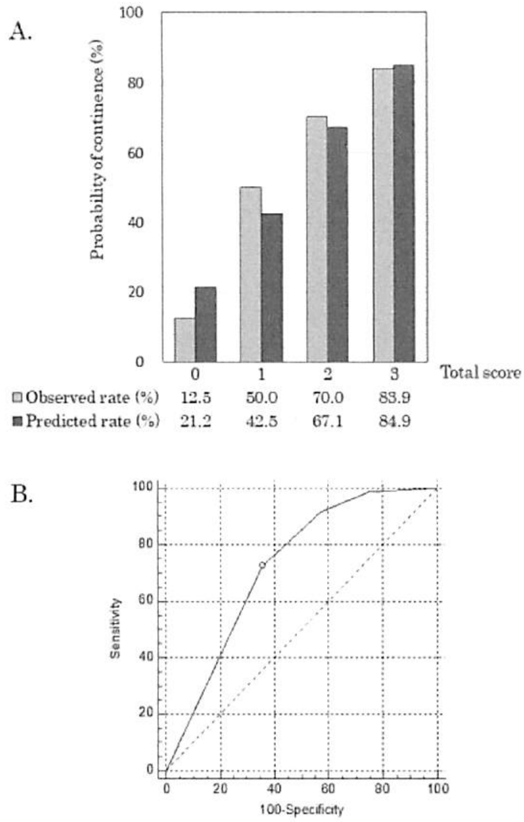
AUC = area under the curve

BMI = body mass index

Figure Legends



ItoFig 1. Representative bladder neck angle (BNA) and membranous urethral length (MUL) postoperatively assessed by magnetic resonance imaging. (A) BNA = 77° (B) BNA = 70° (C) BNA = 51° (D) MUL on the coronal plane = 10 mm (E) MUL on the sagittal plane = 9 mm



ItoFig 2. (A) Calibration plot of observed and predictive rates of patients with recovery of urinary continence 6 months after robot-assisted radical prostatectomy according to the scoring model developed in this study. P = 0.49 by the Hosmer-Lemeshow test. (B) Receiver operating characteristics curve of the scoring model developed in this study. Area under the curve = 0.723 (95% confidence interval, 0.66-0.78; cutoff value, ≥2; P <0.001).

Table 1. Patient characteristics regard with correlation between the BNA and clinical parameters

Parameter		BNA≥70°	BNA<70°	P
Age, years (range)		70 (42-78)	68 (47-80)	0.22
BMI, kg/m^2 (range)		24.0 (16.0-30.0)	24.0 (17.0-31.0)	0.12
Total prostate volume, mL (range)		26.8 (10.0-100.0)	27.5 (10.0-171.9)	0.47
Nerve preservation, n (%)	none	22 (11.0)	21 (10.5)	0.62
	unilateral or bilateral	87 (43.5)	70 (35.0)	
postoperative MUL, mm (range)		12.0 (5.0-19.0)	11.0 (6.0-18.0)	0.083

BNA, bladder neck angle: BMI, body mass index: MUL, membranous urethral length

Table 2. Predictive factors of urinary continence 6 months after surgery

	Univariate			Multivariate		
	OR	95% CI	P	OR	95% CI	P
Age	0.95	0.90 to 1.01	0.100	–	–	–
BMI	0.89	0.80 to 0.99	0.026	–	–	–
TPV	0.99	0.98 to 1.01	0.29			
NVB preservation	1.15	0.55 to 2.40	0.71			
postoperative MUL	1.47	1.27 to 1.74	<0.0001	1.47	1.23 to 1.71	<0.0001
BNA	1.06	1.03 to 1.09	0.00010	1.05	1.02 to 1.09	0.0016

OR, odds ratio; CI, confidence interval; BMI, body mass index; NVB, neurovascular bundle; MUL, membranous urethral length; TPV, total prostate volume; BNA, bladder neck angle

Table 3. Optimal scores for postoperative MUL and BNA in the final predictive model

	Coefficient	OR	95% CI	P	Score
postoperative MUL (≥ 9 mm)	1.9889	7.45	3.30 to 16.3	<0.0001	2
BNA (≥ 65°)	1.0054	2.84	1.38 to 5.83	0.004	1

MUL, membranous urethral length; BNA, bladder neck angle, OR, odds ratio; CI, confidence interval