The Association of Length of the Resected Membranous Urethra With Urinary Incontinence After Radical Prostatectomy

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Purpose: To retrospectively determine whether recovery of urinary continence after radical prostatectomy is associated with the preoperative length of membranous urethra (MU), the amount of rhabdosphincter and the length of MU removed with the prostate.

Materials and Methods: The study cohort comprised 179 consecutive patients who underwent laparoscopic radical prostatectomy (LRP: n = 98) and robot-assisted radical prostatectomy (RARP: n = 81) at Wakayama Medical University between July 2010 and May 2014. The length of MU was measured by preoperative MRI. The amount of resected rhabdosphincter and the length of resected MU were assessed in hematoxylin and eosin sections at the apical margin of prostate specimens. Patient-reported urinary continence status was determined at 3, 6, 12 and 24 months postoperatively, with urinary continence considered as 0-1 pads/day. Kaplan-Meier analysis and the log-rank test were used to compare time to urinary continence recovery. Multivariate Cox regression analyses were performed to determine the predictors of urinary continence.

Results: RARP vs LRP ($p = 0.02$) and shorter length of resected MU ($p = 0.01$) showed significantly better postoperative continence recovery by log-rank test. Nerve-sparing, preoperative length of MU, and amount of resected rhabdosphincter did not significantly correlate with continence recovery. Only the length of resected MU was the independent factor for predicting postoperative urinary continence by multivariate Cox regression analysis (hazard ratio 0.84, $p = 0.01$).

Conclusion: These results demonstrated that the length of resected MU measured by specimen was an independent predictor of urinary incontinence after radical prostatectomy. Care should be taken to preserve maximal length of MU for optimal continence outcomes.

Keywords: Membranous urethral length; Radical Prostatectomy; Urinary Incontinence

INTRODUCTION

Radical prostatectomy is a standard treatment option for localized prostate cancer. Although oncological outcome of radical prostatectomy is fairly satisfactory, postoperative complications including urinary incontinence and erectile dysfunction still remain problems to be solved[1]. Among them, urinary incontinence is a nuisance which affects patient's daily life and quality of life (QOL) directly.

Numerous factors are involved in postoperative urinary continence recovery. Firstly, patient's background including age, comorbidity, body mass index, history of prostate surgery and prostate size should be considered[2-4]. Second, surgical techniques of radical prostatectomy are other considerably important factors. Techniques for improving postoperative urinary incontinence are classified into 2 categories[5,6]. One is a preservation of the anatomical structure related to urinary continence including bladder neck, neurovascular bundle, puboprostatic ligament, rhabdosphincter and membranous urethra, and the other is a reconstrcution of the destroyed structure such as posterior reconstruction of rhabdosphincter (Rocco's stitch) and periurethral suspension stitch. Types of surgery are another concern, i.e. open radical prostatectomy (ORP), laparoscopic radical prostatectomy (LRP) or robot-assisted radical prostatectomy (RARP). Although recent systematic review and meta-analysis showed significantly better urinary continence rate at 12 month in RARP compared to RRP and LRP[7], clear conclusion has not been drawn yet.

In this study, we investigate whether factors concerning membranous urethra (MU) and rhabdosphincter might influence postoperative urinary incontinence using preoperative magnetic resonance imaging (MRI) and resected prostate specimens.

PATIENTS AND METHODS

Patients

The cohort of this retrospective study comprised 179 consecutive patients who underwent LRP (n = 98) and RARP (n = 81) at Wakayama Medical University between July 2010 and May 2014. Indications for radical prostatectomy were as follows; (1) age under 75,

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Table 1. Patient characteristics stratified by surgery (LRP vs RARP)

	Total	LRP	RARP	*p* = (LRP vs. RARP)
No. patients (%)	179	98 (54.7)	81 (45.3)	
Age, year	67(63 – 71)	68 (63 – 72)	67 (64 – 71)	0.94
PSA, ng/mL	8.0 (5.9 – 11.0)	8.1 (5.9 – 12.3)	7.7 (5.9 – 10.1)	0.42
Biopsy Gleason score, n (%)				0.13
≤ 6	50 (27.9)	28 (28.6)	22 (27.2)	
7	74 (41.3)	41 (41.8)	33 (40.7)	
≥ 8	55 (30.7)	29 (29.6)	26 (32.1)	
cT stage, n (%)				0.22
T1c	82 (45.8)	49 (50.0)	33 (40.7)	
T2	90 (50.3)	47 (48.0)	43 (53.1)	
T3a	7 (3.9)	2 (2.0)	5 (6.2)	
Nerve preservation, n (%)	80 (44.7)	18 (18.4)	62 (76.5)	< 0.01
Length of MU – preoperative MRI, mm	17.3 (14.6 – 19.7)	17.5 (14.9 – 19.3)	17.1 (14.5 – 19.8)	0.63
Amount of resected rhabdosphincter – pathology specimen, %	31.7 (25.0 – 40.0)	30.0 (25.0 – 40.0)	34.2 (25.8 – 42.1)	0.13
Length of resected MU – pathology specimen, mm	1.2 (0.5 – 2.0)	1.1 (0 – 2.1)	1.2 (0.6 – 2.0)	0.42

(2) PSA less than 20ng/ml and (3) cT1-2 or cT3a only when the extracapsular invasion was minimum. Demographic data were collected from medical chart. This study was approved by the institutional review board of Wakayama Medical University (No. 1670).

Surgical technique

LRP and RARP were performed using a transperitoneal approach according to the standard techniques, which were previously described [8]. Briefly after cutting endopelvic fascia, we transected bladder neck followed by the dissection of seminal vesicle and prostate in an antegrade fashion. Cavernous nerve-sparing was chosen according to the extent of cancer judged by MRI and digital rectal examination. Posterior rhabdosphincter reconstruction and periurethral suspension stich was performed in RARP but not in LRP. Vesicourethral anastomosis was performed with a running suture. While limited lypmphadenectomy was performed in all patients in LRP, extended lymphadenectomy was performed only in high-risk patients in RARP.

Patient reported outcome

To evaluate the status of urinary continence, we used Expanded Prostate Cancer Index Composite (EPIC) questionnaire as patient reported outcome. The Japanese version of EPIC was purchased from iHope International (Kyoto, Japan) and validation study of Japanese version was reported previously[9]. EPIC questionnaire was mailed to each patient periodically (3, 6, 12 and 24 months after operation). Response rates of the questionnaire at 3, 6, 12 and 24 months were 95%, 93%, 87% and 82%, respectively. Urinary continence status was judged from the response to one of the questions in urinary domain of EPIC and patients who wear 0 - 1 pad/day were considered continent.

Measurement of the length of membranous urethra (MU)

All patients had MRI examination before operation. Length of MU was measured on coronal T2-weighted image of preoperative MRI and determined as the distance from prostatic apex to the entry of urethra into penile bulb (**Figure 1, red arrow**).

Measurement of the amount of resected rhabdosphincter and the length of resected MU

A 3-4mm cone of tissue around the urethra at the apex of resected prostate was amputated and divided into left and right halves. Each half was serially sectioned perpendicularly, typically resulting in 3 wedges of tissue from each half. These wedges were embedded in paraffin blocks and standard hematoxylin and eosin sections were made. The length of resected MU was measured in the cross section including urethra (**Figure 2, red arrow**). The amount of resected rhabdosphincter was expressed as the percentage of total apical margin surface area occupied by rhabdosphincter (**Figure 2, blue arrow**), and the overall percentage of resected rhabdosphincter was calculated as average of typically 6 wedges.

These measurements were assessed by two independent uropathologists. When the inter-rater reliability was examined by Pearson correlation coefficient, it showed high agreement ($r = 0.867$, $p < 0.0001$).

Statistical analyses

Clinical data, including age at surgery, preoperative PSA, biopsy Gleason score, cT stage, nerve preservation, length of MU, amount of resected rhabdosphincter, and length of resected MU were compared between LRP and RARP groups by Wilcoxon signed-rank test for continuous variables and chi square test for categorical variables. Kaplan-Meier analysis and the log-rank test were used to compare time to urinary continence recovery and the cumulative incidence of urinary continence at follow-up. The first response to EPIC report-

Table2. Cox regression analysis of factors predictive of urinary continence recovery

	HR	95% CI	*p*
Age (year)	1.00	0.97 – 1.03	0.85
Type of surgery, RARP/LRP	1.37	0.92 – 2.03	0.11
Nerve preservation , Yes/No	1.01	0.67 – 1.51	0.95
Length of MU – preoperative MRI (mm)	1.04	0.99 – 1.09	0.06
Amount of resected rhabdosphincter – pathology (%)	0.99	0.98 – 1.00	0.57
Length of resected MU - pathology (mm)	0.84	0.73 – 0.97	0.01

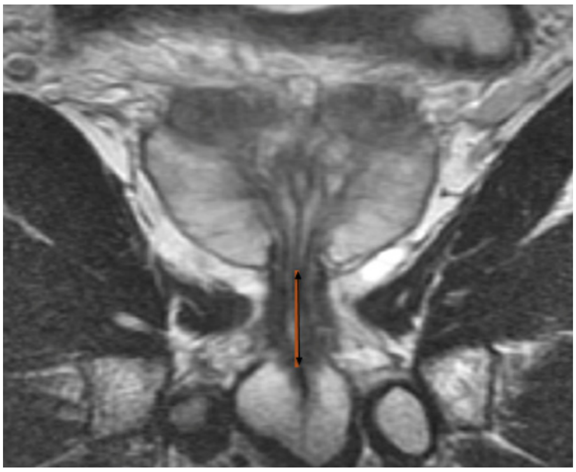

Figure 1. Measurement of the length of membranous urethra (MU). Length of MU was measured on coronal T2-weighted image of preoperative MRI and determined as the distance from prostatic apex to the entry of urethra into penile bulb (red arrow).

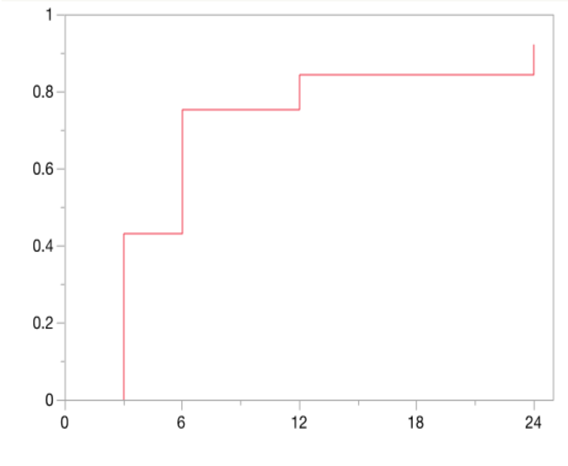

Figure 3. Overall cumulative incidence of urinary continence, defined as 0-1 pad/day, following radical prostatectomy.

ing urinary continence recovery (0 – 1 pad/day) was considered the event at that time. Patients incontinent at their last response were censored at that time. Multivariate Cox regression analyses were performed to determine the predictors of urinary continence recovery time. Clinically important or previously reported variables (age, type of surgery, nerve preservation, length of MU, amount of resected rhabdosphincter and length of resected MU) were included in the model. Proportional hazards assumption was confirmed by plotting Schoenfeld residuals and the fitness of the model was estimated by likelihood ratio test. In addition, multicollinearity of the model was assessed using variance inflation factor. Data analyses were conducted by using the statistical software JMP Pro 12 (SAS Institute, Cary, USA). All p-values were 2 tailed, and $p < 0.05$ was defined as statistically significant.

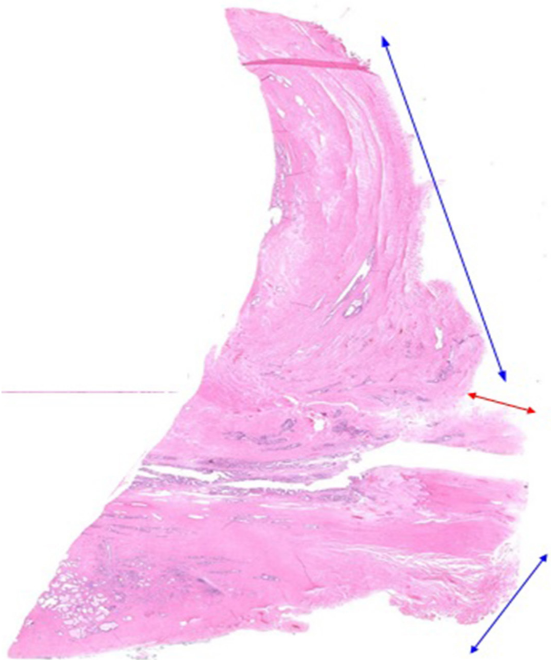

Figure 2. Measurement of the amount of resected rhabdosphincter and the length of resected membranous urethra (MU). The amount of resected rhabdosphincter was expressed as the percentage of total apical margin surface area occupied by rhabdosphincter (blue arrow, 50% in this section) and the overall percentage of resected rhabdosphincter was calculated as average of typically 6 wedges. The length of resected MU was measured in the cross section including urethra (red arrow).

RESULTS

Patients' characteristics

Baseline characteristics for all 179 patients are shown in **Table 1**. Although nerve preservation rate in RARP group (76.5%) was significantly higher than that in LRP group (18.4%), no significant differences were observed between LRP and RARP groups in other variables.

Length of MU, amount of resected rhabdosphinter and length of resected MU

Table 1 shows length of MU, amount of resected rhabdosphinter and length of resected MU. Median length of MU measured by preoperative MRI was 17.3mm (IQR, 14.6 – 19.7). Median amount of resected rhabdosphinter and length of resected MU measured by pathology specimen was 31.7% and 1.2mm, respectively. No significant differences were found between LRP and RARP group in these variables.

Status of urinary continence according to various variables

Figure 3 shows Kaplan-Meier curve representing the percentage of patients achieving urinary continence recovery. The percentage of patients achieving urinary continence recovery after 3, 6, 12 and 24 months was 43.2%, 75.4%, 84.4% and 92.2%, respectively.

Figure 4 (a) shows the same Kaplan-Meier curve according to the type of surgery. Continence rates after 12 months from surgery were 87.8% (RARP) and 81.6% (LRP). RARP showed significantly better continence recovery comparing to LRP (log-rank test, $p = 0.02$).

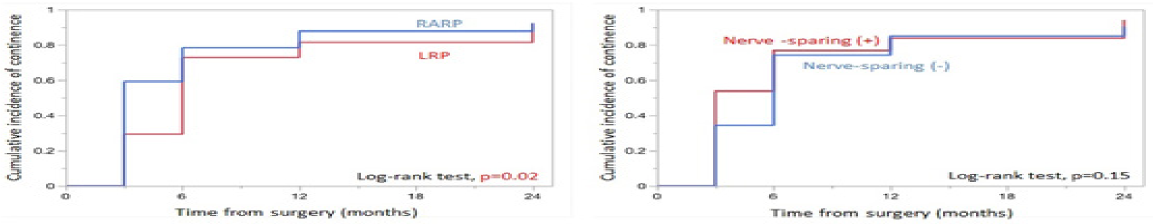

Figure 4. Cumulative incidence of urinary continence following radical prostatectomy stratified by **(a)** type of surgery (RARP vs LRP) and **(b)** nerve-sparing status.

Figure 4 (b) shows the same Kaplan-Meier curve according to nerve-sparing. Continence rates after 12 months from surgery were 83.7% (nerve-sparing (+)) and 84.9% (nerve-sparing (-)). No significant difference was observed between nerve-sparing (+) and nerve-sparing (-) groups (log-rank test, p = 0.15). Figure5 (a) shows the same Kaplan-Meier curve according to the length of MU measured by preoperative MRI. Continence rates after 12 months from surgery were 86.5% (length of MU ≥ 17.3mm) and 81.7% (length of MU < 17.3mm). No significant difference was observed between longer (≥17.3mm) and shorter (< 17.3mm) MU groups (log-rank test, p = 0.20). Figure 5 (b) shows the same Kaplan-Meier curve according to the amount of resected rhabdosphincter. Continence rates after 12 months from surgery were 90.5% (resected rhabdosphincter < 31.7%) and 78.3% (resected rhabdosphincter ≥31.7%). No significant difference was observed according to the amount of resected rhabdosphincter by pathology (log-rank test, p = 0.14). We also compared the apical positive surgical margin (PSM) rates according to the amount of resected rhabdosphincter. Apical PSM rates were 10.3% and 16.3% in the resected rhabdosphincter < 31.7% group and ≥31.7% group, respectively. No statistical significance was observed (chi square test, p = 0.24).

Fig. 5 (c) shows the same Kaplan-Meier curve according to the length of resected MU measured by resected specimen. Continence rates after 12 months from surgery were 88.5% (resected MU < 1.2mm) and 80.2% (resected MU ≥1.2mm). Longer resected MU group (≥ 1.2 mm) showed significantly worse continence recovery comparing to shorter resected MU group (< 1.2 mm) (log-rank test, p = 0.01). We also compared apical PSM rates according to the length of resected MU. Apical PSM rates was 16.9% and 10.0% in the resected MU < 1.2 mm group and ≥1.2mm group, respectively. No statistical significance was observed (chi square test, p = 0.18).

Multivariate analysis determining the factors influencing urinary continence recovery

Table 2 showed Cox regression analysis of factors predicting urinary continence recovery. Only the length of resected MU measured by specimen was independent predictive factor for urinary continence recovery (hazard ratio 0.84, p = 0.01). The length of MU measured by preoperative MU seems to be marginal predictive factor for urinary continence recovery, however the difference did not reach statistically significant (p = 0.06).

DISCUSSION

Postoperative urinary incontinence is most annoying

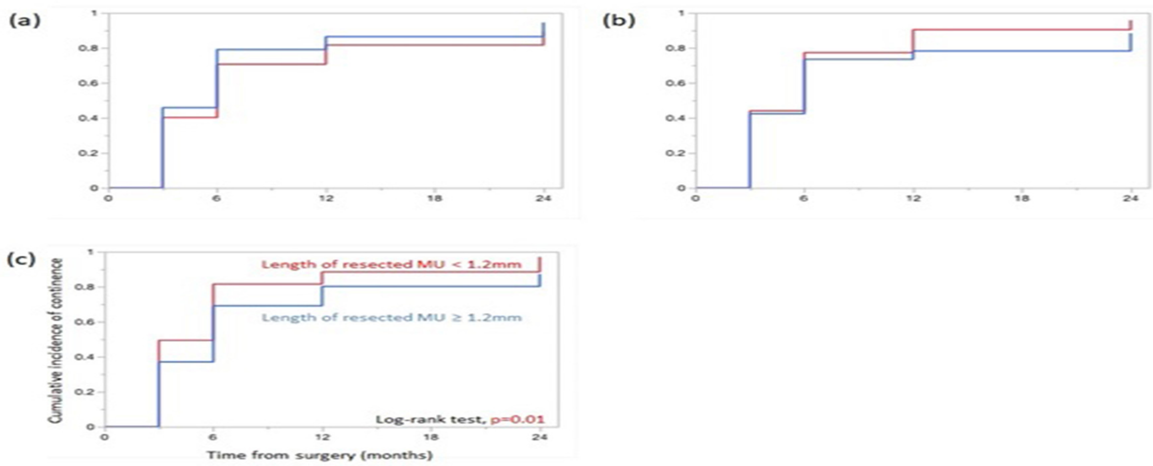

Figure 5. Cumulative incidence of urinary continence following radical prostatectomy stratified by (a) length of membranous urethra (MU) measured by preoperative MRI, (b) amount of resected rhabdoshpincter measured by pathology specimen, and (c) length of resected MU measured by pathology specimen.

complication after radical prostatectomy. Recently, the anatomical mechanism regarding urinary continence in male has been gradually revealed by many vigorous studies[10-13]. Basically, the anatomical mechanism for urinary continence consists of 2 systems; a sphincteric system and a supportive system[5]. The sphincteric system is composed of inner smooth muscle layer (longitudinal and circular smooth muscle) and striated urogenital sphincter muscle (rhabdosphincter). Rhabdosphincter extends from the prostatic apex to the proximal bulbar urethra and considered the most important structure for urinary continence after radical prostatectomy. Strasser et al. showed that the contractility of the remaining rhabdosphincter after transurethral resection of prostate or radical prostatectomy was associated with postoperative urinary incontinence by 3-dimensional ultrasound[14]. The other system is supportive system of pelvic floor surrounding MU and bladder neck. In males, Denonvilliers' fascia, puboprostatic ligament, endopelvic fascia, levator ani muscle and arcus tendinous fascia pelvis correspond to this system. Radical prostatectomy impairs this supportive system inevitably.

In this study, we focused on the sphincteric system in urinary incontinence after LRP and RARP since the sphincteric system is more directly controlling urinary continence than the supportive system is. We selected several measurements concerning the sphincteric system. First one was preoperative length of MU measured by MRI. Paparel et al. demonstrated that both preoperative and postoperative membranous urethral length measured by preoperative and postoperative MRI were correlated with urinary continence status after radical prostatectomy[15]. Unfortunately, we evaluated only preoperative membranous urethral length since we did not examine postoperative MRI. Second, we measured the amount of resected rhabdosphincter histologically using resected prostate specimens. Such evaluation was conducted by Skeldon et al. first[16]. They measured the amount of striated muscle observed in apex of resected prostate specimen and expressed semiquantitatively as percentage of total apex tissue. They showed that the odds of a patient whose resected striated muscle occupied more than 11% of total apex tissue being incontinent was 11.7 times that of a patient whose resected striated muscle occupied less than 10%. We followed their methods exactly in this study. Third, we measured the length of resected MU histologically using resected prostate specimen. To our knowledge, such measurement is firstly tried in this study.

Other variables we analyzed for postoperative urinary incontinence were age[17], type of surgery (RARP/LRP)[7], nerve preservation[18]. All these variables were reported to be significant factors for postoperative incontinence, although negative reports were also observed. We performed Cox regression analysis to identify the most relevant factor for postoperative urinary continence using the above-mentioned variables (age, type of surgery, nerve preservation, length of MU by preoperative MRI, amount of resected rhabdosphincter by pathology, and length of resected MU by pathology). As a result, length of resected MU by pathology was the only independent factor for predicting postoperative urinary continence (**Table 2**). Although it did not reach statistically significant ($p = 0.06$), length of MU by preoperative MRI also showed tendency to predict postoperative urinary continence. Our results are consistent with Paparel's repot[15]. They showed that both preoperative and postoperative membranous urethral length measured by preoperative and postoperative MRI were correlated with urinary continence status after radical prostatectomy. The only difference is that our resected urethral length is an absolute length, whereas Paparel et al. showed the resected urethral length in proportion to the original length of MU.

Another concern is the PSM at the apex of prostate. We wondered if the PSM rate would increase in cases where rhabdosphincter or MU at the apical region of prostate was preserved as much as possible to obtain good urinary continence. However, no significant differences were found in PSM rates according to the amount of resected rhabodsphincter or the length of resected MU.

Limitations of this study were retrospective fashion and the relatively small number of patients. Another limitation is that we could only evaluated the amount of resected rhabdosphincter semi-quantitatively.

In conclusion, length of resected MU was the most important factor to predict urinary incontinence after LRP or RARP. In LRP or RARP, sophisticated manipulation is possible in a magnified field of view with less bleeding. To the extent that we do not sacrifice complete resection of the tumor, we should preserve maximal length of MU to prevent postoperative urinary incontinence.

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