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[Review]

Comprehensive approach for post-prostatectomy incontinence in the era of robot-assisted radical prostatectomy

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Abstract

Robot-assisted radical prostatectomy (RARP) has enabled steady and stable surgical procedures due to both meticulous maneuvers and magnified, clear, 3-dimensional vision. Therefore, better surgical outcomes have been expected with RARP than with other surgical modalities. However, even in the RARP era, post-prostatectomy incontinence has a relatively high incidence as a bothersome complication. To overcome post-prostatectomy incontinence, it goes without saying that meticulous surgical procedures and creative surgical procedures, i.e., “Preservation”, “Reconstruction”, and “Reinforcement” of the anatomical structures of the pelvis, are most important. In addition, medication and appropriate pad usage might sometimes be helpful for patients with post-prostatectomy incontinence. However, patients who have 1) BMI ≥ 26 kg/m², 2) prostate volume ≥ 70 mL, 3) eGFR ≤ 60 mL/min, or a 4) Charlson comorbidity index ≥ 2 have a tendency to develop post-prostatectomy incontinence despite undergoing the same surgical procedures. It is important for patients who have a high risk for post-prostatectomy incontinence to be given information about delayed recovery of post-prostatectomy incontinence. Thus, not only the surgical procedures, but also a comprehensive approach, as mentioned above, are important for post-prostatectomy incontinence.

Key words : robot, prostate cancer, urinary incontinence, lower urinary tract, radical prostatectomy

Introduction

Radical prostatectomy for localized prostate cancer started with the open procedure, progressed to the laparoscopic procedure, and then evolved to the robot-assisted procedure with changing times. Because it is difficult to control bleeding with open radical prostatectomy (ORP), the thrust of ORP is safely removing the prostate by hemostasis of the dorsal vein complex. On the other hand, because laparoscopic radical prostatectomy (LRP) provides magnified, clear vision, it is easier to remove the prostate with it than with ORP. However, after removing the prostate, it is difficult to perform the vesicourethral anastomosis with two-dimensional

vision, except for some skilled surgeons. Hence, although the importance of trifecta and pentapecta were recognized by our urologists, it was hard for them to accomplish the trifecta and pentapecta. In Japan, robot-assisted radical prostatectomy (RARP) has been allowed by the national medical insurance system since 2012. After the introduction of RARP, the number of patients who underwent RARP increased steadily in Japan. Because RARP enabled steady and stable surgical procedures due to both meticulous maneuvers and magnified, clear, 3-dimensional vision, better surgical outcomes have been expected with RARP than with both ORP and LRP.

Post-prostatectomy incontinence has a relative-

ly high incidence as a bothersome complication after radical prostatectomy. Even in the RARP era, because the continence rate is only 17% just after urethral catheter withdrawal in high-volume institutions¹, various trials for early acquisition of urinary continence have been conducted². As mentioned above, because a steady and stable surgical procedure has been enabled under RARP, creative surgical procedures, medication, and physical therapy have become more important for early acquisition of urinary continence in the RARP era. In addition, prediction of which patients are more likely to have prolonged urinary incontinence after surgery and countermeasures for such patients are now becoming more important. In the present review, we provide a critical summary of current knowledge on this outcome in the literature and discuss the pathophysiology of post-prostatectomy incontinence and the various countermeasures for early acquisition of urinary incontinence.

1. Surgical modalities for early acquisition of urinary continence

Due to the clear view and meticulous maneuvers possible with RARP, we presumed that surgeons who have once performed RARP are not willing to perform ORP and LRP. However, is RARP the surgical approach that offers the earliest acquisition of urinary continence among the three surgical modalities, i.e., RARP, LRP, and ORP? While RARP was reported to be associated with the earliest acquisition of urinary continence among the three surgical modalities^{2,3}, a multi-institutional study in Sweden, which was a prospective non-randomized design involving 2,625 patients, demonstrated that there was no significant difference in the continence rate 12 months after surgery between RARP and ORP⁴. Further, a randomized, controlled trial recently demonstrated similar urinary function evaluated by patient-reported outcomes at 6 and 12 weeks after surgery with RARP and ORP⁵. Ferronha *et al.* reported that there were no significant differences in the postoperative continence rate among RARP, LRP, and ORP in their systematic review⁶. However, because individual Japanese physicians could not perform as many cases of RARP as physicians in high-volume Western centers, these data about continence status with each surgical modality might not reflect the situation in Japan.

Regarding the achievement of mastery of the surgical procedures, while LRP needs no less than

40–100 cases, RARP needs about 12–20 cases if the physicians have performed ORP before performing RARP⁷. With respect to the vesicourethral anastomotic technique for acquisition of urinary continence, Good *et al.* reported that a shorter period is needed to master the vesicourethral anastomosis with RARP than with LRP⁸. A report from Japan demonstrated that the pad-free rate 12 months after RARP was 88% following procedures performed by surgeons with previous experience with ORP, and 75% following procedures performed by surgeons with no previous experience with ORP⁹. In addition, even though LRP had not been performed before introduction of RARP in that institution, perioperative outcomes, including the continence rate, were good from the introduction of RARP⁹. As just described, RARP might be easier to master within a shorter period than other surgical modalities even by surgeons with no experience with LRP and/or ORP. Therefore, the number of cases in which RARP was performed has increased in Japan, instead of there being an increase in LRP cases, as in the United States of America in the past.

2. “Preservation”, “Reconstruction”, and “Reinforcement” of the anatomical structures of the pelvis

We have previously reported the effects of surgical techniques for “preservation”, “reconstruction”, and “reinforcement” of anatomical structures of the pelvis on the early acquisition of urinary continence after RARP^{10,11}. Because all these surgical procedures are important for early acquisition of urinary continence after radical prostatectomy, we could not determine which techniques are most important at the present.

However, our previous study demonstrated that “preservation” of membranous urethral length was the most important factor, at least in the early postoperative period after RARP (Figure 1)¹². Based on our study, we take minimal bites of the needle at the anterior aspect of the Ω -shaped membranous urethra during RARP to leave it long postoperatively (Figure 2). We also demonstrated that the postoperative membranous urethra was significantly retained in the nerve-sparing group compared with the non-nerve-sparing group¹². In addition, the nerve-sparing procedure in RARP has the possibility to improve not only erectile function, but also lead to early improvement of lower urinary tract symptoms (LUTS), due to both the increase of maximum voided volume and the decrease of nocturia¹³. There-

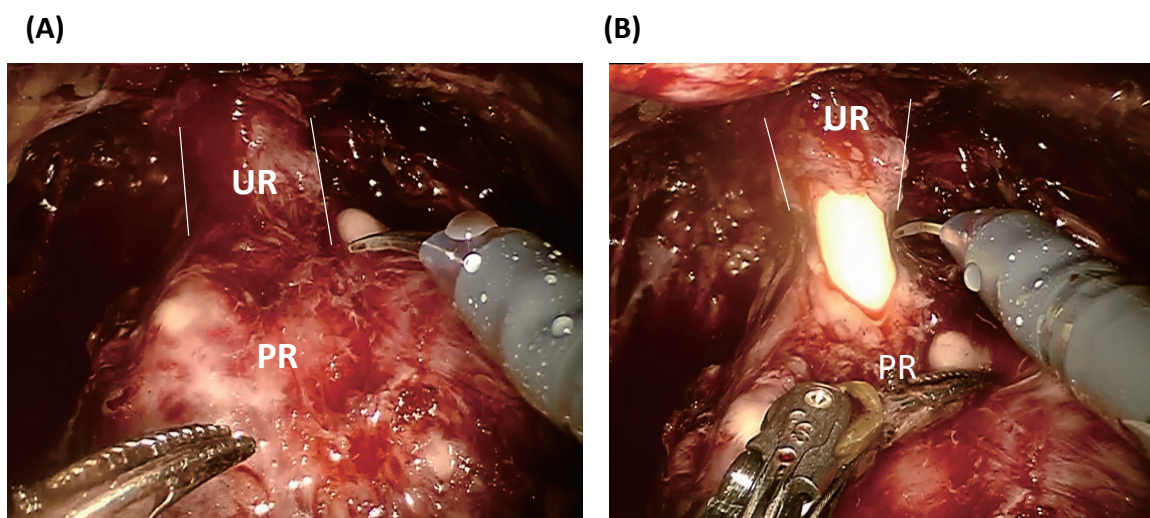


Fig. 1. Preservation of membranous urethral length during robot-assisted radical prostatectomy

(A) Representative photograph before dividing between urethra and prostate

Before dividing urethra and prostate, it is important to clearly show the association between urethra and prostate to preserve the postoperative membranous urethral length.

(B) Representative photograph during the dividing between urethra and prostate

Urethra was cut as nearly as possible at the prostatic apex.

UR ; urethra, PR ; prostate

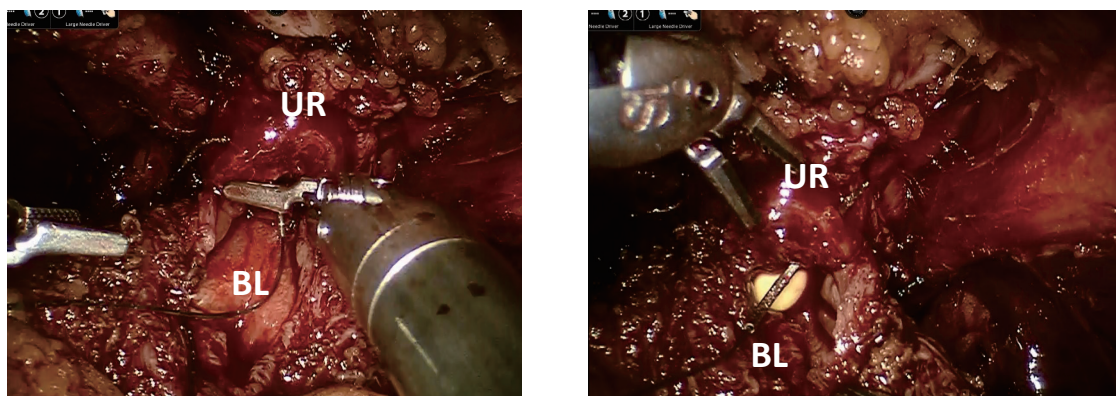


Fig. 2. Artifice of preserving the membranous urethral length

We take minimal bites of the needle at the anterior aspect of the Ω -shaped membranous urethra during vesico-urethral anastomosis at robot-assisted radical prostatectomy to leave it long postoperatively.

UR ; urethra, BL ; bladder

fore “preservation” of erectile nerves is involved in the early acquisition of urinary continence and in the early improvement of LUTS after radical prostatectomy.

However, although “preservation” of erectile nerves was significantly associated with this early acquisition of urinary continence 6 months after radical prostatectomy in meta-analyses¹⁴, the procedure is not associated with urinary continence both 12 months and 24 months after RARP. Thus, this meta-analysis concluded that, because evidence for acquisition of urinary continence was not sufficient with the nerve-sparing procedure, whether the

nerve-sparing procedure is performed should be decided based on the degree of spread of the cancer both on imaging findings and the results of prostatic needle biopsy, especially in patients with preoperative erectile dysfunction¹⁴.

Regarding the “reconstruction” of pelvic organs, the Rocco technique for posterior reconstruction of Denonvilliers’ fascia¹⁵ is performed in many institutions, because it is easy to perform and it is completed in a short amount of time (Figure 3). In a systematic review of the effect of posterior musculofascial reconstruction for urinary continence, posterior musculofascial reconstruction was significant-

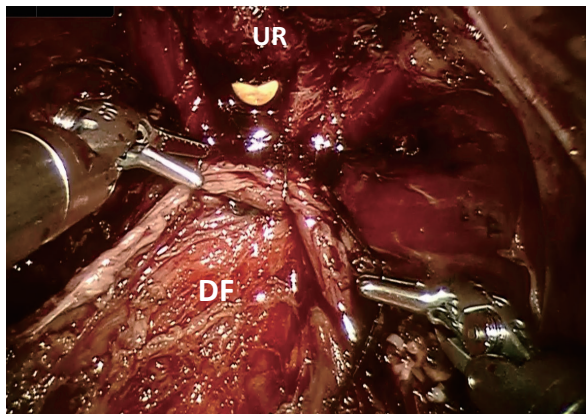


Fig. 3. Representative photograph of posterior reconstruction of Denonvilliers' fascia by using modified Rocco technique
 Disconnected rhabdosphincter in the posterior aspect of the urethra and Denonvilliers' fascia in the bladder neck were attached to enhance the suspension of the posterior aspect of the urethra and prevention of shortening of the membranous urethra.
 UR ; urethra, DF ; Denonvilliers' fascia

ly associated with early acquisition of urinary continence just 1 month after radical prostatectomy¹⁶). The mechanism for acquisition of urinary continence by posterior musculofascial reconstruction was that, in association with the disconnected rhabdosphincter in the posterior aspect of the urethra and Denonvilliers' fascia in the bladder neck, enhancement of suspension of the posterior aspect of the urethra and prevention of shortening of the membranous urethra by decreased tugging of the urethra in the caudal direction were achieved. To obtain further early acquisition of urinary continence, we developed a new technique for posterior reconstruction using peritoneum for additional support of the posterior aspect both of the urethra and the bladder neck. In this new technique, urinary incontinence was significantly improved at 1 month after RARP, compared with the usual posterior reconstruction using Denonvilliers' fascia. In addition, there were no obvious adverse events and no elongation of operative time with this new technique.

With respect to "reinforcement" of anatomical structures in the pelvis, we developed a bladder neck sling suspension technique during RARP (Figure 4)¹⁷). This new suspension procedure was significantly involved in the early acquisition of urinary continence¹⁷). Lee *et al.* also reported the usefulness for early acquisition of urinary continence with the bladder neck plication technique during RARP (Figure 5)¹⁸). However, another group conducted a

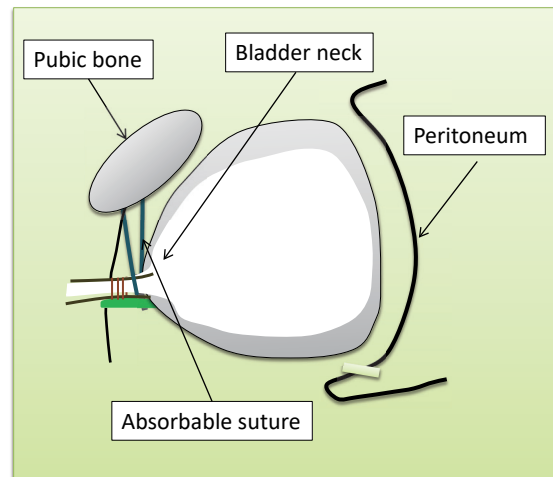


Fig. 4. Bladder neck suspension technique
 Bladder neck is lifted by absorbable suture situated under the vesicourethral anastomotic site. This absorbable suture was fixed at the posterior part of the pubic bone in the periosteum.

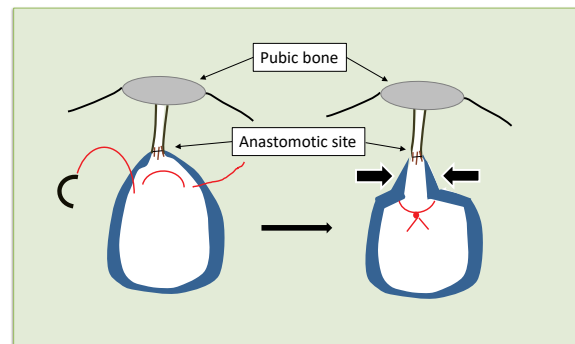


Fig. 5. Bladder neck plication technique
 Bladder neck was plicated by running stitch at the 2 cm proximal site of vesicourethral anastomosis.

randomized study of the bladder neck plication technique for the early acquisition of urinary continence¹⁹); they found no benefit for urinary continence in the plication group. Therefore, the effect of the bladder plication technique for urinary continence remains controversial.

3. The effect of sutures for urinary continence during vesicourethral anastomosis

Vesicourethral anastomosis for LRP or RARP is usually performed using running sutures in many institutions (Figure 6), because the use of interrupted sutures is more difficult in LRP or RARP than in ORP²⁰⁻²²). One of the drawbacks of using running sutures in vesicourethral anastomosis is easy slippage of the suture during the procedure²²). A polyglyconate, unidirectional barbed synthetic absorb-

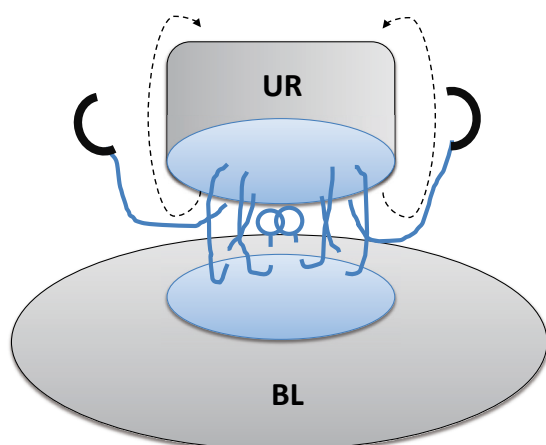


Fig. 6. Vesicourethral anastomosis by using running suture

Vesicourethral anastomosis for laparoscopic radical prostatectomy or robot-assisted radical prostatectomy is usually performed using running sutures in many institutions. This anastomosis technique represents the Van Velthoven stitch.

UR ; urethra, BL ; bladder

able suture (V-Loc Wound Closure Device ; Covidien, Mansfield, MA) consists of a unidirectional barbed absorbable thread. The barbs are present at regular intervals throughout the strand, thereby preventing slippage of the suture, precluding the need for assistance and eliminating the need for knot tying. Therefore, the unidirectional barbed suture has been preferred for vesicourethral anastomosis in LRP or RARP, and several reports have demonstrated excellent perioperative outcomes with respect to shortening of the vesicourethral anastomosis time^{22,23}.

However, regarding tissue damage associated with barbed sutures, an increasing number of reports has cited a risk of small bowel obstruction after laparoscopic gastrointestinal tract surgery^{24,25}. Our study showed that, after RARP, barbed sutures during vesicourethral anastomosis induced more severe tissue damage as seen on MRI (Figures 7) and greater transient aggravation of quality of life (QOL) and lower urinary tract function than non-barbed sutures²⁶. The present findings suggest that using non-barbed sutures during vesicourethral anastomosis may facilitate earlier acquisition of urinary QOL and urinary continence.

4. Patient factors and postoperative pelvic anatomical features for post-prostatectomy incontinence

Body mass index (BMI), prostate volume,

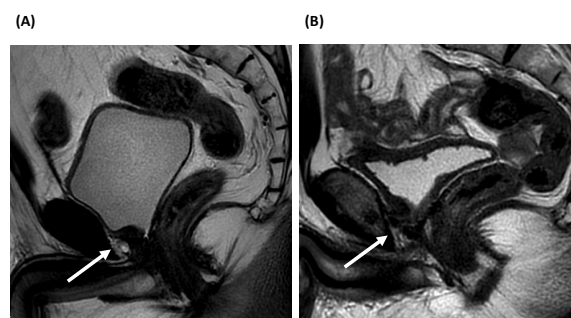


Fig. 7. Postoperative urethral and periurethral tissue on sagittal T2-weighted images from postoperative magnetic resonance imaging (MRI).

(A) Mild damage to the urethra and surrounding tissue.

(B) Severe damage to the urethra and surrounding tissue.

Charlson comorbidity index, age, and so on have been shown to be predictors of delayed recovery of urinary continence after radical prostatectomy². In recently developed nomograms for predicting the recovery of urinary continence after radical prostatectomy, preoperative membranous urethral length, surgical modality (RARP), and age (younger age) were important factors for early urinary continence²⁷. In our study, 1) $\text{BMI} \geq 26 \text{ kg/m}^2$, 2) prostate volume $\geq 70 \text{ mL}$, 3) $\text{eGFR} \leq 60 \text{ mL/min}$, and 4) Charlson comorbidity index ≥ 2 points were predictors of delayed recovery of urinary continence after RARP²⁸. Because the above-mentioned factors 1)-4) were considered to negatively affect each other for the recovery of urinary continence, urinary incontinence has been significantly prolonged in patients with several of the above-mentioned factors.

The Charlson comorbidity index was primarily developed to predict patients' survival based on the sum of scores composed of patients' comorbidities affecting their survival²⁹. This index was found to be significantly correlated with overall survival after radical prostatectomy³⁰. Therefore, our study suggests that a Charlson comorbidity index of more than 2 points was not only a risk factor for overall survival after radical prostatectomy, but also a risk factor for delayed recovery of urinary continence after radical prostatectomy. In our institution, informed consent, focusing on the possibility of prolonged urinary incontinence after radical prostatectomy, is obtained from such high-risk patients. Furthermore, additional surgical procedures for alleviating post-prostatectomy incontinence, i.e., total reconstruction, might be needed, as suggested by Nuguyan *et al.*³¹.

We also investigated the factors contributing to

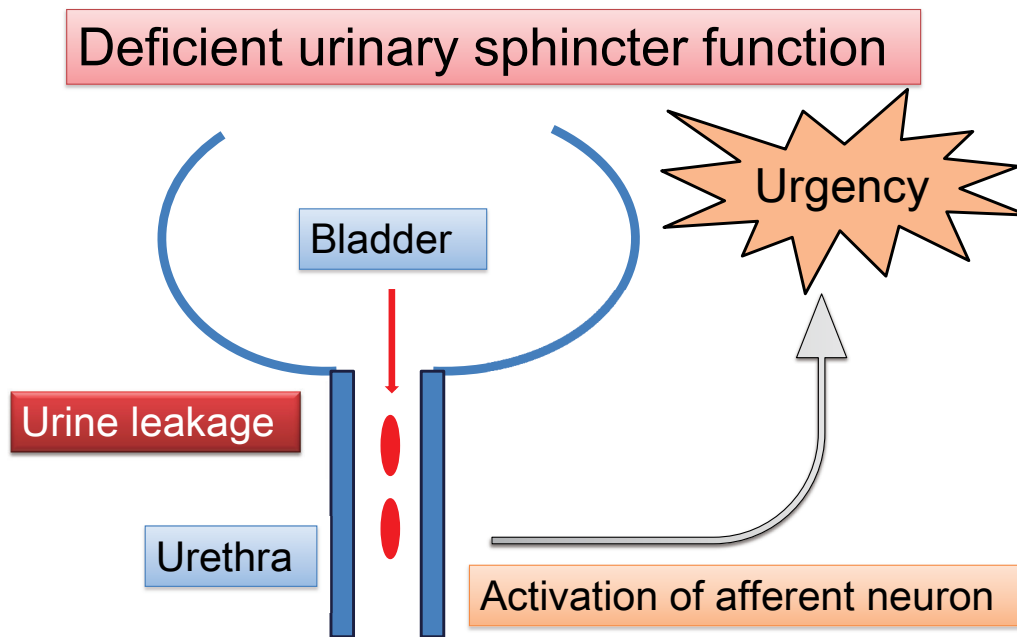


Fig. 8. Putative mechanism of de novo overactive bladder after radical prostatectomy induced by urinary pooling inside the urethra

Urinary leakage into the urethra owing to deficient urethral sphincter function stimulates afferent nerve activity, resulting in inducing urgency after radical prostatectomy.

early recovery of urinary continence after radical prostatectomy from the perspective of postoperative urethral and vesical anatomical features^{12,32}. Post-operative membranous urethral length, descent of the bladder neck, and atony of the external urethral sphincter on postoperative cystourethrography are significantly associated with post-prostatectomy incontinence. In addition, a study of postoperative pelvic anatomical features on MRI demonstrated that urinary pooling inside the urethra on postoperative MRI was significantly associated with urgency after radical prostatectomy³². Therefore, preservation of the nerves involved in continence to prevent inflow of urine into the urethra was recommended from the perspective of averting de novo overactive bladder (OAB) after radical prostatectomy (Figure 8). Thus, we could predict which patients would have prolonged post-prostatectomy incontinence and de novo OAB based on both patients' factors and postoperative pelvic anatomical features.

5. Association between post-prostatectomy incontinence and nocturia

The causes of post-prostatectomy incontinence are considered to be decreased sphincter function³³, decreased maximum bladder capacity³⁴, de novo OAB, and so on³⁵. The same underlying mechanism that induces post-prostatectomy incontinence

might lead to nocturia after radical prostatectomy. We investigated the effect of post-prostatectomy incontinence on nocturia after radical prostatectomy³⁶. Our study demonstrated that, although the number of nocturia episodes was not significantly different between the continent and incontinent patients after radical prostatectomy, nocturia-specific QOL was significantly worse in incontinent patients. In incontinent patients after radical prostatectomy, other than the number of nocturia episodes, psychological stress might worsen nocturia-specific QOL. Therefore, prevention of post-prostatectomy incontinence might be important to avoid aggravating nocturia-specific QOL.

6. Effects of medication on urinary incontinence after radical prostatectomy

Several studies investigated the effects of medications on urinary incontinence after radical prostatectomy^{27,28}. Bianco *et al.* performed a randomized, double-blind, multicenter study investigating the efficacy of solifenacin succinate in 640 patients with urinary continence after RARP³⁷. Although the primary end point, which was the time from the day of the first dose to the day of urinary continence, showed no significant difference between the drug and control groups, a significant increase of the proportion of continent patients at the end of study, a

significant decrease of the average change of number of pads per day, and a significant improvement of QOL were achieved in the drug-administration group as secondary endpoints. Shim *et al.* conducted a prospective, randomized, controlled study to elucidate the therapeutic effect of solifenacin succinate on recovery from voiding dysfunction after radical prostatectomy in 78 men with clinically localized prostate cancer³⁸. They concluded that solifenacin succinate might result in early recovery of urinary incontinence and prevent worsening of QOL, which might be attributed to increased bladder capacity after drug administration. From these above-mentioned studies, medication was considered to provide a certain level of effect to decrease urinary incontinence and improve QOL after radical prostatectomy.

7. Efficacy of pelvic floor muscle training for post-prostatectomy incontinence

One of the conservative management techniques for early acquisition of urinary continence after radical prostatectomy is pelvic floor muscle training. In our institution, preoperative pelvic floor muscle training is given to almost all patients who undergo RARP. Anderson *et al.* recently reported a systematic review to elucidate the effectiveness of conservative management including pelvic floor muscle training for early acquisition of urinary continence after radical prostatectomy³⁹. Fifty trials were investigated in their systematic review. The trials included 4,717 men, of whom 2,736 had an active conservative intervention. This systematic review did not demonstrate the usefulness of conservative management for post-prostatectomy incontinence because urinary incontinence improved with time regardless of the type of conservative management. The causes why this systematic review did not demonstrate the superiority of conservative management were that a wide variety of conservative therapies, of evaluation methods of urinary continence, and of populations evaluated were included in the review. However, because pelvic floor muscle training was not demonstrated to be invalid for early acquisition of urinary continence after radical prostatectomy, less invasive pelvic floor muscle training should be continued at the institutions that have already introduced it.

8. The effect of pad usage for post-prostatectomy incontinence on urinary QOL after radical prostatectomy

To date, counts of pads for protection against urinary incontinence have been used as an objective measure of the severity of urinary incontinence⁴⁰⁻⁴³. However, there have been no reports regarding the relationship between pad usage and urinary QOL after radical prostatectomy. Our study showed that increases in the frequency of pad exchange and pad wetness had a significantly negative effect on urinary QOL after RARP in the early postoperative period⁴⁴. Although we predicted that most patients after RARP would select the “liner-type” pads due to a sense of shame associated with wearing “diaper-type” pads due to their lack of discreetness, 39% (35/90) of patients selected “diaper-type” pads for post-prostatectomy incontinence in the early postoperative period. Moreover, there was no significant difference in urinary QOL between patients with “liner-type” pads and patients with “diaper-type” pads. Because patients were informed of the occurrence of urinary incontinence in the early postoperative period and about its improvement with time, most patients might not be bothered about the temporary wearing of “diaper-type” pads in the early postoperative period. However, there is a possibility that not only pad usage, i.e., pad form and pad size, but also wearing pads in itself^{45,46}, could affect urinary QOL in the late postoperative period after radical prostatectomy.

9. Several problems in the evaluation methods of post-prostatectomy incontinence

There are several issues related to the evaluation methods for post-prostatectomy incontinence. First, there are no obvious criteria for post-prostatectomy incontinence. Although the number of pad exchanges is an objective measure of the severity of urinary incontinence in many studies⁴⁰⁻⁴³, several studies reported that pad count was a poor measure of the severity of urinary incontinence⁴⁷⁻⁴⁹. In addition, as we mentioned above (see Section 8), many kinds of pads were used in the early postoperative period after radical prostatectomy⁴⁴. Thus, it is possible that the volume of urinary incontinence would be different even in patients who exchanged the same number of pads per day.

Second, although a longer duration of pad test is a reliable measure of urinary continence, a longer duration of pad test decreases patients' compli-

ance⁵⁰). Looking at the pad test in a comprehensive manner, a 24-h pad test might be the most appropriate for evaluating post-prostatectomy incontinence. However, in our institution, although the 1-h pad test was performed in almost all patients after radical prostatectomy under the close scrutiny of an expert nurse, only half of the patients performed the 24-h pad test regardless of the physician's reminders to do so at the time of every visit to the outpatient clinic. The completion rate of the 24-h pad test in our present cohort was consistent with that of another study⁵⁰.

Finally, because the perception of the severity of urinary incontinence differs in each patient, it is possible that increased urinary incontinence is not always correlated with decreased QOL as evaluated by patient-reported outcomes⁴⁴. Therefore, if urinary incontinence were only judged by QOL, the volume of urinary incontinence could not be evaluated objectively. Thus, because there are several limitations in the evaluation method of post-prostatectomy incontinence, urinary continence should be judged by the number of pad exchanges per day, the pad test, and a QOL questionnaire in an integrated fashion^{12,44}.

10. The effect of radical prostatectomy on postoperative LUTS

Although patients who undergo radical prostatectomy have preoperative LUTS at a relatively constant rate, LUTS has gradually improved with time after radical prostatectomy⁵¹⁻⁵³. However, the mechanism of improvement of LUTS after radical prostatectomy has not yet been fully clarified. We demonstrated that improvements of LUTS and lower urinary tract dysfunction were seen with acquisition of the vesical adaptation response to diuresis after RARP in patients with preoperative LUTS⁵⁴.

On the other hand, some cases may require a long period for resolution of LUTS after radical prostatectomy⁵⁵. However, the causes of protracted voiding symptoms after radical prostatectomy have yet to be clarified. We investigated the effect of atherosclerosis, which was associated with the occurrence of benign prostatic hyperplasia and male LUTS^{56,57}, on the resolution of LUTS after radical prostatectomy. The result was that atherosclerosis delayed the improvement of both voiding symptoms and voiding function after RARP, leading to aggravation of QOL in the early postoperative period⁵⁸. Therefore, we demonstrated that atherosclerosis might be a predictor of slower recovery from tran-

sient lower urinary tract dysfunction immediately after RARP.

As seen from the above, while several studies demonstrated that RARP provides earlier acquisition of urinary continence^{2,59-61}, recent attention has shifted the focus to the effect of RARP on lower urinary tract function and LUTS⁶²⁻⁶⁵. Thus, early improvement of post-prostatectomy incontinence and LUTS after radical prostatectomy are important in the RARP era.

Conclusions

In the RARP era, high levels of good postoperative outcomes for urinary continence after radical prostatectomy have been expected. The ideal outcome would be quick recovery of post-prostatectomy incontinence and pad-free status for all patients. To achieve this ideal, it goes without saying that surgical procedures are the most important aspect. However, in fact, there are individual variabilities in post-prostatectomy incontinence despite the same surgical procedures.

It is important for patients at high risk of post-prostatectomy incontinence to be given information about delayed recovery of post-prostatectomy incontinence. Medications and appropriate pad usage might sometimes be helpful for patients with post-prostatectomy incontinence. Not only surgical procedures, but also a comprehensive approach, are important for post-prostatectomy incontinence.

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