Received: 8 January 2018 | Accepted: 18 February 2018
DOI: 10.1002/nau.23556

ORIGINAL CLINICAL ARTICLE

WILEY Neurourology Urodynamics ICS SUFU

# De novo overactive bladder after robot-assisted laparoscopic radical prostatectomy

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**Aims:** To investigate storage symptoms following robot-assisted laparoscopic radical prostatectomy (RARP), focused on de novo overactive bladder (OAB), and to evaluate the factors related to de novo OAB occurrence.

**Methods:** We prospectively examined 245 patients without OAB who underwent RARP for localized prostate cancer. Subjective and objective symptoms in the lower urinary tract were evaluated before and after surgery. At 3 months after RARP, the patients were divided into two groups: patients with de novo OAB (de novo OAB group) and those without OAB (OAB-free group). We compared the operative and urodynamic parameters between both groups and evaluated the factors related to OAB.

**Results:** De novo OAB was observed in 37.8% (87/230) of patients. Post-operative continence rate was significantly higher in the OAB-free group (79.7%) than in the de novo OAB group (8.0%). Although the International Prostate Symptom Score (IPSS) and Overactive Bladder Symptom Score (OABSS) in the de novo OAB group significantly deteriorated from 9.7 to 14.1 and from 2.4 to 8.3, respectively, no corresponding significant changes occurred in the OAB-free group. Additionally, there was a significant difference in pre-operative IPSS-QOL score, continence rate, pre-and post-operative maximum urethral closing pressure (MUCP), and post-operative functional profile length (FPL) between both groups. Multivariable logistic regression analysis showed pre-operative IPSS-QOL score and post-operative MUCP were significant predictive factors for de novo OAB.

**Conclusions:** The incidence rate of de novo OAB after RARP was about 40%, and seemed unexpectedly high. Decreased urethral function was significantly related to de novo OAB after surgery.

**KEYWORDS**
overactive bladder, prostatectomy, urethral function, urodynamics

## 1 | INTRODUCTION

Robot-assisted laparoscopic radical prostatectomy (RARP) is becoming a popular treatment option for localized prostate

Yoshihisa Matsukawa and Momokazu Gotoh led this review process.

  

cancer and is now performed globally.[1,2] Urinary incontinence after prostatectomy, which is one of the most important complications of this procedure, is reported to have a negative impact on quality of life (QOL).[3–5] The incidence of urinary continence following prostatectomy differs depending on definition of continence, patient selection, surgical technique, and time of assessment.[6,7] In some papers, the incidence of post-operative urinary continence was reported to be significantly higher after RARP than after open prostatectomy because of the minimally invasive nature of RARP.[2,8] However, the continence rate after RARP was reported to be 50-70% at 3 months and around 90% at 12 months, which means that a significant number of patients are still suffering from urinary incontinence.[7,9]

Urinary incontinence comprises stress urinary incontinence (SUI) and urgeny urinary incontinence (UUI). Epidemiology and pathophysiology of SUI after RARP has been assessed in detail and the decrease of urethral sphincter function has been reported as the main etiologic factor of SUI.[10–12] Storage symptoms such as urinary urgency and UUI are reported to be more bothersome and more prone to reduce QOL than voiding and post-micturition symptoms.[13,14] However, few studies have described and clarified the cause of storage dysfunctions such as UUI and de novo overactive bladder (OAB) after RARP. In a urodynamic study, the occurrence of OAB was thought to be related to detrusor overactivity (DO) and a low-compliance bladder after surgery. A review study reported that the rate of de novo DO in urodynamic studies after prostatectomy ranged from 2 to 77%.[15] However, the mechanism regarding de novo storage dysfunctions after prostatectomy is still incompletely understood.

In the present study, we investigated storage function following RARP, with a focus on de novo OAB. The aims of the present study were: (i) to investigate the rate of de novo OAB following RARP for the localized prostate and (ii) to evaluate the factors related to the occurrence of de novo OAB after RARP.

## 2 | MATERIALS AND METHODS

This was a single-center prospective study and was conducted in accordance with the ethical principles of the declaration of Helsinki. The protocol was approved by the ethics committee of the Nagoya University Graduate School of Medicine. All participants provided written informed consent before enrolment. The study included patients without OAB who had undergone RARP for prostate cancer at our hospital between April 2012 and March 2015. The inclusion criteria were as follows: localized prostate cancer (clinical stages ranging from T1c to T3a, N0, and M0); urgency subscore (Q3) of Overactive Bladder Symptom Scores (OABSS) <2 (ie urgency episodes <1 per week)[16]; Total IPSS < 30; and age ≥ 50 years. Patients were excluded if they received oral or surgical treatment for lower urinary tract symptoms (LUTS); had neurogenic bladder dysfunction, bladder calculi, or active urinary tract infections; or had severe cardiac disease, renal dysfunction, or hepatic dysfunction.

RARP was carried out by five surgeons (YM, YY, MK, NS, and MG) via the transperitoneal approach using the da Vinci S system (Intuitive Surgical, Sunnyvale, CA). After bunching of the dorsal vein complex, the procedure for dissecting the prostate was via an antegrade approach from the bladder neck. A nerve-sparing procedure was performed in some cases depending on the cancer status. In non-nerve-sparing cases, the neurovascular bundle was resected. After prostate resection, double-layered posterior reconstruction was performed, and urethrovesical anastomosis was performed by running a single suture using double-armed 3-0 VLoc™ (Medtronic Japan Co., Ltd., Tokyo, Japan), according to Clayman's method.[17] The urethral catheter was removed at post-operative day 5 by cystographic evaluation.

To evaluate lower urinary tract symptoms, the IPSS, IPSS-QOL, and OABSS were assessed before surgery (1-2 days pre-operatively) and at 3 months after surgery. The patients also underwent urethral pressure profiling (UPP) in order to evaluate urethral function before surgery and 3 months after surgery. Maximum urethral closing pressure (MUCP) and functional profile length (FPL) were evaluated as UPP parameters. UPP was performed using a 6-Fr transurethral catheter with a side hole which was removed at 60 mm/min using an electronic puller with a perfusion rate of 2 mL/min, according to the standard methods defined by the International Continence Society.[18,19] The UPP data were de-identified and analyzed independently by our research group members who were not involved in conducting the UPP.

At the evaluation 3 months after RARP, we divided the patients into two groups: those with de novo OAB (de novo OAB group) and those without OAB (OAB-free group). We compared the operative and urodynamic parameters between the two groups and evaluated the factors related to the occurrence of de novo OAB by univariate and multivariate analyses. In the present study, OAB was defined as a score of two or more on the urgency component of OABSS (ie, urgency episodes ≥1 per week), and a total OABSS of three or more. Additionally, urinary continence was defined as the use of no pad per day. Patients were excluded from the analysis if they received adjuvant therapy such as radiotherapy or if urodynamic or LUTS assessment data were not collected at 3 months after surgery.

All statistical values are represented as mean ± standard deviation. The Wilcoxon signed-rank test and McNemar-test were performed to evaluate changes in subjective symptoms, including IPSS, OABSS, and urethral function obtained by

UPP. The analysis of variance multivariable logistic regression was performed to determine significant predictive factors of de novo OAB after RARP. All tests were two-sided, and a $P$-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (IBM, Armonk, NY).

## 3 | RESULTS

Of 245 patients who met the entry criteria, UDS was not performed after the surgery in seven patients and the evaluation of OAB after the surgery was not performed in three patients. Five patients received radiation therapy after surgery. As a result, the final analysis included 230 patients. The mean age at surgery was 65.7 years. Patient characteristics before surgery are shown in Table 1.

According to the evaluation of pre—and post-operative OABSS, de novo OAB after RARP was observed in 87 patients (37.8%) (de novo OAB group) while 143 patients (62.2%) had no OAB symptoms after RARP (OAB-free group). The comparison of operative parameters between the two groups is shown in Table 2. The mean age of the de novo OAB group was 67.1 years and was significantly higher than that of the OAB-free group (65.0 years). There were no differences in initial prostate specific antigen (PSA) level, blood loss, resected prostate volume, and pathological stage between the two groups. However, there was a significant difference in the nerve-sparing rate between the two groups and the continence rate at 3 months after operation was significantly higher in the OAB-free group (79.7%) than in the de novo OAB group (8.0%).

**TABLE 1** Patients' characteristics before surgery

| $N = 230$ | RARP group Mean ± SD |
|---|---|
| Age (years) | 65.7 ± 6.4 |
| Body-mass index | 23.4 ± 2.6 |
| Initial-PSA (ng/mL) | 9.3 ± 7.2 |
| IPSS | 8.5 ± 5.0 |
| IPSS-storage | 3.7 ± 2.1 |
| IPSS-voiding | 4.8 ± 3.7 |
| IPSS-QOL | 2.3 ± 1.4 |
| OABSS | 2.3 ± 1.3 |
| OABSS-urgency sub score (Q3) | 0.5 ± 0.5 |
| MUCP ($cmH_2O$) | 85.0 ± 21.6 |
| FPL (mm) | 48.1 ± 11.7 |

Regarding LUTS, IPSS, IPSS-storage score, IPSS-voiding score, and IPSS-QOL score before surgery were significantly higher in the de novo OAB group (Table 3). Regarding urethral function before surgery, although there was no difference in FPL between the two groups, MUCP was significantly lower in the de novo OAB group (mean 80.8 $cmH_2O$) than in the OAB-free group (87.6 $cmH_2O$). IPSS and OABSS in the de novo OAB group significantly increased from 9.7 to 14.1 and from 2.4 to 8.3, respectively, whereas, in the OAB-free group, no significant change was noted (Table 3).

**TABLE 2** The comparison of operative parameters between the two groups

| | De novo OAB group | OAB free group | |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | $P$ |
| $N$ (%) | 87 (37.8%) | 143 (62.2%) | |
| Age (years) | 67.1 ± 6.0 | 65.0 ± 6.4 | 0.01 |
| Body-mass index | 23.6 ± 2.6 | 23.3 ± 2.5 | 0.38 |
| Initial-PSA (ng/mL) | 10.0 ± 9.1 | 8.8 ± 5.8 | 0.20 |
| Blood loss (g) | 165 ± 177 | 188 ± 213 | 0.41 |
| Prostate volume (g) | 38.5 ± 14.1 | 39.4 ± 12.0 | 0.62 |
| pT stage | | | 0.10 |
| pT0 | 5 | 6 | |
| pT2a,b | 18 | 32 | |
| pT2c | 38 | 69 | |
| PT3a | 22 | 29 | |
| pT3b | 4 | 7 | |
| Nerve-sparing rate | 20/87 (23.0%) | 57/143 (39.9%) | 0.01 |
| Continence rate at 3 months after surgery | 7/87 (8.0%) | 114/143 (79.7%) | <0.001 |

**TABLE 3** The change of LUTS and urodynamic parameters between the two groups

| | De novo OAB group | | OAB-free group | | |
|---|---|---|---|---|---|
| | Mean ± SD | *P* (intra) | Mean ± SD | *P* (intra) | *P* (inter-group) |
| *N* (%) | 87 (37.8%) | | 143 (62.2%) | | |
| IPSS | | | | | |
| Before | 9.7 ± 4.7 | | 7.7 ± 4.8 | | 0.002 |
| After | 14.1 ± 5.5 | <0.001 | 6.7 ± 3.7 | 0.05 | <0.001 |
| IPSS-storage | | | | | |
| Before | 4.1 ± 1.9 | | 3.4 ± 2.2 | | 0.01 |
| After | 7.8 ± 2.3 | <0.001 | 3.7 ± 1.9 | 0.09 | < 0.001 |
| IPSS-voiding | | | | | |
| Before | 5.6 ± 3.8 | | 4.3 ± 3.6 | | 0.01 |
| After | 6.3 ± 3.9 | 0.13 | 3.0 ± 2.5 | <0.001 | <0.001 |
| IPSS-QOL | | | | | |
| Before | 2.7 ± 1.3 | | 2.1 ± 1.4 | | 0.002 |
| After | 4.7 ± 1.2 | <0.001 | 2.2 ± 1.3 | 0.31 | <0.001 |
| OABSS | | | | | |
| Before | 2.4 ± 1.2 | | 2.2 ± 1.4 | | 0.47 |
| After | 8.3 ± 2.6 | <0.001 | 2.7 ± 1.3 | 0.08 | <0.001 |
| OABSS-urgency (Q3) | | | | | |
| Before | 0.5 ± 0.5 | | 0.4 ± 0.4 | | 0.34 |
| After | 3.2 ± 0.9 | <0.001 | 0.5 ± 0.5 | 0.84 | <0.001 |
| MUCP ($cmH_2O$) | | | | | |
| Before | 80.8 ± 19.7 | | 87.6 ± 22.3 | | 0.02 |
| After | 44.3 ± 11.5 | <0.001 | 62.8 ± 15.5 | <0.001 | <0.001 |
| ΔMUCP (%) | 43.6 ± 14.8 | | 27.1±13.1 | | <0.001 |
| FPL(mm) | | | | | |
| Before | 48.0 ± 11.8 | | 48.2 ± 11.6 | | 0.88 |
| After | 22.3 ± 4.7 | <0.001 | 25.8 ± 4.6 | <0.001 | <0.001 |
| ΔFPL (%) | 50.3 ± 17.2 | | 43.5 ± 17.2 | | 0.004 |

Urethral function such as MUCP and FPL significantly decreased in both groups after RARP. However, in the comparison of post-operative urethral function, both MUCP, and FPL were significantly lower in the de novo OAB group. The reduction rates of MUCP and FPL in the de novo OAB group was 43.6% and 50.3%, respectively, and was significantly higher than in the OAB-free group (27.1 and 43.5%, respectively) (Table 3).

Regarding factors related to de novo OAB after RARP, IPSS-QOL score before surgery, and post-operative MUCP were the significant factors related to the occurrence of de novo OAB in the multivariable logistic regression analysis (Table 4). Receiver-operating curve (ROC) analysis identified 50 $cmH_2O$ as the optimal cut-off value for post-operative MUCP; this value yielded a sensitivity of 81% and a specificity of 72% (Figure 1). Additionally, pre-and intra-operative factors related to the occurrence of de novo OAB were evaluated by the multivariable logistic regression analysis, and nerve spearing procedure was found to be the only significant factor (Table 5).

## 4 | DISCUSSION

Although some studies have evaluated OAB and storage symptoms following radical prostatectomy (RP),[15] to our knowledge, this is the first study to prospectively investigate the factors related to de novo OAB after RARP. In our study, the decrease of urethral function, especially MUCP, was found to be the most relevant variable related to de novo urgency and UUI after RARP. Although lower MUCP after RP was reported to be a significant factor related to post-operative SUI,[10–12] it is noteworthy that MUCP was found to be significantly associated not only with SUI but also with de novo OAB after prostatectomy. In this study, 37.8% of all patients (87/230) had de novo OAB at 3 months after RARP.

**TABLE 4** The factors related to de novo OAB after RARP by multivariable logistic regression

| | *P* | HR | 95%CI | |
|---|---|---|---|---|
| Age | 0.593 | 1.017 | 0.996 | 1.089 |
| Total IPSS before surgery | 0.733 | 1.017 | 0.840 | 1.258 |
| IPSS-QOL before surgery | **0.018** | **1.555** | **1.068** | **2.219** |
| Pre-operative MUCP | 0.124 | 1.073 | 0.814 | 1.321 |
| Post-operative MUCP | **0.002** | **0.783** | **0.670** | **0.916** |
| Post-operative FPL | 0.214 | 0.940 | 0.851 | 1.037 |
| Change ratio of MUCP | 0.137 | 0.916 | 0.817 | 1.028 |
| Change ratio of FPL | 0.695 | 0.995 | 0.971 | 1.028 |
| Nerve spearing procedure | 0.196 | 0.640 | 0.326 | 1.259 |

Bold value emphasize the significant difference.

Hosier et al reported that 19% of patients developed de novo OAB at a median follow-up of 2.7 years after RP and quite a few patients were found to have storage symptoms such as urgency and UUI after RP.[20] Additionally, in this study, the continence rate in the de novo OAB groups was only 8.0% at 3 months after surgery, which was obviously lower than that in the OAB-free group (79.7%). It may be assumed that many patients developed post-operative urinary incontinence associated with storage dysfunctions such as detrusor overactivity although SUI was central component for the incontinence after RP.

In the de novo OAB group, not only OABSS but also IPSS-total, IPSS-voiding sub-score, and IPSS-QOL score significantly increased before and after surgery. We previously reported that a failure to improve storage dysfunction such as DO contributed to the inadequate improvement of LUTS completely after α1-blocker treatment in patients with benign prostatic hyperplasia.[21] In a large population-based study, Agarwal et al[13] reported that urinary urgency was the most common troublesome symptom. In this way, the worsening of storage symptoms after surgery was thought to have an influence on the worsening of QOL and LUTS. Considering the background that, a large number of patients receive RP for localized prostate cancer globally, it seemed meaningful to investigate factors and mechanisms related to de novo OAB after RARP.

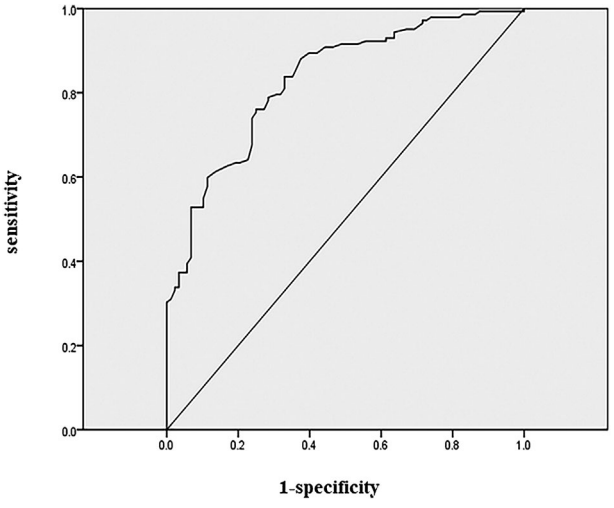


**FIGURE 1** ROC curve of post-operative MUCP regarding de novo OAB after RARP: ROC analysis identified 50 $cmH_2O$ as the optimal cut-off value for postoperative MUCP; this value yielded a sensitivity of 81% and a specificity of 72%

OAB is usually attributable to DO, which is characterized by involuntary contractions of the detrusor muscle during the filling phase.[15,22] We have previously reported that 33% of patients at 3 months after laparoscopic prostatectomy had DO in urodynamic studies.[23] Leach et al[24] also reported that DO contributed to incontinence in 60% of 215 patients. Thus, since many patients were found to have DO after RP, the occurrence of de novo OAB after RP was thought to be attributable to de novo DO. However, few studies have focused on the cause of DO and OAB after RP. In our study, the decrease of sphincter function by surgery was the strongest factor related to de novo OAB after RP in multivariable logistic regression analysis. We were unable to determine the precise reason for the relationship between the decrease of sphincter function and de novo OAB; however, we can offer one plausible hypothesis. In the field of female urology, about 50% of women with SUI also complain of urinary urgency and/or UUI. In women with mixed stress and urge incontinence, successful surgical repair of SUI is associated with the cure of UUI in 50% to 75% of patients. Conversely, de novo SUI after RP may occur in conjunction with de novo OAB and UUI. Jung et al[25] reported that the passage of fluid through the urethra of the rat increased the frequency of reflex bladder contractions. Thus, in patients with SUI due to decreased sphincter function, leakage of urine into the proximal urethra could increase bladder activity by stimulating C-fiber urethral afferent nerves which in turn modulate the micturition reflex.

In our study, the nerve spearing procedure was the only significant factor to reduce de novo OAB among pre-and intra-operative factors. Kadono et al[12] reported the nerve spearing procedure contributed to preservation of urethral function such as MUCP and FPL. This preservation of urethral function by nerve spearing procedure was thought to

**TABLE 5** The pre- and intra-operative factors related to de novo OAB after RARP by multivariable logistic regression

| | *P* | HR | 95%CI | |
|---|---|---|---|---|
| Age | 0.243 | 1.030 | 0.980 | 1.083 |
| Total IPSS before surgery | 0.124 | 1.061 | 0.984 | 1.145 |
| IPSS-QOL before surgery | 0.123 | 1.235 | 0.944 | 1.616 |
| Pre-operative MUCP | 0.054 | 0.988 | 0.972 | 1.008 |
| Nerve spearing procedure | **0.033** | **0.550** | **0.318** | **0.952** |

Bold value emphasize the significant difference.

contribute to reduce de novo OAB after RALP. Nerve spearing was considered to be a useful procedure to prevent UUI besides SUI after RARP.

The present study has several limitations. First, the diagnosis of de novo OAB was performed based on patient-reported outcomes; cystometrography to evaluate storage functions such as the presence or absence of DO and bladder compliance in the storage phase was not performed in this study. Consequently, it was unclear whether the decrease of urethral function was related to not only de novo OAB after surgery but also de novo DO. Another limitation was that the period of assessment in the present study was only at 3 months after surgery. Generally, urethral function is reported to be restored gradually and the change in the incidence of de novo OAB should be evaluated for the long term after surgery (eg, 12 months). The long-term evaluation of storage symptoms after RARP seems necessary for future studies.

## 5 | CONCLUSIONS

The incidence rate of de novo OAB after RARP was 37.8%, which was considered to be unexpectedly high. The decrease in urethral function was related to de novo OAB after surgery and may be attributable to the increased reflex response of the urethral afferent pathway. Nerve spearing procedure might be useful to reduce de novo OAB after RARP.

## ACKNOWLEDGMENTS

The authors thank all patients for participating and all trial investigators for their contribution to data acquisition and patient care.

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**How to cite this article:** Matsukawa Y, Yoshino Y, Ishida S, et al. De novo overactive bladder after robot-assisted laparoscopic radical prostatectomy. *Neurourology and Urodynamics*. 2018;1–7. https://doi.org/10.1002/nau.23556