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Impact of postoperative sexual function on health-related quality of life after robot-assisted radical prostatectomy

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Abstract

Background: We investigated potential disparities in health-related quality of life, particularly concerning urinary function, between patients with preserved and those with impaired sexual function after robot-assisted radical prostatectomy (RARP).

Materials and methods: Between December 2012 and April 2020, 704 men underwent RARP in our hospital. This study included 155 patients with a preoperative 5-item International Index of Erectile Function (IIEF-5) of ≥12 points and an assessable IIEF-5 at 12 months postoperatively. Health-related quality of life was assessed using the 8-item Short-Form Health Survey and Expanded Prostate Cancer Index Composite (EPIC) preoperatively and at 3, 6, and 12 months postoperatively. A logistic regression analysis and Wilcoxon rank sum tests were performed.

Results: Patients were grouped according to the median IIEF-5 score 12 months after surgery: those with preserved sexual function (n = 71) and those with impaired sexual function (n = 84). The mental component summary of the 8-item Short-Form Health Survey was better in the group with preserved sexual function at 6 months postoperatively than in the group with impaired sexual function ($p < 0.01$). In the EPIC, the group with preserved sexual function performed better not only in the sexual domain but also in the urinary domain at all time points compared with the group with impaired sexual function ($p < 0.01$). In the comparison of the urinary subdomains of the EPIC, there were no significant differences in urinary function or incontinence, but there were significant differences in urinary distress and irritative/obstructive scores ($p < 0.01$).

Conclusions: Patients with preserved postoperative sexual function after RARP showed better urinary function than those with impaired sexual function. Hence, preserved sexual function is closely associated with urinary function.

Keywords: Prostatectomy; Robot-assisted radical prostatectomy; Health-related quality of life; Sexual function; Urinary function

1. Introduction

Radical prostatectomy (RP) and radiation therapy are the primary treatment options for patients with localized prostate cancer. Although the oncological outcomes of these therapies are similar, each has distinct adverse effects. Major complications of RP include postoperative erectile dysfunction (ED) and urinary incontinence. Many studies have been conducted on health-related quality of life (HRQOL) to assess these issues.[1–4] The relationship between sexual function and urinary incontinence has also been previously investigated. Gandaglia et al.[5] reported that patients with good preoperative sexual function had better postoperative urinary continence. Another report comparing laparoscopic radical prostatectomy (LRP) and open RP showed that patients with good preoperative sexual function who underwent nerve-sparing surgery for LRP had better early postoperative urinary continence.[6] Patients with good preoperative sexual function were expected to have good postoperative urinary continence.

However, no study has compared HRQOL, including urinary status, between patient groups with preserved and impaired sexual function after RP. Previous reports have been limited to patients with good preoperative sexual function. Improving sexual function after RP is difficult in patients with preoperatively deteriorated sexual function. However, in patients who maintain preoperative sexual function, the influence on HRQOL, particularly sexual and urinary functions, is an important concern. The influence on HRQOL after treatment is an important factor when determining the treatment plan because oncological outcomes will be similar irrespective of whether patients receive RP or radiation therapy for localized prostate cancer. If improvements in HRQOL can be clearly attributed to the preservation of postoperative sexual function, surgeons should be more active in attempting to preserve sexual function. Conversely, nerve sparing is associated with the risk of a positive surgical margin, which is related to biochemical recurrence.[7] Hence, selection of patients suitable for nerve sparing is important. This study therefore aimed to investigate potential disparities in HRQOL, specifically in terms of urinary function, between patients with preserved sexual function and those with impaired sexual function after robot-assisted radical prostatectomy (RARP).

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2. Materials and methods

2.1. Study population

Between December 2012 and April 2020, 704 men underwent RARP at Wakayama Medical University Hospital in Wakayama, Japan (Fig. 1). This clinical study was approved by the Wakayama Medical University Institutional Review Board (authorization number, 1670) and performed in accordance with the Declaration of Helsinki. We targeted cases with no preoperative impairment of sexual function in which sexual function could be evaluated 12 months after surgery. Of the 704 patients, 13 who received neoadjuvant hormone therapy and 102 who lacked preoperative 5-item International Index of Erectile Function (IIEF-5) scores were excluded. Therefore, the preoperative sexual function was assessed in 591 patients. Among them, 398 patients who originally had impaired preoperative sexual function (IIEF-5 score, <12 points) and 38 patients who did not answer the questionnaire 12 months after surgery were excluded. Erectile dysfunction severity is typically classified into 5 categories based on IIEF-5 scores: severe (5–7), moderate (8–11), mild-to-moderate (12–16), mild (17–21), and no ED (22–25). The average IIEF-5 score for a 50-year-old Japanese man has been reported as 16 points.[8] Furthermore, sexual function declines with age.[9] In the current study, the mean age of the patients was 66 years; therefore, the cutoff for sexual function was set at 12 points (indicating more than moderate function). Finally, 155 patients were selected for this study and divided into 2 groups according to the median value of –13 of IIEF-5 12 months after surgery. The preserved sexual function group comprised 71 patients who had an IIEF-5 score of ≥–13, whereas the impaired sexual function group comprised 84 patients with an IIEF-5 score of <–13.

We investigated the differences in the changes in postoperative HRQOL between the 2 groups according to the 8-item Short-Form Health Survey (SF-8) and Expanded Prostate Cancer Index Composite (EPIC) (details shown in the paragraph hereinafter).

The following clinical and pathological parameters were collected: age, body mass index, preoperative prostate-specific antigen (PSA) level, clinical stage, pathological Gleason Score, National Comprehensive Cancer Network criteria, nerve preservation, length of the membranous urethra, bladder neck size, prostate volume, and PSA recurrence. The length of the membranous urethra and bladder neck size were measured during surgery. As for nerve sparing, if none of the following factors were met, we attempted nerve sparing: palpable induration during digital rectal examination, Prostate Imaging Reporting and Data System score of 4 or 5 in the peripheral zone region on prostate magnetic resonance imaging, and 3 or more positive cores in systematic biopsy.

2.2. HRQOL questionnaires

Health-related quality of life questionnaires were collected before surgery and 3, 6, and 12 months after surgery. The assessments were self-administered, without the need for interviews. To evaluate the HRQOL, we used the SF-8, EPIC, and IIEF-5 questionnaires. The SF-8 is a simple version of the 36-item Short-Form Health Survey[10] and was purchased from iHope International (Kyoto, Japan). In the SF-8, the physical component summary (PCS) and mental component summary (MCS) scores were calculated, which are equivalent to the 36-item Short-Form Health Survey. The EPIC is an advanced version of the University of California-Los Angeles Prostate Cancer Index.[10] It consists of 4 summary domains: urinary, sexual, bowel, and hormonal. In each domain, scores for function and discomfort were calculated. In the urinary domain, the urinary incontinence and irritation/obstruction scores were calculated. The Japanese version of EPIC was purchased from iHope International.[11] The IIEF-5 consists of 5 questions and is used to screen for ED and determine the effectiveness of ED treatment. In our study, the SF-8, EPIC, and IIEF-5 questionnaires were mailed to each patient both preoperatively and postoperatively on a periodic basis and returned to our hospital. Postoperative changes in HRQOL were assessed by subtracting the preoperative HRQOL scores from each postoperative HRQOL score.

2.3. Statistical analyses

Patient demographics and HRQOL were compared using the Mann-Whitney-Wilcoxon test for continuous variables and Pearson χ^2 test for categorical variables. Univariate and multivariate logistic regression analyses were performed to identify predictive factors associated with postoperative urinary function. Two-sided p values

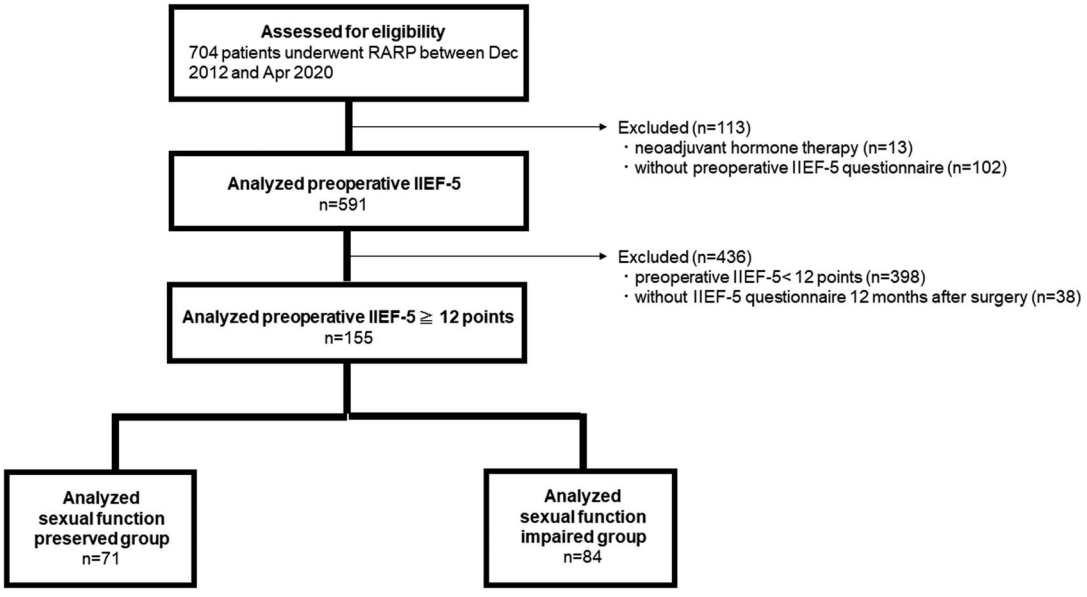

Figure 1. Patient flow diagram. IIEF-5 = 5-item International Index of Erectile Function; RARP = robot-assisted radical prostatectomy.

Table 1

Comparison of patient characteristics between those with impaired and those with preserved sexual function.

	Overall	Sexual function impaired group	Sexual function preserved group	*p*
No. patients	155	84	71	
Age, yr	66 (61–69)	66 (62–69)	67 (61–70)	0.38
BMI, kg/m^2	24.1 (22.0–26.3)	23.9 (22.1–26.3)	24.4 (22.0–26.3)	0.76
Preoperative PSA, ng/mL	7.4 (5.6–11.4)	6.8 (5.1–11.2)	8.1 (6.1–11.6)	0.10
Postoperative Gleason score, n (%)				0.71
6	18 (11.7)	9 (10.8)	9 (12.7)	
7	117 (76.0)	62 (74.7)	55 (77.5)	
≥8	19 (12.3)	12 (14.5)	7 (9.8)	
Clinical stage, n (%)				0.34
T1c	39 (25.1)	16 (19)	23 (32.4)	
T2a-c	88 (67.9)	62 (73.9)	26 (60.6)	
T3a,b	11 (7.0)	6 (7.1)	5 (7.0)	
NCCN criteria, n (%)				0.30
Low	27 (17.4)	11 (13.1)	16 (22.6)	
Intermediate	75 (48.4)	43 (51.2)	32 (45.1)	
High	53 (34.2)	30 (35.7)	23 (32.3)	
Nerve sparing, n (%)				<0.01
Non–nerve sparing	30 (19.4)	23 (27.4)	7 (9.9)	
Unilateral nerve sparing	87 (56.1)	47 (56.0)	40 (56.3)	
Bilateral nerve sparing	38 (24.5)	14 (16.6)	24 (33.8)	
Urethral length, mm	15 (14–18)	16 (14–18)	15 (14–18)	0.52
Bladder neck size, mm	18 (14.8–20.3)	17 (14–21)	18 (15–20)	0.85
PSA recurrence, n (%)	22 (14.2)	15 (17.8)	7 (9.8)	0.15
PSA recurrence within 12 mo, n (%)	7 (4.5)	6 (8.4)	1 (1.2)	0.08
Salvage EBRT		0 (0)	1 (1.2)	
Salvage ADT		6 (8.4)	0	

ADT = androgen deprivation therapy; BMI = body mass index; EBRT = external beam radiation therapy; NCCN = National Comprehensive Cancer Network; PSA = prostate-specific antigen.
Continuous variables are presented as medians (quartiles).

were used, with the significance set at 0.05. Data analyses were performed using JMP software version 13 (SAS Institute, Cary, NC).

3. Results

3.1. Patient characteristics

Regarding age, body mass index, and oncological background, including preoperative PSA level, Gleason score, clinical stage, National Comprehensive Cancer Network risk criteria, and rate of PSA recurrence, there were no significant differences between the groups with impaired and preserved sexual function (Table 1). Intraoperative anatomical factors that may be involved in postoperative urinary continence, such as the length of the membranous urethra and bladder neck size, also showed no significant differences between the groups. Seven patients experienced recurrence within 12 months; 1 underwent salvage external beam radiation therapy, and 6 underwent salvage hormone therapy. A total of 125 patients (80.6%) underwent nerve preservation (unilateral or bilateral). In the group with preserved sexual function, nerve

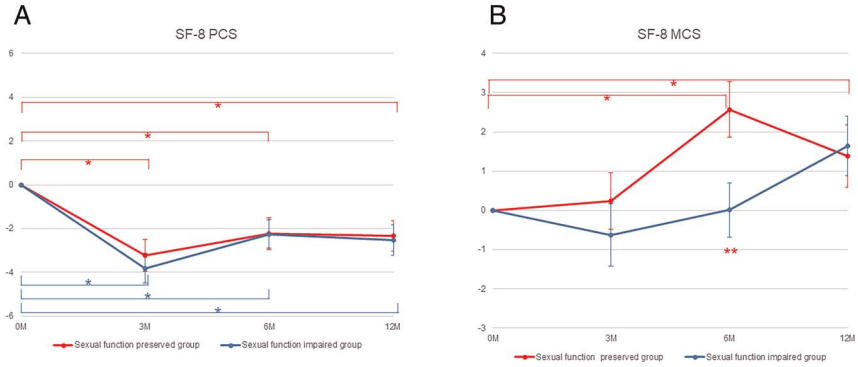

Figure 2. Comparison of summary score of SF-8. (A) shows PCS. (B) shows MCS. *Significantly different from baseline value ($p < 0.01$). **Significantly different at 6 months postoperatively between sexual function preserved group and impaired group ($p = 0.01$). MCS = mental component summary; PCS = physical component summary; SF-8 = 8-item Short-Form Health Survey.

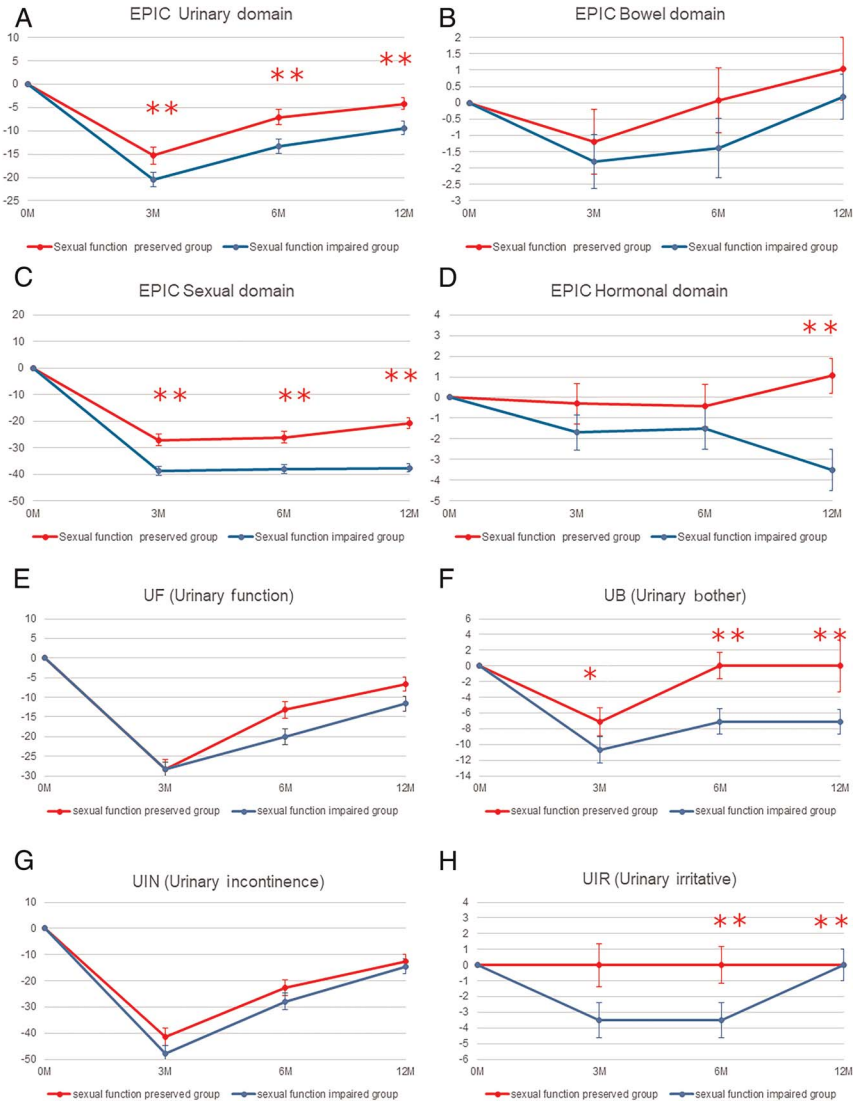

Figure 3. (A–D) Comparison of summary domains score of EPIC. *Significantly different between sexual function preserved group and impaired group ($p < 0.01$). (E–G) shows urinary subscales of EPIC. *Significantly different ($p < 0.05$); **significantly different ($p = 0.01$). EPIC = Expanded Prostate Cancer Index Composite.

preservation was performed in 64 patients (90.1%), whereas, in the group with impaired sexual function, it was performed in significantly fewer patients (61 patients [72.6%]). At 12 months postoperatively, 137 patients (87.4%) had an IIEF-5 score of <11 and 18 patients (13.6%) had an IIEF-5 score of ≥12.

3.2. Comparison of SF-8 between the groups

The PCS scores were not significantly different between the 2 groups at any time point (Fig. 2A). However, when compared with the preoperative scores, the HRQOL scores significantly decreased at 3, 6, and 12 months postoperatively in each group. Conversely, the MCS scores were better in the group with preserved sexual function at 6 months postoperatively than in the group with impaired sexual function ($p = 0.01$) (Fig. 2B). The HRQOL score significantly improved compared with the preoperative scores at 6 and 12 months postoperatively in the group with preserved sexual function.

3.3. Comparison of EPIC between the groups

According to the EPIC, the group with preserved sexual function performed better not only in the sexual domain but also in the urinary domain at all time points ($p < 0.01$) (Figs. 3A–C). In the hormonal domain, the group with preserved sexual function showed better scores 12 months after surgery than the group with impaired sexual function ($p < 0.01$) (Fig. 3D).

3.4. Comparison of urinary subdomains of EPIC between the groups

To analyze quality of life related to urinary function in detail, we compared the urinary subdomains of the EPIC, and there were no significant differences in terms of urinary function or incontinence (Figs. 3E, G). Conversely, significant differences were observed in the scores related to urinary bother and urinary irritation/obstruction (Figs. 3F, H). Urinary bother showed significant differences at all time points ($p = 0.04$, $p < 0.01$, and $p < 0.01$, respectively), and urinary irritative/obstructive exhibited significant differences at 6 and 12 months postoperatively ($p < 0.01$ and $p < 0.01$, respectively). We performed a subgroup analysis to clarify the relationship between incontinence and urinary bother. Continence was defined as the use of no pads per day for 12 months postoperatively. Patients with incontinence had a greater decrease in HRQOL related to

Table 2

Univariate and multivariate logistic regression analyses of predictive factors associated with the urinary function.

	3 mo						6 mo						12 mo					
	Univariable			Multivariable			Univariable			Multivariable			Univariable			Multivariable		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age	1.1	0.11–0.11	0.89	0.97	0.91–1.04	0.52	1.03	0.97–1.09	0.23	1.02	0.95–1.10	0.46	1	0.95–1.06	0.76	0.97	0.90–1.04	0.51
BMI	0.93	0.84–1.03	0.2	0.94	0.84–1.05	0.31	0.9	0.81–1.00	0.06	0.88	0.78–1.00	0.05	0.93	0.84–1.03	0.17	0.96	0.85–1.08	0.52
Nerve sparing	0.97	0.43–2.19	0.95	0.95	0.38–2.39	0.92	0.91	0.40–2.06	0.83	0.69	0.24–1.68	0.36	1.09	0.48–2.47	0.82	0.96	0.38–2.43	0.94
Urethral length	1.09	0.99–1.19	0.06	1.06	0.96–1.17	0.18	1.08	0.98–1.19	0.07	1.07	0.96–1.19	0.17	1.07	0.97–1.17	0.12	1.04	0.94–1.16	0.35
Sexual function	2	0.93–4.29	0.07	2.38	0.98–5.78	0.05	2.46	1.23–4.89	0.01	2.5	1.12–5.55	0.02	2.78	1.32–5.83	<0.01	2.35	0.99–5.58	0.05

BMI = body mass index; CI = confidence interval; OR = odds ratio.

urinary bother than continent patients ($p < 0.01$). Incontinence was not significantly different between the sexual function–preserved and sexual function–impaired groups; however, the EPIC of the urinary bother was significantly worse in the group with impaired sexual function. Thus, urinary bother was influenced not only by incontinence but also by other factors (e.g., frequency and dysuria).

3.5. Logistic analysis of HRQOL about urinary domain

Logistic regression analysis was performed to identify the factors associated with postoperative urinary function (Table 2). The urinary function was divided into 2 groups based on the median difference in the urinary domain at each time point. We examined factors contributing to urinary function using univariate and multivariate analyses. Regarding sexual function, patients were divided into 2 groups according to the optimal cutoff at each postoperative time point calculated using receiver operating characteristic curves (3 months, <–47 points; 6 months, <–30 points; and 12 months, <–21 points). In univariate analyses, sexual function was a significant factor at 6 and 12 months postoperatively ($p = 0.01$ and $p < 0.01$, respectively). Sexual function tended to be related to urinary function 3 months postoperatively ($p = 0.05$). In multivariate analyses, sexual function was an independent factor for urinary function at 6 months postoperatively ($p = 0.02$). Sexual function tended to be related to urinary function at 3 and 6 months ($p = 0.05$). Nerve sparing was not a significant factor at any time point.

4. Discussion

In this study, we assessed the impact on the HRQOL of patients with good preoperative sexual function, depending on whether their sexual function was preserved after RARP. In the comparison of patient characteristics between the 2 groups, only nerve sparing was found to be significantly different. Nerve sparing has been identified as a predictor of postoperative erectile function in several reports,[12–15] and our results align with this observed pattern. Logistic regression analysis showed no significant difference between nerve sparing and urinary function; however, this may be attributed to the inclusion of patients with preserved sexual function in this study and the limited number of cases where nerves were not spared ($n = 30$ [19.4%]).

Non–disease-specific SF-8 and disease-specific EPIC were examined in this study. Miyake et al.[16] reported changes in SF-8 and EPIC after RARP in Japanese patients; the PCS of SF-8 was impaired 1 month after surgery, whereas the MCS of SF-8 was maintained even after surgery. In the current study, the SF-8 PCS was impaired at 3 months postoperatively and did not improve at 6 or 12 months postoperatively when compared with the preoperative scores in each group. Conversely, there was some postoperative improvement in MCS, and this tendency was more apparent in the group with preserved sexual function. These results are similar to those reported by Miyake et al.[16] Recovery of sexual function has been suggested to have a positive impact on patients' mental health.[16]

According to the EPIC results, there was a tendency for a temporary decrease at 3 months and improvement at 6 and 12 months postoperatively in all 4 domains; nonetheless, 2 domains (urinary and sexual) showed significant differences between the 2 groups. The findings related to the sexual domain were considered reasonable, as the patients were divided into 2 groups based on their IIEF-5 scores. However, in the urinary domain, our initial assumption was that the result would reflect the impact of improved urinary continence in the group with preserved sexual function, as nerve preservation was more frequently performed in that group. However, urinary domain analysis revealed no significant difference in urinary incontinence between the 2 groups but a difference in urinary irritation/obstruction. Although there were no significant differences in urinary function, there was a significant difference in urinary distress. One possible explanation for this finding is that patients with urinary incontinence may have been more aware of the issues related to their urinary function. The worsening of irritative/obstructive symptoms, such as increased urinary frequency and dysuria, could have contributed to a heightened sense of bother or distress associated with urination. Nonetheless, the initial hypothesis that "urinary domain–related HRQOL would be better in the group with preserved sexual function because of better urinary continence" was incorrect; HRQOL related to urinary domain was maintained in the group with preserved sexual function owing to the lower frequency of irritative/obstructive symptoms.

The ProtecT trial reported no difference in long-term cancer-specific survival between the active monitoring, prostatectomy, and radiotherapy groups in patients with localized prostate cancer.[17] Health-related quality of life in the ProtecT trial also showed higher urinary incontinence but lower nocturia in the prostatectomy group than in the other treatment groups.[18] Meanwhile, fecal incontinence was significantly higher in the radiotherapy group, suggesting that different treatments have different impacts on HRQOL. Therefore, considering the adverse effects of short- and long-term treatment when deciding on a treatment is very important. In the present study, there was a significant difference in the urinary domain of the EPIC because of changes in urinary bother and irritation between the 2 groups; however, there was no significant difference in urinary incontinence at 12 months postoperatively. Therefore, it is very important that HRQOL is related not only to incontinence but also to urinary bother and irritation.

Numerous reports have suggested that nerve preservation improves postoperative urinary continence.[12,19–21] A systematic review also

reported that nerve preservation has a favorable effect on urinary continence, especially in the early postoperative period.[22] However, patients with good preoperative sexual function have been previously reported to have good urinary continence regardless of nerve preservation,[15] and our results seem to be similar.

The impact of nerve preservation on lower urinary tract function was also reported by Haga et al.[23] In patients with nerve preservation, there was increase of maximum voided volume and decrease of nocturia, and in the nerve preservation group, there was less damage to the nerves distributed in the bladder trigone at the time of bladder neck dissection. Spradling et al.[24] found that the autonomic innervation of the bladder is highly concentrated in the proximal urethra and posterior bladder neck. The nerve preservation procedures indirectly preserved the intrapelvic branches of the pudendal nerves that innervated the membranous urethra, facilitating the function of the rhabdosphincter of the urethra. This could explain why there were fewer urinary irritation/obstruction symptoms in the group with preserved sexual function. Moreover, basic research using mice has suggested that nerve preservation causes the depletion of nitric oxide synthase and damages endothelial cells and smooth muscle in the corpus cavernosum of the penis, suggesting a relationship between sexual and bladder function.[25]

The present study had some limitations. First, we could not examine the degree of storage and voiding symptoms in detail because we did not collect data from the International Prostate Symptom Score questionnaire. The EPIC results did not provide a clear indication of how irritation or obstruction symptoms specifically impact HRQOL. It is plausible that prostatectomy may have improved obstructive symptoms or alleviated irritative symptoms, as described by Haga et al.[23] Either or both of these factors may be involved; however, it was challenging to attain conclusive findings from the current study. Second, we analyzed only a small number of patients because our sample was limited to those with unimpaired preoperative sexual function. In the future, it will be necessary to include a larger number of patients. Third, the preserved sexual function group should have been divided by an IIEF-5 score of ≥12 (more than mild-to-moderate) at 12 months postoperatively; however, sexual function was significantly reduced after surgery, and most patients had an IIEF-5 score of <11 at 12 months postoperatively. In this study, those who had relatively little decline in sexual function on the IIEF-5 were defined as the preserved sexual function group. Despite these limitations, our results suggest that patients with preserved postoperative sexual function had good postoperative urinary function.

5. Conclusions

Patients with preserved postoperative sexual function had better urinary function after RARP than those with impaired sexual function. In the urinary domain, urinary bother and irritation/obstruction were better in patients with preserved sexual function than in those with impaired sexual function. Preservation of sexual function is closely related to urinary function.

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Statement of ethics

This clinical study was approved by the Wakayama Medical University Institutional Review Board (authorization number, 1670) and performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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None.

Author contributions

YI: Manuscript writing, protocol development;
RD, SM, TW, SY, KK: Data analysis;
YK, IH: Protocol development.

Data availability

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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