Lower Urinary Tract Symptoms after Radical Perineal Prostatectomy

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Objective: To clarify the impact of radical perineal prostatectomy (RPP) on lower urinary tract symptoms (LUTS) in patients with clinically localized prostate cancer.

Methods: A total of 117 patients with a median age of 69 years who underwent RPP alone between August 2002 and August 2005 were included in the study. We measured LUTS on the basis of the International Prostate Symptom Score (IPSS) and IPSS quality of life (QOL) questionnaire before, and 3, 6 and 12 months after surgery.

Results: The overall mean total IPSS and IPSS QOL score decreased over time after RPP and was significantly reduced at 12 months after surgery. The decrease of the score was more prominent and rapid in patients with moderate to severe symptoms (IPSS ≥ 8), whereas in those with no or only mild symptoms (IPSS ≤ 7), the score did not change significantly after RPP. When the patients were divided into groups with baseline scores of 0–1 and 2–5 for each of the seven composites of the IPSS, scores for the 2–5 group improved significantly after RPP in all composites, whereas the 0–1 group had significantly worse scores for voiding frequency and nocturia. No significant change was noted in any of the other five composites.

Conclusion: This longitudinal study shows that RPP is significantly beneficial for moderate to severe LUTS, but also has adverse effects on voiding frequency and nocturia in some men with no or mild symptoms. This information is important when counseling patients about treatment options for localized prostate cancer.

Key words: prostate cancer – radical perineal prostatectomy – lower urinary tract symptoms

INTRODUCTION

It is well known that irritative and obstructive voiding symptoms are common in men with prostate cancer who undergo radical prostatectomy (RP) and that these symptoms significantly affect their quality of life (QOL) (1–3). Because many of these patients have bladder outlet obstruction (BOO) and detrusor overactivity before treatment (4,5), it is important to understand the impact of RP on lower urinary tract symptoms (LUTS) in addition to urinary incontinence.

However, in contrast to the retropubic approach, for which a lot of information on LUTS is available (1,2,4–7), no detailed study has yet been done on radical perineal prostatectomy (RPP). In RPP surgeons can directly access the bladder neck with less manipulation of the urinary bladder (8), and therefore the degree of invasiveness and denervation around the bladder neck, which affect voiding function and LUTS, may differ from those associated with the retropubic approach.

Here we present the results of a longitudinal study that we conducted to clarify the impact of RPP on LUTS.

PATIENTS AND METHODS

Between August 2002 and August 2005, 131 men who underwent RPP without neoadjuvant hormonal therapy for clinically localized prostate cancer at Hiroshima University Hospital and Shimane University Hospital were included in the study. The RPP was performed by four attending
surgeons (A.M., M.I., H.Y., and K.M.) according to the techniques described by Weldon (8).

LUTS was assessed on the basis of the International Prostate Symptom Score (IPSS) and the IPSS QOL score, which are both validated instruments (9,10). The IPSS is a self-administered seven-item questionnaire comprising items on incomplete emptying, intermittency, weak stream and straining (voiding symptom composites, VSC), and voiding frequency, urgency and nocturia (storage symptom composites, SSC). Each scale is scored separately from 0 to 5, with a higher score representing a worse outcome. The IPSS is totally scored from 0 to 35, with scores of 0 to 7, 8 to 19 and 20 to 35 indicating absent or mild, moderate and severe symptoms, respectively (9,10). The IPSS QOL score is a questionnaire that quantifies the QOL for specific LUTS and is scored from 0 to 6, with a lower score indicating a better health state.

All of the patients agreed to participate and signed an informed consent form. They then received from their urologists a questionnaire and a pre-paid envelope for returning it before, and 3, 6, and 12 months after surgery. Statistical analyses were conducted with the Wilcoxon test or \( \chi^2 \) test using the ‘JMP’ software package (ver. 6.02, SAS Institute, Cary, NC, USA). The level of statistical significance was set at \( P < 0.05 \).

RESULTS

CLINICAL CHARACTERISTICS OF THE STUDY PATIENTS

Although 131 patients were enrolled, 14 had undergone adjuvant or salvage radio- and/or hormonal therapy during or up to 12 months after RPP and were therefore excluded from the study analysis because such additional therapies may have an affect on LUTS. Therefore, our present analysis was based on the remaining 117 patients who provided longitudinal follow-up with LUTS surveys. The numbers of study patients at the measurement points 3, 6 and 12 months after RPP were 96 (82%), 92 (79%) and 101 (86%), respectively.

The clinical characteristics of the study patients are listed in Table 1. The median patient age and the median PSA value at diagnosis were 69 years (range 53–79 years) and 6.8 ng/ml (range 2.0–39.6 ng/ml), respectively. The median prostate volume was 27.0 cm\(^3\) (range 10.7–65.0 cm\(^3\)). Thirty-one per cent of the patients underwent unilateral or bilateral nerve-sparing surgery. Three of the 117 patients (2.6%) developed anastomotic stricture within 12 months after RPP. Of the 117 patients, 59 (50.5%) and 58 (49.5%) had total IPSS scores of 0–7 and 8–35, respectively. The 8–35 group had a significantly larger prostate volume than the 0–7 group (mean 30.7 versus 26.5 cm\(^3\), \( P = 0.0324 \)). The mean ages of the 8–35 and 0–7 groups were 68.6 and 67.3 years, respectively, with no significant difference.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. of patients (%)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>12 (10)</td>
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<tr>
<td>60–69</td>
<td>51 (44)</td>
</tr>
<tr>
<td>≥70</td>
<td>54 (46)</td>
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<tr>
<td>PSA at diagnosis (ng/ml)</td>
<td></td>
</tr>
<tr>
<td>≤4</td>
<td>20 (17)</td>
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<tr>
<td>4.1–10</td>
<td>74 (63)</td>
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<tr>
<td>10.1–20</td>
<td>19 (16)</td>
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<tr>
<td>&gt;20</td>
<td>4 (4)</td>
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<tr>
<td>Clinical tumor classification</td>
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<tr>
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<td>92 (79)</td>
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<tr>
<td>T2</td>
<td>25 (21)</td>
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<td>≤6</td>
<td>56 (48)</td>
</tr>
<tr>
<td>7</td>
<td>53 (45)</td>
</tr>
<tr>
<td>≥8</td>
<td>8 (7)</td>
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<tr>
<td>Prostate volume* (cm(^3))</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>24 (21)</td>
</tr>
<tr>
<td>20–40</td>
<td>73 (62)</td>
</tr>
<tr>
<td>&gt;40</td>
<td>12 (10)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Nerve sparing</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>33 (28)</td>
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<tr>
<td>None</td>
<td>81 (69)</td>
</tr>
</tbody>
</table>

PSA, prostate specific antigen.

*Prostate volumes were calculated from transrectal ultrasound data using the ellipse formula [volume = (\( \pi/6 \) \times length \times width \times height)].

ASSESSMENT OF LUTS

The overall mean total IPSS score, which was 9.6 before RPP, decreased over time after RPP and was reduced significantly to 7.4 at 12 months after surgery (23% reduction, \( P = 0.0367 \)) (Fig. 1). The decrease of the score was more prominent and rapid in patients with IPSS 8–35, in whom compared with the baseline score (15.7), the values were reduced by 3.6 (23%, \( P = 0.0083 \)), 4.2 (27%, \( P = 0.0019 \)) and 5.2 (33%, \( P = 0.0003 \)) at 3, 6 and 12 months after surgery, respectively. The percentage of patients with IPSS 8–35 decreased from 50% (58/117) at the baseline to 35% (35/101) at 12 months after RPP (\( P = 0.0288 \)). Meanwhile, in patients with IPSS 0–7, the mean score did not change significantly before and after RPP, except for a transient increase at 3 months after surgery.

The overall mean IPSS QOL score decreased with time after RPP in parallel with the IPSS score and the difference from the baseline became significant at 6 months after
surgery and beyond \( (P = 0.0033 \text{ and } 0.0002 \text{ for 6 and 12 months after surgery, respectively}) \). The IPSS QOL score in patients with IPSS 8–35 also improved significantly at 6 months after surgery and beyond, whereas that in patients with IPSS 0–7 did not change significantly after RPP. These changes of IPSS QOL score also paralleled those of the corresponding IPSS score.

Analysis of each item of the IPSS demonstrated that the symptoms of incomplete emptying and weak stream were significantly relieved after surgery \( (P = 0.0005, 0.0018 \text{ and } 0.0002 \text{ for weak stream and } 0.0029, 0.0313 \text{ and } 0.0151 \text{ for emptying, versus the baseline values at 3, 6 and 12 months after RPP, respectively}) \), while those of the remaining components did not change significantly throughout the study period (Fig. 2).

We further performed the same analysis for patients with baseline scores of 0–1 and those with baseline scores of 2–5. The numbers of patients in the 0–1 and 2–5 groups were 88 (75%) and 29 (25%) for incomplete emptying, 94 (80%) and 23 (20%) for intermittency, 65 (56%) and 52 (44%) for weak stream, 98 (84%) and 19 (16%) for straining, 72 (62%) and 45 (38%) for voiding frequency, 92 (79%) and 25 (21%) for urgency, and 49 (42%) and 68 (58%) for nocturia, respectively. In the 0–1 group, no significant change was noted in any of the 4 VSC. However, of the three SSC voiding frequency and nocturia worsened significantly after RPP. Although the mean scores decreased with time, those at 12 months after surgery were still significantly higher than those at the baseline \( (1.0 \text{ versus } 0.6, P = 0.0042 \text{ and } 1.2 \text{ versus } 0.8, P < 0.0001 \text{ for voiding frequency and nocturia, respectively}) \). Scores for urgency also increased significantly at 3 months after RPP \( (P = 0.003 \text{ versus baseline}) \), but thereafter recovered to the baseline level.

Because voiding frequency and nocturia were the only symptoms that were negatively influenced by RPP in the 0–1 group, we further analyzed the impact of RPP on both of these symptoms. Of the patients with a voiding frequency and nocturia score of 0–1 at the baseline, 41% (26/64) and 44% (20/45), respectively, had \( \geq 1 \) point higher scores than those at the baseline even at 12 months after RPP and their mean IPSS QOL scores at 12 months after surgery were significantly worse than those of patients who declared a \( \leq 0 \) decrease \( (2.9 \text{ versus } 2.0, P = 0.0162 \text{ and } 2.5 \text{ versus } 1.7, P = 0.0218 \text{ for voiding frequency and nocturia, respectively}) \). Among patients who had nocturia scores of 0–1 before RPP, none of the variables at the baseline (age, PSA value, clinical tumor stage, biopsy Gleason score, prostate volume and nerve preservation) differed significantly between those who had a \( \geq 1 \) increase at 1 year after surgery and those who did not. This was also the case for voiding frequency.

Meanwhile, IPSS scores in the 2–5 group were significantly decreased after RPP for all composites (Fig. 2). However, at 12 months after RPP, the average point reduction from the baseline was lowest for nocturia \( (0.5) \) followed by voiding frequency \( (1.4) \). In addition, although significant improvement was obtained for nocturia and voiding frequency, 56% of patients \( (57/101) \) still arose to void two or more times at night and 37% \( (37/101) \) had scores of 2–5 for voiding frequency even at 12 months after RPP. Among patients who had nocturia scores of 2–5 at the baseline, neither age nor prostate volume differed significantly between those who had a \( \geq 1 \) point decrease at 1 year after surgery and those who did not. This was also the case for voiding frequency.

Figure 1. Mean total IPSS and IPSS QOL scores before and after radical perineal prostatectomy. The top and bottom rows indicate the mean total IPSS and IPSS QOL scores, respectively. A and D, overall; B and E, men with IPSS baseline scores of 0–7; C and F, men with IPSS baseline scores of 8 to 35. IPSS, International Prostate Symptom Score; QOL, quality of life. †Baseline; *\( P < 0.05 \) versus baseline (Wilcoxon test).
surgery and those who did not. This was also the case for voiding frequency. Multivariate analysis revealed that of the four factors of age, prostate volume, baseline total IPSS score and nerve preservation, the baseline total IPSS score was the only predictive factor for total IPSS improvement (a \( \geq 2 \) point decrease from the baseline score at 12 months after RPP) \( (P < 0.0001, \text{odds ratio} = 1.25) \). None of age \( (P = 0.9927, \text{odds ratio} = 0.99) \), prostate volume \( (P = 0.0819, \text{odds ratio} = 1.05) \) or nerve preservation \( (P = 0.9299, \text{odds ratio} = 1.06) \) made a significant contribution to IPSS improvement.

DISCUSSION

Previously in the course of investigating the impact of our RPP procedure on urinary continence, we briefly assessed the changes of IPSS after RPP (11). The present study further extended our investigation of the impact of RPP on LUTS and clearly demonstrated that RPP provides major benefits for men with pre-existing LUTS. This was consistent with previous studies of RRP series (5,6,12). The significant improvement in IPSS-related QOL would imply that alleviation of LUTS outweighs the inconvenience caused by mild stress incontinence after surgery. Because as many as 44–57% of men who present for RP have moderate to severe LUTS (1,5,6) (50% in our study), this information is important when counseling patients about treatment options for localized prostate cancer.

The improvement of LUTS is probably attributable mostly to obstruction relief by RP. In our study, men with IPSS 8–35 had a significantly larger prostate volume than those with IPSS 0–7 in whom no apparent alleviation of LUTS was observed. It is well known that benign prostatic hypertrophy (BPH) can cause BOO, and secondary bladder overactivity and reduction of functional bladder capacity, which may result in storage symptoms (13,14). Conversely, these symptoms have been shown to be reversed with obstruction relief by prostatectomy in 60% of BPH patients (13,14). Several investigators have also reported IPSS improvement concurrent with an increase in urinary flow rate after RRP in patients who had moderate to severe LUTS and a flow rate of \( < 10 \text{ ml/s} \) before RP (5,15). Although our study lacked urodynamic or uroflowmetric data, these findings suggest a strong association of BOO relief by RPP with IPSS improvement. However, in the present study the pre-operative IPSS score was the only predictor of LUTS improvement and prostate volume was not. To clarify the mechanism of LUTS improvement, further investigations including urodynamic studies will be needed.

In contrast to the ameliorating effect of RPP on moderate to severe LUTS, RPP caused deterioration of nocturia and voiding frequency in men with no or only mild symptoms. In their own RRP series, Namiki et al. (6,7) obtained similar results to ours, and stated that the severity of nocturia never returned to the baseline level within 2 years after surgery. Therefore, the unfavorable impact of RP on nocturia may be irreversible, while the effect on voiding frequency is unclear.
because no long-term outcome data are available for asymptomatic men. As nocturia is considered to be a major cause of sleep disorder for men aged 50 years and older (16), and it has been reported that elderly people who need to void three or more times per night have a higher mortality rate than those voiding less often (17), this is a real and substantive problem for middle-aged or older men.

The mechanism leading to deterioration of these symptoms remains to be fully elucidated. None of the examined variables was able to predict the impact of RPP on nocturia status or voiding frequency. However, based on the RP-related functional and morphologic changes in the urinary bladder, several mechanisms have been assumed. Recently it was reported that following RP a substantial proportion of patients were affected by detrusor overactivity, impaired detrusor contractility, decreased compliance and sphincter weakness (13,18–20). As one of the reasons for these abnormalities, bladder denervation during surgery has been suggested (13). Wide anatomical dissection around the prostate and bladder neck during surgery may disrupt regional afferent and efferent innervation, causing outlet incompetence and partial denervation of the detrusor muscle (13). Also, Jung et al. (21) demonstrated that leakage of urine into the proximal urethra could increase bladder activity by stimulating urethral afferents, which in turn modulate the micturition reflex and induce detrusor instability. Thus, bladder denervation during surgery and postoperative urine incontinence may be implicated in the deterioration of storage symptoms, although recovery from urinary incontinence after RPP is considerable (11,22). For patients with no or only mild symptoms, these adverse effects may emerge as exacerbation of nocturia or voiding frequency. These mechanisms also might partly explain why the decrease in the scores for nocturia and voiding frequency was not as convincing as that for other composites in symptomatic men. The reversal of detrusor overactivity by relief of BOO might have been dampened by adverse effects such as bladder denervation or subtle urine leakage. Alternatively, men who were less sensitive to the LUTS-ameliorating effect of RPP might have had other pre-existing conditions, which may have resulted in nocturia, including nocturnal polyuria, diabetes mellitus, anxiety or primary sleep disorders, and behavioral and environmental factors (23).

To our knowledge, only one previous study has investigated the differences in the impact of RP on LUTS between surgical approaches, where AUA symptom score and subscales for obstruction and irritation did not differ between RPP and RRP (24). However, that study was a cross-sectional one with a median time between surgery and the survey of 2.7 years. In this context, the present study is the first to longitudinally investigate the impact of RPP on LUTS and QOL for 1 year after surgery in men with localized prostate cancer. In view of our results and those of the previous RRP series (5–7,12,15), RPP and RRP seem to have similar outcomes in terms of LUTS and LUTS-associated QOL for both symptomatic men and men with no or only mild symptoms. Future direct comparative trials between RPP and RRP are warranted to elucidate the superiority of one procedure over the other.

Although our study was relatively small and lacked data on uroflow and urodynamic variables, it provides important and detailed information about the impact of RPP on LUTS and LUTS-related QOL. These data may be useful when informing patients pre-operatively about treatment options for localized prostate cancer.

Conflict of interest statement
None declared.

References

16. Middelkoop HA, Smilde-van den Doel DA, Neven AK, Kamphuisen HA, Springer CP. Subjective sleep characteristics of 1,485 males and females aged 50–93: effects of sex and age, and factors