Intraoperative Electrophysiological Confirmation of Neurovascular Bundle Preservation during Radical Prostatectomy: Long-term Assessment of Urinary and Sexual Function

Shunichi Namiki¹, Akito Terai², Haruo Nakagawa¹, Yoshihiro Ikeda¹, Seiichi Saito¹, Makoto Satoh¹, Shigeto Ishidoya¹, Koji Yoshimura², Kentaro Ichikawa² and Yoichi Arai¹

¹Department of Urology, Tohoku Graduate University School of Medicine, Sendai and ²Department of Urology, Kurashiki Central Hospital, Kurashiki, Okayama, Japan

Received July 3, 2005; accepted September 15, 2005; published online November 8, 2005

Objective: We investigated the longitudinal recovery of urinary and sexual function after radical retropublic prostatectomy (RP) using an intraoperative electrophysiological test to confirm the functional preservation of the neurovascular bundle (NVB).

Methods: A total of 70 patients who underwent RP for localized prostate cancer were prospectively enrolled in our survey. During RP, electrophysiological testing was performed to confirm the NVB preservation. The NVB was electrostimulated and the responses were observed by monitoring the intracavernous or intraurethral pressure changes. All patients were classified into three groups according to the degree of nerve-sparing [a bilateral nerve-sparing group (BNS), a unilateral nerve-sparing group (UNS) and a non-nerve-sparing group (NNS)] based on the macroanatomical as well as the electrophysiological assessment. Both urinary and sexual function were measured before and 3, 6, 12 and 24 months after RP by a self-administered questionnaire.

Results: The concordance rate of nerve-sparing or non-nerve-sparing between the electrophysiological and macroanatomical assessment was 80%. According to the electrophysiological data, the BNS maintained significantly better urinary function at 3 months after RP than the NNS and UNS. After 6 months, each group had almost recovered continence. When considering sexual function, the BNS showed better sexual function scores than the NNS throughout the post-operative periods and the UNS at 2 years. According to the macroanatomical assessment, however, these differences were significant.

Conclusions: Nerve-sparing RP as confirmed by intraoperative electrophysiological test may contribute significantly to the early recovery of continence and greater rate of sexual function after RP.

Key words: prostate cancer – radical prostatectomy – erectile stimulation – nervous system – outcome assessment

INTRODUCTION

Radical prostatectomy (RP) is considered a safe and effective treatment for localized prostate cancer (1). Urinary incontinence and erectile dysfunction represent the principal sources of post-operative adverse events for patients who have undergone RP. Anatomical studies have identified the pelvic course of the cavernous nerves responsible for penile erection (2). Based on these studies, modifications in the surgical technique for RP have been developed to allow better post-operative preservation of continence or erectile function (3).

Intraoperative cavernosal nerve electrical stimulation has been reported for a limited number of patients undergoing RP (4,5). The data regarding its usefulness, however, have been controversial. Accurate evaluation of the effect of the nerve-sparing procedure also requires an assessment of the neurovascular bundle (NVB) preservation. We therefore used intraoperative electrophysiological testing to confirm the functional NVB preservation. Previously, we described that preservation of the bilateral NVB using electrophysiological assessment contributed to the early recovery of urinary continence for 6 months after RP (6). We now report a full cohort study with emphasis on the recovery of urinary function.
continence and erectile function during the first 2 years after RP, using an intraoperative electrophysiological test to assess the NVB preservation.

PATIENTS AND METHODS

PATIENT POPULATION AND OPERATION TECHNIQUE

Between March 2001 and December 2002 at Tohoku University Hospital and Kurashiki Central Hospital, electrophysiological confirmation of the NVB preservation during RP was performed in 88 patients with clinically localized prostate cancer. The operations were performed by three experienced urologists (Y.A., K.Y. and A.T.) who used virtually the same technique originally described by Walsh (7). The indications for the nerve-sparing procedure depended on preoperative [digital rectal examination, magnetic resonance imaging (MRI), the number and Gleason score of the positive biopsies, prostate-specific antigen (PSA) level or preference of the patient] and intraoperative factors, prioritizing cancer control.

INTRAOPERATIVE ELECTROSTIMULATION TECHNIQUE

After prostate removal, the operating surgeon performed a macroanatomical assessment of the nerve-sparing or non-nerve-sparing RP (macroanatomical assessment). Next, electrophysiological testing was performed to confirm the NVB preservation (electrophysiological assessment). Intraoperative electrostimulation was performed according to the method described by Terada et al. (8) and Kurokawa et al. (9). A monopolar stimulating needle electrode (Nippon Kohden) was put on a proximal point of the macroanatomically preserved NVB. For the side on which the NVB was intentionally resected, the electrode was placed on a point near the resected proximal stump of the NVB. Electrical stimulation was maintained for 10 s at 30 mA (20–50 mA)/10 Hz; monophasic rectangular pulse with pulse duration of 1.0 ms. The response to the electrical stimulation was observed as changes of cavernous pressure measured by a 23-G needle that was inserted into the corpus cavernosum of the penis. However, recently we have also used a balloon catheter inserted from the external urethral orifice and positioned at the middle portion of the penile urethra to measure the intraurethral pressure instead of using the 23-G needle to measure the intracavernous pressure. The needle or catheter was connected to a disposable pressure transducer set, and the changes of pressure were recorded on a pen recorder to observe the responses to the stimulation. An increase in the pressure of >4 cmH2O was considered a ‘positive’ response (9).

The difference between the macroanatomical assessment and the electrophysiological functional assessment was noted. We then classified all patients into three groups according to the degree of NVB preservation [a bilateral nerve-sparing group (BNS), a unilateral nerve-sparing group (UNS) and a non-nerve-sparing group (NNS)] based on the electrophysiological testing.

QUALITY-OF-LIFE ASSESSMENT

Urinary continence and sexual function were estimated by using the urinary and sexual function and bother domains of the University of California Los Angeles Prostate Cancer Index (UCLA PCI), which assesses the prostate-specific health-related quality-of-life (HRQOL) (10). The questionnaire had already been translated into Japanese, and its validity and reliability had been previously tested (11). The questionnaire was administered at five points in time. The baseline interview (t0) was conducted within 1 month before the surgery. Follow-up interviews were conducted in person at scheduled study visits of 3 (t1), 6 (t2), 12 (t3) and 24 (t4) months after RP.

All patients were informed of their cancer diagnosis before being asked to fill out the questionnaires. In the study, we collected self-reported outcome data directly from patients so as to avoid any physician-generated bias. All patients who agreed to participate in this study received a questionnaire, an informed consent form and a prepaid postage envelope for returning the questionnaire from their urologists. They voluntarily provided the self-reported questionnaire by mail.

STATISTICAL ANALYSIS

At baseline, comparison between the three groups was performed by \( \chi^2 \)-test, one-way analyses of variance (ANOVA). UCLA PCI scores for the various domains are shown as the mean ± standard deviation (SD) on 0–100 scales, with higher scores always representing better outcomes. For the study of associated factors, we used a logistic regression model. These statistical analyses for intergroup differences were performed using Mann–Whitney \( U \)-test. \( P \)-values of <0.05 were considered significant.

RESULTS

Intraoperative electrostimulation and observation of the responses to confirm nerve preservation were performed in 88 patients. Of these patients, 18 who received neoadjuvant therapy or post-operative salvage therapy were excluded. Thus, the study population comprised of 70 patients. Intraoperative electrostimulation and observation of the responses to confirm nerve preservation were performed in these 70 patients (140 NVBs). Of 79 sides in which the NVB appeared to be preserved macroanatomically, 11 NVBs (14%) did not demonstrate a positive response. However, of 61 sides in which the NVB was intentionally resected, 17 NVBs (28%) showed a positive response. Thus, the total concordance rate was 80%.

Use of the assessment to confirm NVB preservation made it possible to objectively divide the patients into three groups: 24 patients in the BNS; 37 in the UNS; and 9 in the NNS. However, use of the macroanatomical assessment to classify the patients resulted in 17 patients of the BNS, 43 of the UNS and 10 of the NNS.
DISCUSSION

Our study demonstrated several important findings. First, macroanatomical and electrophysiological assessments of nerve preservation showed different outcomes. The intraoperative
electrophysiological assessment revealed that about 20% of the macroanatomical assessments were incorrect. Terada et al. (8) reported that 6 (21.4%) of 28 sides on which the NVB was macroanatomically preserved did not have a positive response. A possible explanation is that the nerve function might be lost owing to electrocautery damage or nerve manipulation even if the NVB appears to be macroanatomically preserved.

The few previous reports on nerve-sparing benefit for urinary continence or sexual function, as measured by physician reports, were single surgeon series and identified only the patient age as a significant covariate (12–14). Previous studies using validated HRQOL instruments showed that cavernous nerve preservation enhanced the post-RP sexual recovery (15,16). However, these studies were limited because the nerve-sparing status was determined retrospectively or based on macroanatomical assessments by the surgeons. First, our study combines the longitudinal disease-specific HRQOL outcomes followed for 2 years after RP, using a validated e-survey methodology, with electrophysiological assessments of the nerve preservation outcomes.

**Table 2.** Urinary domain scores of patients in the treatment groups: electrophysiological assessment

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>BNS</th>
<th>UNS</th>
<th>NNS</th>
<th>P-value for comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BNS versus UNS</td>
<td>BNS versus NNS</td>
<td>UNS versus NNS</td>
<td></td>
</tr>
<tr>
<td>Urinary function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (t0)</td>
<td>92.1 ± 13.5</td>
<td>93.4 ± 6.0</td>
<td>94.7 ± 16.0</td>
<td>NS</td>
</tr>
<tr>
<td>3 Months (t1)</td>
<td>79.1 ± 22.7**</td>
<td>71.2 ± 22.3**</td>
<td>67.0 ± 21.5**</td>
<td>0.047</td>
</tr>
<tr>
<td>6 Months (t2)</td>
<td>87.4 ± 18.3*</td>
<td>86.2 ± 20.3*</td>
<td>81.5 ± 20.1**</td>
<td>NS</td>
</tr>
<tr>
<td>12 Months (t3)</td>
<td>87.8 ± 14.4</td>
<td>87.2 ± 18.1*</td>
<td>80.0 ± 20.2**</td>
<td>NS</td>
</tr>
<tr>
<td>24 Months (t4)</td>
<td>88.0 ± 15.3</td>
<td>87.1 ± 17.7*</td>
<td>84.5 ± 18.2*</td>
<td>NS</td>
</tr>
<tr>
<td>Urinary bother</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (t0)</td>
<td>88.2 ± 22.6</td>
<td>88.8 ± 18.7</td>
<td>85.0 ± 25.5</td>
<td>NS</td>
</tr>
<tr>
<td>3 Months (t1)</td>
<td>81.3 ± 24.2</td>
<td>76.4 ± 24.2*</td>
<td>72.5 ± 14.2*</td>
<td>0.016</td>
</tr>
<tr>
<td>6 Months (t2)</td>
<td>90.2 ± 14.7</td>
<td>85.3 ± 24.3</td>
<td>92.4 ± 15.7</td>
<td>NS</td>
</tr>
<tr>
<td>12 Months (t3)</td>
<td>91.5 ± 12.2</td>
<td>91.0 ± 15.8</td>
<td>93.0 ± 10.0</td>
<td>NS</td>
</tr>
<tr>
<td>24 Months (t4)</td>
<td>88.3 ± 18.0</td>
<td>84.7 ± 23.0</td>
<td>87.5 ± 20.0</td>
<td>NS</td>
</tr>
</tbody>
</table>

BNS, bilateral nerve-sparing; UNS, unilateral nerve-sparing; NNS, non-nerve-sparing; NS, not significant.

Data are presented as mean ± standard deviation.

Statistically significant changes from baseline are indicated as *P < 0.05 and **P < 0.01, respectively (Mann–Whitney U-test).

**Table 3.** Sexual domain scores of patients in the treatment groups: electrophysiological assessment

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>BNS</th>
<th>UNS</th>
<th>NNS</th>
<th>P-value for comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BNS versus UNS</td>
<td>BNS versus NNS</td>
<td>UNS versus NNS</td>
<td></td>
</tr>
<tr>
<td>Sexual function</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (t0)</td>
<td>33.7 ± 21.1</td>
<td>38.8 ± 22.1</td>
<td>26.9 ± 22.1</td>
<td>NS</td>
</tr>
<tr>
<td>3 Months (t1)</td>
<td>14.2 ± 20.7**</td>
<td>5.6 ± 5.6**</td>
<td>1.8 ± 3.0**</td>
<td>0.048</td>
</tr>
<tr>
<td>6 Months (t2)</td>
<td>13.3 ± 11.7**</td>
<td>9.8 ± 13.1**</td>
<td>1.6 ± 4.1**</td>
<td>0.001</td>
</tr>
<tr>
<td>12 Months (t3)</td>
<td>17.1 ± 18.0**</td>
<td>11.5 ± 14.3**</td>
<td>2.4 ± 5.9**</td>
<td>0.001</td>
</tr>
<tr>
<td>24 Months (t4)</td>
<td>24.3 ± 11.4**</td>
<td>13.6 ± 11.6**</td>
<td>5.7 ± 5.9**</td>
<td>0.011</td>
</tr>
<tr>
<td>Sexual bother</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (t0)</td>
<td>69.3 ± 23.6</td>
<td>70.5 ± 27.1</td>
<td>63.9 ± 20.8</td>
<td>NS</td>
</tr>
<tr>
<td>3 Months (t1)</td>
<td>47.4 ± 34.3**</td>
<td>52.9 ± 42.9**</td>
<td>66.7 ± 33.1</td>
<td>0.044</td>
</tr>
<tr>
<td>6 Months (t2)</td>
<td>46.3 ± 28.1**</td>
<td>60.0 ± 31.6*</td>
<td>68.8 ± 32.5</td>
<td>NS</td>
</tr>
<tr>
<td>12 Months (t3)</td>
<td>52.3 ± 29.1*</td>
<td>62.8 ± 27.3*</td>
<td>72.2 ± 32.2</td>
<td>0.043</td>
</tr>
<tr>
<td>24 Months (t4)</td>
<td>41.1 ± 28.1**</td>
<td>57.3 ± 29.1**</td>
<td>68.8 ± 27.2</td>
<td>0.048</td>
</tr>
</tbody>
</table>

BNS, bilateral nerve-sparing; UNS, unilateral nerve-sparing; NNS, non-nerve-sparing; NS, not significant.

Data are presented as mean ± standard deviation.

Statistically significant changes from baseline are indicated as *P < 0.05 and **P < 0.01, respectively (Mann–Whitney U-test).
Second, the electrophysiological assessment revealed that bilateral nerve-sparing RP is beneficial for the early recovery of post-operative urinary continence. However, when the nerve-sparing groups were classified based on the macro-anatomical assessment, no statistically significant difference could be found. We extended the follow-up period up to 2 years and compared these results with those from our earlier report, which described that, based on the electrophysiological assessment, bilateral nerve-sparing RP was beneficial for the early recovery of post-operative urinary continence during the

**Figure 1.** Sequential changes in average urinary function scores in the BNS, bilateral nerve-sparing group; UNS, unilateral nerve-sparing group and NNS, non-nerve-sparing group. (A) The changes in the scores of the three groups when classified according to the macroanatomical assessment. (B) The changes in the average urinary function scores for the three groups classified according to the electrophysiological assessment.

**Figure 2.** Sequential changes in average sexual function scores in the BNS, bilateral nerve-sparing group; UNS, unilateral nerve-sparing group and NNS non-nerve-sparing group. (A) The changes in the scores of the three groups when classified according to the macroanatomical assessment. (B) The changes in the average sexual function scores for the three groups classified according to the electrophysiological assessment.
first 6 months (6). The initial study showed significant differences in the recovery of urinary continence at 3 months post-operatively. Interestingly, the present study revealed that the BNS and UNS groups differed in urinary continence at 3 months after prostatectomy but were almost identical at 6 months or later. Thus BNS appears to contribute to early recovery of continence and similar outcome of urinary function is finally obtained with longer follow-up, irrespective of BNS and UNS procedures. Third, nerve-sparing RP, particularly that with bilateral NVB preservation, significantly contributed to the recovery of the post-operative sexual function compared with patients without nerve preservation. Notably, the BNS showed better sexual function than the UNS at 2 years after RP. Litwin et al. (17) described that nerve-sparing RP continued to show improved sexual function in the second year after RP, finding similar to ours. Kim et al. (18) examined 35 patients who underwent bilateral preservation and 25 patients who underwent unilateral preservation and found no correlation between the intraoperative findings and post-operative recovery. In part, this may have been due to the length of the follow-up period (minimum 6 months, median 365 days), which was shorter than that of our investigation. However, the BNS and UNS reported lower sexual bother than baseline throughout the post-operative periods. Although the small number of patients might limit the reliability of our results, those who underwent RP with nerve-sparing procedure were potentially more interested in or motivated to maintaining their sexual function post-operatively. Therefore, it is possible that they were more inclined to report lower sexual bother scores because of their disappointment with post-operative sexual dysfunction. These findings will be helpful in counseling men who are more motivated to resume sexual activity when they are weighing a decision about RP. In other words, greater emphasis needs to be placed on the risk of post-operative erectile dysfunction in preoperative counseling.

Another important aspect of the electrophysiological assessment of NVB preservation is that the method could provide immediate feedback to the surgeons during the operation. Despite attempts at direct visualization of the nerves, it is currently impossible to predict at that time of surgery whether the apparently preserved nerves will be functionally normal or whether vascular damage will affect the continence or erectile function (19). Thus, the success or failure of the nerve-sparing procedure is recognized 1 or 2 years after the surgery. Moreover, the recovery of urinary and sexual functions may be multifactorial in nature. Therefore, it is difficult for the surgeon to know whether the nerve-sparing procedure contributes beneficially to the outcome. Using the method described by the present study, a surgeon could immediately obtain some information about the results of his nerve-sparing procedure. This early feedback may further contribute to the improvement of the surgical technique.

In our study, multivariate logistic regression analysis did not reveal earlier recovery of urinary continence in patients undergoing a nerve-sparing technique. However, the ability to investigate this was severely limited by the fact that only a small subset of patients underwent non-nerve-sparing procedure. A larger number of patients are necessary to confirm this finding.

This prospective observational study has several limitations. The cohort of this study was not randomly sampled and might not be representative of all men with prostate cancer who choose RP. Thus, the patients undergoing NNS were significantly older than those who underwent BNS and UNS. Age has been shown to be a significant predictor of the recovery of sexual function and post-operative continence status (20). Our study had a relatively small sample size, especially in the NNS group, consistent with its design as a feasibility study of longitudinal collection. Finally, we did not distinguish among patients who used erectile aids such as sildenafil, a vacuum erection device. This factor may have influenced the assessment of the sexual function recovery.

Despite these limitations, our findings have important implications for men choosing RP for localized prostate cancer. It is expected that in the future the instruments and associated procedures for intraoperative electrophysiological assessment will become simpler and more convenient to use, enabling this technique to be more widely used.

Overall, bilateral nerve-sparing RP was beneficial for the early recovery of urinary continence just after RP. More than 6 months later, however, no differences were observed among each of the nerve-sparing procedure groups. Bilateral nerve-sparing RP contributed significantly to improve the recovery of post-operative sexual function compared with non-nerve preservation but also compared with the unilateral nerve preservation procedure for 2 years after RP.

Acknowledgment

This study was supported in part by a grant from the Ministry of Health and Welfare of Japan.

References


