LONG-TERM EFFECT OF SILDENAFIL CITRATE ON ERECTILE DYSFUNCTION AFTER RADICAL PROSTATECTOMY: 3-YEAR FOLLOW-UP

RUPESH RAINA, MILTON M. LAKIN, ASHOK AGARWAL, RAKESH SHARMA, KUSH K. GOYAL, DROGO K. MONTAGUE, ERIC KLEIN, AND CRAIG D. ZIPPE

ABSTRACT

Objectives. To evaluate the long-term effect and safety of sildenafil citrate for the treatment of erectile dysfunction after radical prostatectomy (RP).

Methods. The study consisted of 91 patients with erectile dysfunction from our institution who received oral sildenafil citrate after RP. We surveyed these patients using a self-administered questionnaire during the first year of sildenafil citrate use to determine treatment satisfaction, patient compliance, and safety. Those who had responded positively to the drug were surveyed again 3 years later (n = 48). Sildenafil citrate was prescribed at a dose of 50 mg and increased to 100 mg if needed. Data were collected from a self-administered questionnaire using the abridged five-item version of the International Index of Erectile Function questionnaire, referred to as the Sexual Health Inventory of Men, and the Erectile Dysfunction Inventory of Treatment Satisfaction. The patients were stratified according to the type of nerve-sparing (NS) RP procedure they underwent: bilateral NS, unilateral NS, and non-NS.

Results. At 3 years, 31 (71%) of the 43 patients who had returned the second surveys were still responding to sildenafil. Of these 31 respondents, 10 (31%) had augmented their dose from 50 to 100 mg. The dropout rate was 27%; 6 of 12 had discontinued because of the return of natural erections, 5 because of a loss of efficacy, and 1 because his spouse had died. No differences were found in the 1-year and 3-year five-item International Index of Erectile Function (Sexual Health Inventory of Men) and Erectile Dysfunction Inventory of Treatment Satisfaction scores between the NS groups. The most common side effects at 3 years were headache (12%), flushing (10%), and blue or blurred vision (2%). No patient discontinued the drug at 3 years because of side effects.

Conclusions. The results of this study indicate that the vast majority of patients with erectile dysfunction after RP who initially respond to sildenafil continue to do so at 3 years and are satisfied and compliant with the treatment regimen.

had undergone RP, such as the impact of the presence or absence of the neurovascular bundles.³

Earlier research from our clinic investigated the effects of this new oral medication in patients after RP and studied the impact of the presence or absence of the neurovascular bundles.⁶ Our initial publication reported that 12 of 15 patients undergoing bilateral nerve-sparing (NS) procedures showed efficacy with vaginal penetration with sildenafil at 1 year after RP.⁶ This initial study showed the role and value of neurovascular preservation in determining the response to sildenafil citrate.

Subsequently, we updated our experience to include 91 patients treated with sildenafil after RP.⁷ In the bilateral NS group, 71.7% (38 of 53) achieved vaginal intercourse; in the unilateral NS group, 50% (6 of 12) did so. In the non-NS group, only 15.4% (4 of 26) achieved vaginal penetration.⁷ Our study showed that sildenafil citrate can improve erectile dysfunction in about 70% of impotent, motivated patients after RP if a bilateral NS procedure is performed and in 50% of patients if a unilateral NS procedure is done.

This finding was confirmed by Lowentritt et al.⁸ 1 year later when they reported a response rate to sildenafil citrate in 58% of men undergoing bilateral NS procedures. The impact of nerve preservation and the efficacy of sildenafil was also reported by Zagaja et al.⁹ from the University of Chicago, who showed an 80% response rate in men younger than 55 years old when both nerve bundles were spared and a 40% response when one bundle was spared. However, in the 56 to 65-year-old group, the response rate dropped to 45% in the group with two nerves spared and to 0% in those with one nerve preserved.⁹

After the launch of sildenafil citrate, much has been learned about the mechanism of action of the drug, its safety profile, and its clinical efficacy specific to various etiologies of ED. However, no reports have been published on its long-term effects and durability in patients with ED after RP. We conducted this study to evaluate the long-term efficacy of sildenafil citrate at the 3-year interval.

MATERIAL AND METHODS

INITIAL STUDY: PATIENT RECRUITMENT

We obtained and reviewed the records of two experienced surgeons (C.Z., E.K.) who, between 1994 and 1998, performed RP on 330 sexually active patients with localized prostate cancer. At a mean follow-up of 3 months, 208 (68%) or 350 patients experienced severe ED, with no patient able to achieve vaginal penetration. All 208 patients with ED were initially evaluated by an internist in our group (M.L.) who took a comprehensive sexual history and performed a physical examination. At that time, the patients were offered standard ED treatments, including a vacuum constriction device, intracavernous injection, or the medicated urethral system for erections. The patients who had not received preoperative or postoperative hormonal or radiation therapy, who were not using any concurrent form of ED treatment, and who did not have any contraindications to the use of sildenafil citrate (eg, ischemic cardiovascular disease or the use of oral, sublingual, or transdermal nitrates) were prescribed oral sildenafil citrate (50 mg, 44%).

We retrospectively stratified these 91 patients according to the type of NS procedure they had undergone: bilateral NS (n = 53), unilateral NS (n = 12), and non-NS (n = 26). The surgeon recorded the anatomic status of the neurovascular bundle at the time of surgery; no intraoperative function tests were performed. The type of NS procedure was confirmed by reviewing the operative records.

DRUG THERAPY

All patients waited at least 3 months after surgery before they were prescribed sildenafil. The starting dose was 50 mg, which was titrated to 100 mg if the patient did not have a positive response. Patients were instructed to take one sildenafil tablet approximately 1 hour before sexual activity, as per the manufacturer’s instructions, and to engage in adequate foreplay before attempting sexual intercourse.

THREE-YEAR UPDATE: SURVEYS AND DATA ASSESSMENT

The patients’ response to sildenafil citrate was assessed using the International Index of Erectile Function (IIEF-15) questionnaire, and the efficacy of sildenafil citrate for ED after RP was assessed using the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire.¹⁰–¹² The EDITS questionnaire is a psychometrically validated measure of patient satisfaction with ED treatments. We asked 2 of the 11 questions that comprise the questionnaire: (a) how satisfied are you with sildenafil citrate; and (b) how has sildenafil citrate met your expectations. The two questions were scored using a 5-point scale (0 to 4), and the mean score was multiplied by 25 to get the total EDITS score. The total scores were calculated as follows: 0 = very dissatisfied; 25 = satisfied; 50 = neither satisfied nor dissatisfied; 75 = satisfied; and 100 = very satisfied. A score of 50 or more was defined as “satisfied with treatment” and a score of 50 or less was defined as “not satisfied with treatment.”¹²

A third questionnaire was used to determine the sexual satisfaction of the patients’ spouses/partners. The spouses/partners were specifically asked how often they were satisfied with intercourse and how often the patient was able to achieve and maintain an erection. This questionnaire was scored from 1 to 5: 1 = never/occasionally; 2 = less than half of the time; 3 = sometimes/half the time; 4 = more than half of the time; and 5 = almost always. Total spousal satisfaction was calculated from these questions and expressed as a percentage.⁴,¹⁰

Patients completed the IIEF-15 questionnaire before (preoperative, baseline) and at a mean interval of 36 weeks (range 24 to 48) after RP. All three surveys were mailed to all 91 patients and their spouses/partners 1 year after they began taking sildenafil citrate. At this time, we also performed a retrospective chart review to collect data on treatment effect, mean duration of intercourse, number of patient attempts at intercourse, number of successful attempts (vaginal penetration), and side effects. All 91 patients and their spouses/partners completed the IIEF-15, EDITS, and spousal questionnaires.

Data from the IIEF-15 questionnaire were condensed into the IIEF-5 questionnaire, which is an abridged 5-item version of the IIEF-15 questionnaire referred to as the Sexual Healthy Inventory of Men (SHIM). The SHIM is a validated, multidimensional, self-administered questionnaire that is a sensitive indicator of changes in erectile function and treatment outcomes. It is scored from 1 to 5: 1 = never/occasionally; 2 =
TABLE I. Characteristics of 91 patients after radical prostatectomy who had erectile dysfunction before sildenafil citrate therapy

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (n = 91)</th>
<th>Bilateral NS (n = 53)</th>
<th>Unilateral NS (n = 12)</th>
<th>Non-NS (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yr)</td>
<td>61.8</td>
<td>60.5</td>
<td>61.2</td>
<td>65.6</td>
</tr>
<tr>
<td>Preoperative erectile status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full</td>
<td>89.4 (82)</td>
<td>93.9 (50)</td>
<td>100 (12)</td>
<td>76.9 (20)</td>
</tr>
<tr>
<td>Partial</td>
<td>10.6 (9)</td>
<td>6.1 (3)</td>
<td>0 (0)</td>
<td>23.1 (6)</td>
</tr>
<tr>
<td>None</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Predrug erectile status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Partial</td>
<td>42 (38)</td>
<td>49 (26)</td>
<td>41 (5)</td>
<td>27 (7)</td>
</tr>
<tr>
<td>None</td>
<td>58 (53)</td>
<td>51 (27)</td>
<td>59 (7)</td>
<td>73 (19)</td>
</tr>
</tbody>
</table>

Key: NS = nerve sparing
Data presented as the percentage, with the number of patients in parentheses.

less than half of the time; 3 = sometimes/half of the time; 4 = more than half of the time; and 5 = almost always. The total IIEF-5 score was calculated by totaling the response to all five questions. A positive response to drug therapy was defined as successful vaginal intercourse.

Of the 91 patients who completed the first round of surveys, 48 (52%) were “positive responders.” We mailed these 48 patients the IIEF-15, EDITS, and spousal questionnaires 3 years after the first surveys to assess long-term efficacy and compliance. At this time, we performed a follow-up chart review (M.L.) to determine any change in drug efficacy, dose, and frequency of use, compliance, return of natural erections, and development of new side effects. Data from the IIEF-15 at 3 years was also condensed into the IIEF-5 (SHIM).

Statistical Analysis

Comparisons between the respondent groups at 1 year and at 3 years were performed using the chi-square test or Fisher’s exact test as appropriate. Comparisons of percentages within a group between follow-up times were performed using McNemar’s test. Comparisons of continuous variables between groups were performed using Student’s t test or the Wilcoxon rank sum test. The paired t test or Wilcoxon signed-rank tests were used to compare changes within a group. All statistical tests were two-tailed, and P was considered statistically significant when <0.05. All computations were performed using Statistical Analysis System software, version 8.1 (SAS Institute, Cary, NC). The continuous variables are summarized as the mean and standard deviation.

Results

No statistically significant differences were found between the non-NS and NS groups in age, interval between RP and start of sildenafil, preoperative and predrug erectile status, nocturnal erections, and ability to penetrate, as assessed by our retrospective chart review (Table I).

First Survey

During the first survey, 48 (52.7%) of 91 patients reported having successful vaginal intercourse. The mean ± SD EDITS score was 73.6 ± 3.2, and the spousal satisfaction rate was 69.2%. In the 53 patients who had had a bilateral NS RP, 38 (71.7%) responded; in those in the unilateral NS group, 6 (50%) of 12 responded; and in those with non-NS, 4 (15.4%) of 26 responded. The magnitude of improvement in responses was greater in the bilateral NS group than in the unilateral NS and non-NS groups (P < 0.05). Table II shows the baseline (postoperative, before sildenafil use) and 1-year post-treatment scores for the abridged IIEF-5 questionnaire, total EDITS score, and spousal satisfaction. Of the positive responders, 14 (29.1%) required the 50-mg dose and 34 (70.9%) the 100-mg dose. The two most common side effects were transient headache (30.7%) and flushing (21%), which were not related to dose increase.

Second Survey

Forty-three (89%) of the 48 patients who responded to sildenafil therapy favorably at 1 year returned the questionnaires 3 years later. Five patients did not return the questionnaires despite a second request. Of these 43 patients, 33 had had bilateral NS surgery, 6 unilateral NS surgery, and 4 non-NS surgery. At 3 years, 31 (72%) of 43 patients were still using sildenafil citrate for sexual intercourse. All these patients were sildenafil dependent, with a variable degree of partial erections. The spousal satisfaction rate was 72.6%. Ten (31%) of the 31 responders augmented their dose from 50 to 100 mg, with no correlation between the frequency of use and the need to increase the dose.

Table III shows the reasons the 12 patients stopped taking the drug after the first survey. The drop out rate was 27%; 6 (50%) of 12 discontinued because of the return of natural erections sufficient for vaginal intercourse (mean use 2.1 years), 5 stopped because of a loss of efficacy (mean use 1.5 years), and 1 discontinued because his spouse had died. Table IV shows the scores for the SHIM (abridged 5-item version of IIEF) and EDITS questionnaires stratified by the type of NS surgery.
Mean EDITS score: 5.18

Total mean IIEF-5 score 5.18

Sildenafil at 1 year (72%) continued to have efficacy and compliance. Most patients who responded at 1 year (72%) continued to have effective erections with sildenafil citrate at 3 years. The SHIM (IIEF-5) and EDITS scores were comparable at 1 and 3 years. When the responses at 1 and 3 years were stratified according to neurovascular bundle status, the magnitude of improvement in SHIM (IIEF-5) was still greater in the bilateral NS group than in the unilateral NS and non-NS groups. The degree of neurovascular preservation continued to stratify the response rates to sildenafil.

Sildenafil citrate should be offered as the first treatment option for the subset of patients with ED after RP. Various factors correlate with the sildenafil response in men with ED after RP. Pretreatment variables include preoperative sexual function and frequency, patient age, type of NS procedure, degree of postoperative potency before drug therapy, and the length of time after surgery before sildenafil administration.6–9,13

The etiology of ED after RP appears to be transient or permanent injury to the neurovascular bundles that innervate the corpora cavernosum.2,3 Although the etiology can be mixed, with both vasculogenic and neurogenic insults, the primary problem appears to be neurologic injury.1,2 With a neurologic injury, the release of nitric oxide is decreased across the neuromuscular junction, limiting the amount of available cyclic guanosine monophosphate (cGMP). Sildenafil citrate works by inhibiting the phosphodiesterase type 5 (PDE5) enzyme, and thus increases the amount of cGMP.14 Thus, the presence or absence of the neurovascular bundles, which significantly influences the relative amount of nitric oxide secretion, influences a man’s ability to achieve vaginal intercourse. Without nitric oxide, cGMP is not activated and, therefore, cannot convert guanosine triphosphate into cGMP. cGMP is metabolized through enzymatic breakdown by PDE5, which closes the potassium channel and results in increased intracellular calcium and smooth muscle contraction.15,16

### TABLE II. Comparison of IIEF-5 and EDITS score of positive responders to sildenafil citrate at baseline, 1 year, and 3 years

<table>
<thead>
<tr>
<th>IIEF-5 Domains</th>
<th>Baseline After Surgery (n = 48)</th>
<th>At 1 yr of Sildenafil Use (n = 48)</th>
<th>At 3 yr of Sildenafil Use (n = 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q5 (maintenance ability)</td>
<td>1.34 ± 0.13 (1-2)</td>
<td>3.42 ± 0.36 (3-4)</td>
<td>4.12 ± 0.19* (4-5)</td>
</tr>
<tr>
<td>Q15 (erection confidence)</td>
<td>1.11 ± 0.04 (1-2)</td>
<td>3.87 ± 0.29 (3-4)</td>
<td>3.91 ± 0.28 (3-5)</td>
</tr>
<tr>
<td>Q4 (maintenance frequency)</td>
<td>1.17 ± 0.06 (1-2)</td>
<td>3.81 ± 0.06 (3-4)</td>
<td>4.31 ± 0.22* (4-5)</td>
</tr>
<tr>
<td>Q2 (erection firmness)</td>
<td>1.20 ± 0.08 (0-1)</td>
<td>3.57 ± 0.12 (3-4)</td>
<td>3.85 ± 0.29* (3-4)</td>
</tr>
<tr>
<td>Q7 (intercourse satisfaction)</td>
<td>0.36 ± 0.12 (0-1)</td>
<td>3.85 ± 0.40 (3-4)</td>
<td>3.98 ± 0.28 (3-5)</td>
</tr>
<tr>
<td>Total mean IIEF-5 score</td>
<td>5.18 ± 0.43 (4-6)</td>
<td>18.52 ± 1.23 (15-20)</td>
<td>20.01 ± 1.26 (15-25)</td>
</tr>
<tr>
<td>Mean EDITS score</td>
<td>—</td>
<td>73.6 ± 3.2 (50-75)</td>
<td>71.9 ± 2.6 (50-75)</td>
</tr>
</tbody>
</table>

**Notes:**
- IIEF-5 = short form (5 questions) of International Index of Erectile Function; EDITS = Erectile Dysfunction Inventory of Treatment Satisfaction.
- Each IIEF-5 domain scored from 0 to 5: 0 = none; total IIEF-5 score calculated by totaling and taking the mean of the responses to all 5 domains of IIEF-5.
- Significant difference at 3 years. Although some significant differences were found, caution should be used in their interpretation because of the small sample size of the groups.
- None of these measures differed significantly between 1 year and 3 years of follow-up, although the maintenance frequency and ability items had improved significantly at 3 years. Although some significant differences were found, caution should be used in their interpretation because of the small sample size of the groups.
- The most common side effects at 3 years were headaches (12%), flushing (10%), and blue or blurred vision (2%). No patient discontinued the drug at 3 years because of side effects.

### TABLE III. Reason for discontinuation of sildenafil citrate at 3 yr

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bilateral NS (n = 33)</th>
<th>Unilateral NS (n = 6)</th>
<th>Non-NS (n = 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Return of natural erection sufficient for vaginal penetration (mean use ≥ 2.5 yr)</td>
<td>15 (5)</td>
<td>16 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Lack of efficacy</td>
<td>6 (2)</td>
<td>16 (1)</td>
<td>50 (2)</td>
</tr>
<tr>
<td>Death of spouse</td>
<td>3 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Notes:**
- NS = nerve sparing.
- Data presented as the percentage, with the number of patients in parentheses.

**COMMENT**

Our 3-year follow-up study of the effect of sildenafil citrate after RP demonstrates its long-term efficacy and compliance. Most patients who responded at 1 year (72%) continued to have effective erections with sildenafil citrate at 3 years.
cGMP, there is no substrate in which PDE5 can work. Hence, a PDE5 inhibitor such as sildenafil citrate is ineffective.\textsuperscript{6,7} This physiology emphasizes and explains why the presence and amount of neurovascular tissue significantly influences the response rates to sildenafil citrate.

We observed that some patients who received sildenafil with good initial responses had a reduction, or complete loss, of efficacy. This loss resulted in some patients requiring a greater dose or eventually discontinuing treatment. Ten (31\%) of 31 patients who were still using sildenafil observed a reduction in efficacy that required them to increase the dose to 100 mg to achieve adequate results. A trend, but no significant relationship, was noted between the frequency of use and the need to increase the dose. The percentage in the reduction in efficacy of sildenafil ranged from 15\% to 50\%, and the time for diminished efficacy was 15 months (average 12 to 18). Patients who took sildenafil four or fewer times per month had to increase the dose (51\%) more often than those who took it four or more times per month (16\%), but this difference was not statistically significant.

El-Galley \textit{et al.}\textsuperscript{17} evaluated the long-term efficacy and tachyphylaxis effect of sildenafil in patients who initially responded to the drug and frequently became resistant with time. The results of their study suggested a possible tachyphylaxis effect with sildenafil after 2 years of use. Twenty percent of the patients increased their dose to sustain the same effect and 17\% discontinued the drug because of a loss of efficacy.\textsuperscript{17} Tachyphylaxis is a pharmacologic process referring to a reduction in tissue response to a drug that occurs in the presence of a constant concentration of the drug. Additional confirmatory studies are required to document possible causes and the interval for the reduction or loss of efficacy in subgroups of patients using sildenafil citrate for ED after RP.

At the 3-year mark, 12 of 43 patients stopped using sildenafil citrate after a mean use of 2.5 years. Of the 12 patients who reported a good initial response on the first survey, 6 had spontaneous erections (mean time 2.1 years after RP) and no longer needed treatment, suggesting a potential therapeutic benefit. However, 5 (12\%) of 43 patients stopped taking sildenafil because of a gradual loss of efficacy (mean use of drug 1.5 years); 1 patient discontinued treatment because his spouse had died. Intracavernous injection can salvage many sildenafil nonresponders, as reported by Thukral \textit{et al.}\textsuperscript{18} and Shabsigh \textit{et al.}\textsuperscript{19} In patients who have undergone non-NS surgery or those for whom treatment with sildenafil citrate has failed, alternative treatments (intracavernous injections, vacuum constriction devices, medicated urethral system for erections) should all be offered on an individual basis, as the efficacy and compliance vary on an individual basis.

Our data suggest that ED after RP can be effectively treated with sildenafil citrate if some degree of neurovascular preservation is performed. Long-term results show that 76\% of preoperative sexually potent men with good bilateral NS surgery can recapture that function with sildenafil treatment. Perhaps 50\% or more of those undergoing a unilateral procedure can also have function restored. Four (15\%) of 26 men in the non-NS cohort also recovered sexual function, with 2 of the 4 patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Bilateral NS (25/33)</th>
<th>Unilateral NS (4/6)</th>
<th>Non-NS (2/4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q5 (maintenance ability)</td>
<td>4.35 ± 0.21* (4–5)</td>
<td>3.42 ± 0.57 (3–4)</td>
<td>2.38 ± 0.72 (2–3)</td>
</tr>
<tr>
<td>Q15 (erection confidence)</td>
<td>3.54 ± 0.13* (5–4)</td>
<td>3.28 ± 0.52 (3–4)</td>
<td>1.96 ± 0.18 (2–3)</td>
</tr>
<tr>
<td>Q4 (maintenance frequency)</td>
<td>4.38 ± 0.21* (4–5)</td>
<td>3.34 ± 1.46 (3–4)</td>
<td>1.85 ± 0.40 (1–2)</td>
</tr>
<tr>
<td>Q2 (erection firmness)</td>
<td>3.93 ± 0.28* (5–5)</td>
<td>3.14 ± 0.55 (3–4)</td>
<td>2.14 ± 0.50 (2–3)</td>
</tr>
<tr>
<td>Q7 (intercourse satisfaction)</td>
<td>3.87 ± 0.29* (5–4)</td>
<td>2.71 ± 0.28 (2–3)</td>
<td>1.73 ± 0.20 (1–2)</td>
</tr>
<tr>
<td>Total mean IIEF-5 score</td>
<td>19.97 ± 1.12* (15–25)</td>
<td>15.89 ± 3.38 (15–20)</td>
<td>10.06 ± 2.0 (5–15)</td>
</tr>
<tr>
<td>Mean EDITS score</td>
<td>74.2 ± 3.4 (50–100)</td>
<td>63.9 ± 8.1 (50–75)</td>
<td>47.6 ± 7.5 (25–50)</td>
</tr>
</tbody>
</table>

Abbreviations as in Tables I and II.

Data presented as the mean ± SD, with the range in parentheses, unless otherwise noted. Each IIEF domain scored from 0 to 5: 0 = did not attempt intercourse; 1 = never/occasionally; 2 = less than half the time; 3 = sometimes/half the time; 4 = more than half the time; 5 = almost always; total IIEF-5 score calculated by totaling and taking mean of response to all 5 domains of IIEF-5.

EDITS scored using a 5-point scale (0–4); mean score multiplied by 25 to get total EDITS score; total scores calculated as follows: 0 = very dissatisfied; 25 = neither satisfied nor dissatisfied; 75 = satisfied; 100 = very satisfied. A score of ≥ 30 was defined as “satisfied with treatment” and a score of < 30 was defined as “not satisfied with treatment.”

Spousal questionnaire scored from 1 to 5: 1 = never/occasionally; 2 = less than half the time; 3 = sometimes/half the time; 4 = more than half of the time; 5 = almost always; total spousal satisfaction was calculated from these questions and expressed as a percentage.

*P < 0.05 bilateral vs. non-NS IIEF-5 domain was considered as significant (Wilcoxon rank sum test).
continuing to use sildenafil at 3 years. This merits further exploration to determine whether this was a placebo effect or whether sexual function might be influenced by mechanisms outside the primary neurovascular bundles.

Our study has important clinical implications in the surgical management of prostate cancer. The introduction of sildenafil citrate coincides with the highly effective screening programs that detect localized prostate cancer at stages associated with high cure rates. The mean age of patients with newly diagnosed prostate cancer has dropped to the late 50s and early 60s, significantly extending sexual life expectancy. This period of sexual longevity should encourage urologists to advance their understanding of uroepithelial anatomy and recognize that subtle refinements in their surgical technique can have a significant impact on the sexual outcomes of their patients.

**CONCLUSIONS**

After NS RP, patients who initially respond to sildenafil continued to show excellent long-term efficacy and compliance at 3 years by SHIM analysis. The degree of neurovascular preservation continued to determine the response rates to sildenafil. Discontinuation was primarily due to a return of natural erections (15%) and loss of efficacy (12%), with no patient stopping because of adverse side effects.

**REFERENCES**