

EFFICACY AND FACTORS ASSOCIATED WITH SUCCESSFUL OUTCOME OF SILDENAFIL CITRATE USE FOR ERECTILE DYSFUNCTION AFTER RADICAL PROSTATECTOMY

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ABSTRACT

Objectives. To assess the efficacy and factors associated with successful treatment of sildenafil citrate for erectile dysfunction after radical prostatectomy (RP).

Methods. Of the 470 patients who underwent RP at our institution between July 1998 and January 2000, 227 (48%) sought treatment for erectile dysfunction, and 174 (37%) were prescribed sildenafil citrate. The starting dose was 50 mg, which was increased to 100 mg if the patient did not have a positive response. Of the 174 patients, 104 (59.8%) had undergone a bilateral nerve-sparing (NS) procedure, 28 (16.1%) had undergone a unilateral NS procedure, and 42 (24.1%) had undergone a non-NS procedure. Erectile function was assessed by the abridged five-item version of the International Index of Erectile Function questionnaire, referred to as the Sexual Health Inventory for Men (SHIM), at baseline and 1 year after sildenafil use. The patients' charts were retrospectively reviewed to find factors associated with a successful outcome, which was defined as successful vaginal intercourse. Association with success was assessed by chi-square analysis and the Cochran Armitage test for trend. Bonferroni correction for multiple comparisons was used, with an overall significance level of 0.05 for each factor assessed.

Results. The mean age was 60.1 ± 6.25 years, and the mean interval from RP to drug use was 3 months. After treatment with sildenafil, 100 (57%) of 174 patients responded to the drug: 79 (76%) of 104 in the bilateral NS group, 15 (53.5%) of 28 in the unilateral NS group, and 6 (14.2%) of 42 in the non-NS group. SHIM analysis showed that the magnitude of the improvement was greater in the bilateral NS group (19.97 ± 1.12) than in the unilateral NS (15.89 ± 3.38) or non-NS (10.06 ± 2.0) groups ($P < 0.020$). Four factors were significantly associated statistically with a successful outcome: the presence of at least one neurovascular bundle, a preoperative SHIM score of 15 or greater, age 65 years old or younger, and interval from RP to drug use of more than 6 months ($P < 0.001$).

Conclusions. The efficacy of sildenafil citrate after RP correlated with the degree of neurovascular bundle preservation, preoperative erectile function status, age, and interval before starting treatment. UROLOGY 63: 960-966, 2004. © 2004 Elsevier Inc.

Since the introduction of sildenafil citrate (Viagra, Pfizer Pharmaceutical, New York, NY) in 1988, much has been learned about its safety profile and clinical efficacy specific to various etiolo-

gies of erectile dysfunction (ED), especially radical prostatectomy (RP).¹⁻³ Two studies from our institution found, for example, that the drug is well tolerated and is more effective in men who undergo unilateral or bilateral nerve-sparing (NS) RP than in men whose neurovascular bundles are removed.^{4,5}

In the first study, we reported that 12 of 15 patients who underwent bilateral NS procedures were able to achieve vaginal penetration with sildenafil 1 year after RP.⁴ This initial study showed the role and value of preserving the neurovascular bundles in determining the response to sildenafil citrate.

In the second study, we updated our experience to include 91 patients treated with sildenafil after

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RP.⁵ In the bilateral NS group, 71.7% (38 of 53) achieved vaginal intercourse, in the unilateral NS group, 50% (6 of 12) did so, and in the non-NS group, only 15.4% (4 of 26) achieved vaginal penetration.⁵ Our study showed that sildenafil citrate can improve ED in about 70% of impotent, motivated patients after RP if a bilateral NS procedure was performed and in 50% of patients if a unilateral NS procedure was done. Lowentritt *et al.*⁶ and Zagaja *et al.*,⁷ in subsequent publications, confirmed these findings.

Today, sildenafil citrate is commonly prescribed to treat ED after RP. However, we still do not know the factors determining the drug's clinical efficacy, especially because few published reports have studied the predictors of satisfactory outcome in patients with ED after RP.

In this study, we determined the efficacy of sildenafil citrate and the predictors of satisfactory outcome and identified the prognostic factors for treatment of ED after RP. We assessed the change in the quality of erection before and after treatment using the abridged five-item version of the International Index of Erectile Function (IIEF-15)⁸ questionnaire, referred to as the Sexual Health Inventory for Men (SHIM).^{8,9} The drug response to sildenafil citrate was assessed using the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire.¹⁰ We stratified the responses on the basis of patient age, number of neurovascular bundles preserved, preoperative erectile function as determined by SHIM analysis, and the interval after surgery to the initiation of drug treatment.

MATERIAL AND METHODS

PATIENT RECRUITMENT

We obtained and reviewed the records of 470 preoperatively sexually active patients with localized prostate cancer who underwent RP between July 1998 and January 2000. After a minimal follow-up of 3 months, only 151 patients (32%) were able to have erections sufficient for vaginal penetration and 319 (68%) had experienced severe ED. These 319 patients were not able to have erections sufficient for successful penetration and their mean IIEF-5 (SHIM) score had decreased from 19.65 (preoperative baseline) to 4.27 (3 months after RP). When various factors were delineated for the 151 men capable of successful vaginal penetration, we found that all these men had undergone NS RP with the same surgeon (C.Z.). This subset of patients was younger (55.6 ± 3.78 years), preoperatively sexually potent (mean baseline IIEF-5 [SHIM] score 22 ± 4.27), and had no comorbid conditions (no coronary artery disease, hypertension, or diabetes mellitus).

Of the 319 patients, 227 (71%) sought treatment for ED and were initially evaluated with a comprehensive sexual history and physical examination and pertinent laboratory testing. The remaining 92 patients did not seek any treatment despite sexual counseling. At that time, the patients were offered standard ED treatments, including a vacuum constriction device (VCD), intracavernous injections (IC), the medicated urethral

system for erection, and oral therapy with sildenafil citrate. Of the 227 patients, 174 (76%) preferred treatment with sildenafil citrate. None of the 227 patients had received preoperative or postoperative hormonal therapy or radiotherapy. Of the 227 patients, 32 (14%) chose IC injections and 21 (10%) agreed to try a VCD. The patients who tried standard treatment with a VCD and IC injections had not tried sildenafil citrate for treatment of ED after RP. The 21 patients who tried a VCD had enrolled in our earlier VCD trial in an attempt to encourage early sexual activity and prevent post-RP venoocclusive dysfunction. Of the 32 patients who chose IC injections, 10 did so because they were receiving oral nitrate treatment for cardiovascular disease and sildenafil treatment was contraindicated.

We retrospectively stratified these 174 patients according to the type of NS procedure they had undergone: bilateral NS in 104, unilateral NS in 28, and non-NS in 42. The surgeon recorded the anatomic status of the neurovascular bundle at surgery; no intraoperative function tests were performed. The type of NS procedure was confirmed by reviewing the operative records.

DRUG THERAPY

Sildenafil citrate was prescribed after a mean of 3 months (range 2 to 4) months after RP. The starting dose was 50 mg, which was titrated to 100 mg if the patient did not have a positive response after a minimum of four attempts. Patients were instructed to take one sildenafil tablet approximately 1 hour before sexual activity according to the manufacturer's instructions and to engage in adequate foreplay before attempting sexual intercourse. All 174 patients started drug treatment at a mean of 3 months after RP. The men were allowed four attempts (within a 1-month interval) with sildenafil citrate before titrating the dosage upward. At least four attempts at 100 mg were allowed within 1 month before the treatment was considered a success or failure.

SURVEYS AND DATA ASSESSMENT

The patients' response to sildenafil citrate was assessed using the IIEF-15 questionnaire,⁸ and the efficacy of sildenafil citrate was assessed using the EDITS questionnaire.¹⁰

The EDITS questionnaire is a psychometrically validated measure of patient satisfaction with ED treatment. We asked 2 of the 11 questions that comprise the questionnaire: "How satisfied are you with sildenafil citrate?" and "How has sildenafil citrate met your expectations?" The two questions were scored using a 5-point scale from 0 (no satisfaction or dissatisfaction) to 4 (high satisfaction). The mean satisfaction score for each patient was calculated. To place scores in an easily interpretable metric, each mean score was multiplied by 25 to reach the total EDITS score. The total scores were calculated as follows: 0, extremely low treatment satisfaction; 25, unsatisfied with treatment; 50, neither satisfied nor dissatisfied with treatment; 75, satisfied with treatment; and 100, extremely high treatment satisfaction. 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."¹⁰

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 one half the time; 3, sometimes/one half the time; 4, more than one half the time; and 5, almost always.^{2,8}

Patients completed the IIEF-15 questionnaire before (preoperatively, within 3 months of screening) and again after a mean interval of 36 weeks (range 14 to 48 weeks; baseline

TABLE I. SHIM (IIEF-5) scores: patients treated with sildenafil citrate after radical prostatectomy (n = 100)

SHIM (IIEF-5) Domain	Before Surgery	Before Treatment	After Sildenafil Citrate Use
Q5—maintenance ability	4.25 ± 1.33 (4–5)	0.66 ± 1.32 (0–1)	3.90 ± 1.56* (3–4)
Q15—erection confidence	2.96 ± 2.08 (2–3)	0.58 ± 0.28 (0–1)	3.83 ± 1.66* (3–4)
Q4—maintenance frequency	4.84 ± 0.55 (4–5)	1.42 ± 1.41 (1–2)	3.67 ± 1.66 (3–4)
Q2—erection firmness	4.88 ± 0.56 (4–5)	1.29 ± 1.12 (1–2)	4.45 ± 1.60* (4–5)
Q7—intercourse satisfaction	4.82 ± 0.71 (4–5)	1.43 ± 1.33 (1–2)	3.61 ± 2.02 (3–4)
Total mean SHIM (IIEF-5) score	21.75 ± 5.23 (20–25)	4.23 ± 3.48 (0–5)	19.46 ± 8.78* (15–20)

KEY: SHIM = Sexual Health Inventory for Men; IIEF = International Index of Erectile Function.

Data presented as mean ± SE, with ranges in parentheses.

Each IIEF domain was scored from 0–5: 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 five domains of IIEF-5.

* Difference in mean IIEF-5 domains between pretreatment and after sildenafil citrate use was statistically significant ($P < 0.05$) as assessed with chi-square test.

before drug treatment) after RP surgery. All three surveys were also mailed to all 174 patients and their spouses/partners 1 year after they began taking sildenafil citrate. Data were also collected on treatment effect, duration of intercourse, number of successful attempts (vaginal penetration), and side effects. We stratified patient response by a retrospective chart review on the basis of patient age, number of neurovascular bundles preserved, preoperative erectile function, and the interval between surgery and the start of therapy.

The data from the IIEF-15 questionnaire were condensed into the IIEF-5 (SHIM) questionnaire. 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, less than one half the time; 3, sometimes/one half the time; 4, more than one half the time; and 5, almost always. The total IIEF-5 score was calculated by totaling the response to all five questions.^{8,9} The mean baseline scores to the questions were calculated and compared with the final scores after sildenafil citrate use to determine changes in response. Successful outcome with the drug was defined as successful vaginal intercourse.

STATISTICAL ANALYSIS

Comparisons between the respondents groups before and after sildenafil citrate use 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 test were used to compare changes within a group. Several factors associated with a successful outcome after sildenafil use were found by retrospective chart review. The association with success was assessed with chi-square analysis and the Cochran Armitage test for trend. Bonferroni's correction for multiple comparisons was used, with an overall significance level of 0.05 for each factor assessed. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant. All computations were performed using Statistical Analysis System software, version 8.1 (SAS Institute, Cary, NC). The continuous variables were summarized as the mean and standard error (SE).

RESULTS

After several requests, all 174 patients and their spouses/partners completed the IIEF-15, EDITS, and spousal/partner questionnaires. The mean age

of the patients was 61.8 ± 6.25 years, and the mean interval from RP to drug use was 3 months. No statistically significant differences were found between the non-NS and NS groups in age, interval between RP and start of sildenafil citrate, and pre-treatment erectile status.

After treatment with sildenafil, 100 (57%) of the 174 patients reported having successful vaginal intercourse: 79 (76%) of 104 in the bilateral NS group, 15 (53.5%) of 28 in the unilateral NS group, and 6 (14.2%) of 42 in the non-NS group. The erections were sufficient for vaginal intercourse in all 100 responders (total mean IIEF-5 [SHIM] score greater than 18); the duration of intercourse ranged from 7 to 12 minutes. The total mean (\pm SD) SHIM (IIEF-5) score was 19.46 ± 8.78 (Table I), the total mean (\pm SD) EDITS score was 73.6 ± 3.2 , and the mean spousal/partner satisfaction rate was 58%.

IMPACT OF NEUROVASCULAR BUNDLE PRESERVATION

The magnitude of the improvement by SHIM (IIEF-5) analysis was greater in the bilateral NS group (19.97 ± 1.12) than in the unilateral NS (15.89 ± 3.38) and non-NS (10.06 ± 2.0) groups ($P = 0.020$). Table II shows the mean scores for the abridged IIEF-5 questionnaire, total EDITS score, and spousal/partner satisfaction as stratified by NS procedure.

IMPACT OF PREOPERATIVE ERECTILE FUNCTION STATUS

A statistically significant positive correlation was found between baseline preoperative sexual function and the response to sildenafil citrate. Patients with a preoperative total mean IIEF-5 score of 15 or greater had a response rate of 67% (92 of 137) compared with 22% (8 of 37) for those with a total mean IIEF-5 score of less than 15 (Table III).

IMPACT OF AGE

When all 174 patients were stratified by age alone, 75% of men younger than 60 years old, 57%

TABLE II. SHIM (IIEF-5), EDITS, and spousal satisfaction scores: responses stratified by neurovascular bundle status

Variable	Bilateral NS (79/104)	Unilateral NS (15/28)	Non-NS (6/42)
Mean age (yr)	61.8	60.5	61.2
Able to penetrate (%)	76	53.5	14.2*
IIEF-5 (SHIM) questionnaire			
Q5 (maintenance ability)	4.35 ± 0.21* (4–5)	3.42 ± 0.57 (3–4)	2.38 ± 0.72 (2–3)
Q15 (erection confidence)	3.54 ± 0.13* (3–4)	3.28 ± 0.52 (3–4)	1.96 ± 0.18 (2–3)
Q4 (maintenance frequency)	4.38 ± 0.21* (4–5)	3.34 ± 1.46 (3–4)	1.85 ± 0.40 (1–2)
Q2 (erection firmness)	3.93 ± 0.28* (4–5)	3.14 ± 0.55 (3–4)	2.14 ± 0.50 (2–3)
Q7 (intercourse satisfaction)	3.87 ± 0.29* (3–4)	2.71 ± 0.28 (2–3)	1.73 ± 0.20 (1–2)
Total mean IIEF-5 (SHIM) score	19.97 ± 1.12* (15–25)	15.89 ± 3.38 (15–20)	10.06 ± 2.0 (5–15)
Mean EDITS score [†]	74.2 ± 3.4 (50–100)	63.9 ± 8.1 (50–75)	47.6 ± 7.5 (25–50)
Spousal questionnaire [‡]			
Ability to achieve erection (%)	60/104 (57.7)	13/28 (46.4)	1/47 (2.3)
Spousal satisfaction %	82/104 (78.8)	13/28 (46.4)	6/42 (14.2)

KEY: EDITS = Erectile Dysfunction Inventory of Treatment Satisfaction; NS = nerve sparing; other abbreviations as in Table 1.

Data presented as mean ± SE, with ranges in parentheses, unless otherwise noted.

* P < 0.05 bilateral vs. non-NS IIEF-5 domain considered significant (Wilcoxon rank sum test).

[†] EDITS questions scored using 5-point scale (0–4), and each mean score was multiplied by 25 to reach total EDITS score; total scores were calculated as follows: 0, very dissatisfied; 25, unsatisfied; 50, neither satisfied nor dissatisfied; 75, satisfied; 100, very satisfied; a score of ≥50 was defined as “satisfied with treatment” and a score of ≤50 was defined as “not satisfied with treatment.”

[‡] Spousal response is percentage of spouse/partners who answered positively to questionnaire.

TABLE III. Factors associated with successful outcome of sildenafil citrate after radical prostatectomy

Variable	Percentage (Responders/Total)	P Value*
Neurovascular bundle status (NS vs. non-NS)	71 (94/132) vs. 14 (6/42)	<0.001
Preoperative erectile function (IIEF-5 ≥15 vs. <15)	67 (92/137) vs. 22 (8/37)	<0.001
Age, overall (<60 vs. 60–65 vs. >65 yr)	75 (36/48) vs. 57 (42/74) vs. 42 (22/52) [†]	0.001 [‡]
Interval from RP (3–6 vs. 6–12 vs. 12–18 vs. >18 mo)	24 (4/17) [§] vs. 57 (24/42) vs. 63 (66/104) vs. 91 (10/11)	<0.001 [‡]

KEY: RP = radical prostatectomy; other abbreviations as in Tables I and II.

* Chi-square test for overall association, unless noted.

[†] Significantly different from <60 yr.

[‡] Cochran Armitage test for trend.

[§] Significantly different from <12, 12–18, and >18 mo.

of those 60 to 65 years old, and 42% of those older than 65 years responded to drug therapy. In patients who had undergone bilateral NS RP, the response rate varied from 76% in men younger than 60 years (IIEF-5 19.87 ± 4.67) to 64% in men 60 to 65 years old (IIEF-5 18.34 ± 3.6) to 61% in men older than 65 years (IIEF-5 16.78 ± 4.79). In patients who had undergone unilateral NS RP, 55% of men younger than 60 years old (IIEF-5 15.67 ± 3.69), 50% of men between 60 to 65 years old (IIEF-5 14.32 ± 4.26), and 33% of men older than 65 years (IIEF-5 12.72 ± 5.02) responded to sildenafil citrate. Of the 42 patients who underwent a non-NS procedure, 6 (14%) responded to sildenafil citrate (IIEF-5 10.06 ± 2.0).

IMPACT OF INTERVAL AFTER RP AND DRUG DOSE

When the 100 of 174 patients who responded to sildenafil citrate were analyzed, a statistically sig-

nificant difference in the drug response rate was found when the interval from surgery to drug therapy was stratified: 3 to 6 months (4 of 17, 24%), 6 to 12 months (24 of 42, 57%), 12 to 18 months (66 of 104, 63%) and longer than 18 months (10 of 11, 91%). Most patients responded to sildenafil citrate 12 months after RP.

Of the 174 patients, 59 (34%) required the 50-mg dose, and 115 (66%) required the 100-mg dose. No statistically significant differences in efficacy were found when stratified by the drug dose.

SIDE EFFECTS

The most common side effects of the drug were transient headaches (24%), flushing (14.5%), dizziness (8.6%), dyspepsia (5.6%), and nasal congestion (3%), with an increase in the incidence of headache seen at the higher dose (P = 0.04). The 9 patients (5%) who discontinued the drug because

of side effects also had had no response. None of the patients had any serious cardiovascular effects (defined as fainting, strokes, or myocardial infarction).

COMMENT

The most salient finding in this series was that 76% of the preoperative sexually active men who underwent bilateral NS surgery recaptured their erectile function with sildenafil treatment. Perhaps 50% or more of those undergoing a unilateral NS procedure will also have their function restored. In addition, when the SHIM and EDITS responses were stratified according to neurovascular bundle status, the magnitude of improvement in each SHIM domain was significantly greater in the bilateral NS group than in the unilateral NS and non-NS groups. Thus, the degree of neurovascular preservation continues to affect the response rates to sildenafil. In addition to neurovascular bundle status,¹¹⁻¹³ we found three other factors that were associated with a successful outcome: preoperative erectile function, age, and the interval between RP and the start of drug therapy.

Moreover, patients in this study responded to sildenafil in a dose-dependent fashion: the 100-mg dose produced the greatest response rate. Higher doses of sildenafil were associated with greater mean scores for the questions on the IIEF-5 and EDITS questionnaire. In our study, 61% of the patients required a titration in their dose, from 50 to 100 mg, for a positive response. This increase was well tolerated. The incidence of headache was the only side effect that increased at the 100-mg dose. However, additional confirmatory studies are required to document the incidence and possible causes of tachyphylaxis—an effect that El-Galley *et al.*¹⁴ reported increased at 2 years—and the interval for the reduction or loss of efficacy in subgroups of patients using sildenafil citrate for ED after RP.¹⁴

In our updated study, we also found that preoperative sexual status (Table III) influenced the response to oral sildenafil (67% versus 22%). Lowentritt *et al.*⁶ also found that the proportion of men with pretreatment erectile activity had better outcomes with sildenafil citrate therapy than men without such function (82% versus 20%). Similarly, Marks *et al.*¹⁵ studied patients' responses to sildenafil citrate by stratifying them using a pre-drug ED severity classification system. The men who reported some erectile function (severity class 1 and 2) responded to sildenafil citrate much more efficaciously than those with no function (severity class 4; 80% versus 53%). Unlike other studies, we had clearly defined preoperative sexual status as

potent if the IIEF-5 (SHIM) score was greater than 15 with erections sufficient for vaginal penetration.

The potency rates after RP vary significantly with age. Young men regain natural erections more often than do older men. Zagaja *et al.*⁷ showed that the magnitude of a man's response to sildenafil after RP appears to be inversely correlated with his age. Of the patients who underwent bilateral NS RP in that study, 80% of the patients who were younger than 55 years old reported an adequate response to the drug versus 33% of those who were older than 65 years. When analyzing the patients who had undergone unilateral NS RP, Zagaja *et al.*⁷ found that none of the patients who were older than 55 years—and only 40% of those younger than 55 years—reported an adequate response.

Similarly, Lowentritt *et al.*⁶ showed that patient age at the start of treatment significantly affected the response. In their study, 57% of the patients who were younger than 55 years and treated within 6 months of surgery responded to treatment but only 13% who were older than 55 years and treated in the same manner were sexually satisfied with treatment. These potency rates are quite similar to those reported in our updated series, with one exception. We found that 33% to 50% of patients older than 55 years who had undergone unilateral NS RP also responded to sildenafil citrate therapy. Unlike other studies, 6 (14%) of the 26 men in the non-NS cohort also recovered their sexual function. 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 pathways.

It is unclear whether the recovery of erectile function as related to age is purely a neurologic entity. If the neurovascular bundles are preserved, should the patient respond to sildenafil regardless of age? The observation that the response to sildenafil correlated strongly with age and the number of neurovascular bundles preserved suggests either that the response to nerve injury is age related or that the vascular factor related to age is also an etiologic factor.^{6,7,11,15,16}

Contrasting findings have been reported regarding the latency period after RP during which sildenafil citrate is effective. Our study showed that patients responded most optimally to sildenafil therapy when they began taking the drug at least 6 months after surgery. This finding is similar to that of Lowentritt *et al.*,⁶ who found that patients who began taking the drug before the 6-month mark did not respond well. Zagaja *et al.*⁷ found that none of their patients responded to sildenafil sooner than 9 months after RP. Hong *et al.*¹⁷ found that treatment satisfaction improved from 26% when sildenafil was started

0 to 6 months after RP to 60% when it was started 18 to 24 months after RP. Our study demonstrated that some patients also responded to drug therapy at 3 to 6 months and almost 50% did well after 6 months or longer. Unlike the findings of Zagaja *et al.*,⁷ we had a response rate of 57% at 9 to 12 months compared with 0% at 9 months after RP. Our study also demonstrated that most patients responded to the drug at 12 months (63%) compared with other studies that found that at least 18 to 24 months after RP were required before sildenafil was effective.^{6,7,17}

The results of our study raise several interesting issues regarding the etiology of ED after RP. Although our clinical experience has shown that men can recover natural erections sufficient for vaginal penetration sooner than 12 months after NS RP, no patient in this series did so. During the early postoperative period, patients who undergo non-NS or NS RP usually report the absence of spontaneous erections (both nocturnal and at awakening). This interval of reduced erectile function is potentially associated with impaired blood inflow to the corpora cavernosa, which ultimately leads to tissue hypoxia and significant damage to the cavernous smooth muscle.^{11–13,16,18} Despite the surgeon's best effort to preserve the penile nerves, some dissection around the prostate is necessary, resulting in varying degrees of nerve injury.^{11,16,19,20} Pharmacologic interventions to promote erections during this convalescent period have been shown to enhance the recovery of spontaneous erections.²¹ This neural recovery period appears to be at least 6 to 12 months long and may actually be longer.^{11,16,19–21} Because oral therapy demonstrated limited effect in the early postoperative period, alternative treatments (eg, IC injections, VCD, or medicated urethral system for erection) can be used as adjuvant therapy for treatment of patients with ED after RP during the recovery of temporary neuropraxia.^{11,21}

The potency rates after RP vary a great deal, and the criteria for a positive response or a satisfactory erection have not been universally applied. Ideally, uniformity in using universally validated questionnaires and comprehensive and objective evaluations of erectile function in an institution can address the problem of erectile function more accurately. Our study, using exclusively validated questionnaires, has important clinical implications in the treatment of prostate cancer with surgery. 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 newly diagnosed prostate cancer has dropped to the late 50s and early 60s, significantly extending a man's sexual

life expectancy. This longer period of sexual longevity should encourage urologists to advance their understanding of uropelvic anatomy and recognize that subtle refinements in their surgical technique can have a significant impact on the sexual outcomes of their patients.

CONCLUSIONS

The efficacy of sildenafil citrate after RP is related to the degree of neurovascular bundle preservation, preoperative erectile function status, patient age, and interval before starting treatment. Our study showed that the use of sildenafil citrate could salvage 76% of impotent, motivated patients if they had undergone bilateral NS RP and 53.5% if they had undergone unilateral NS RP. The main side effect was headaches (28.6%); but overall compliance was excellent, with a less than 5% discontinuation rate because of adverse side effects. The interval for the best response appeared to be 12 months or longer after RP, and most patients required the 100-mg dose. The potential impact of oral therapy and its requirement for nerve tissue should encourage urologists to perfect the NS approach.

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