

# SEXUAL FUNCTION AFTER MALE RADICAL CYSTECTOMY IN A SEXUALLY ACTIVE POPULATION

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## ABSTRACT

**Objectives.** To assess sexual dysfunction in sexually active men after radical cystectomy (RC) and to determine whether sildenafil citrate can improve erectile dysfunction after surgery.

**Methods.** The baseline and follow-up data from 49 sexually active male patients (mean age  $57.8 \pm 9.1$  years) undergoing RC (1995 to 2002) were obtained. Of the 49 patients, 16 (33%) had undergone nerve-sparing RC; 38 (78%) had undergone orthotopic diversion; 8 (16%) had undergone ileal conduit diversion; and 3 (6%) had undergone cutaneous continent diversion. The data were assessed using the abridged 5-item International Index of Erectile Function questionnaire, referred to as the Sexual Health Inventory for Men (SHIM).

**Results.** At a mean follow-up of  $47.6 \pm 22.7$  months, the total mean SHIM score decreased from  $22.08 \pm 3.96$  to  $4.33 \pm 5.72$  after RC ( $P < 0.05$ ). Of the 49 patients, 42 (86%) did not have erections sufficient for vaginal penetration. Of these 42 patients, 22 (52%) tried sildenafil citrate. Of these 22 patients, only 2 (9%) responded positively, with a total mean SHIM score of  $23.50 \pm 2.12$ . Although the mean SHIM score after orthotopic substitution ( $5.24 \pm 6.21$ ) was statistically significant compared with that after ileal conduit ( $1.13 \pm 0.33$ ) and cutaneous continent ( $1.33 \pm 0.58$ ) diversions, this was not clinically significant.

**Conclusions.** Male erectile dysfunction after RC is a prevalent problem. In our series, only 9 (14%) of 49 sexually active men were potent after surgery. Of these 9 potent patients, 8 (89%) had undergone nerve-sparing RC. Of concern, only 52% of the patients with erectile dysfunction sought treatment after RC. UROLOGY 64: 682–686, 2004. © 2004 Elsevier Inc.

Radical cystectomy (RC) has been the standard for treatment of aggressive superficial bladder cancer and invasive carcinoma.<sup>1</sup> The endpoints after this operation have focused on cure, urethral recurrence, and continence.<sup>2–5</sup> During RC, the neurovascular bundles are usually removed or damaged with removal of the bladder.<sup>6</sup> Recent interest in quality-of-life issues has stimulated the evolution of orthotopic bladder substitution.<sup>7</sup> This technical advancement has provided the momentum for assessing other quality-of-life issues after RC.<sup>8</sup>

In this study, we addressed sexual function, an-

other quality-of-life issue after RC. We chose a sexually active population in whom erectile function was an important quality-of-life issue before surgery. We validated our responses in this subset, using the abridged 5-item version of the International Index of Erectile Function (IIEF-5) questionnaire, referred to as the Sexual Health Inventory for Men (SHIM).<sup>9</sup> We also asked patients what treatments they had sought and assessed their responses using a validated questionnaire.<sup>9</sup>

## MATERIAL AND METHODS

### STUDY SUBJECTS AND DESIGN

The Cleveland Clinic Institutional Review Board approved this study, and all patients granted informed consent. Study participants were a self-selected, nonrandomized group who had undergone RC, were alive in 2003, and had completed the necessary questionnaires. We obtained data on 49 male patients (mean age  $57.8 \pm 9.1$  years) who were sexually active before surgery and had undergone RC at the Glickman Urological Institute from May 1995 to March 2002. These patients completed the SHIM (IIEF-5) questionnaire or the IIEF-15 (before 1999) before surgery (4 months or less), after RC (1

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**TABLE I. SHIM (IIEF-5) analysis: baseline and after radical cystectomy**

SHIM (IIEF-5) Domains	Baseline Before RC (n = 49)	After RC (n = 49)
Q15, erection confidence	4.12 ± 0.97	1.39 ± 0.76*
Q2, erection firmness	4.41 ± 0.91	0.67 ± 1.20*
Q5, maintenance ability	4.35 ± 1.09	0.69 ± 1.28*
Q4, maintenance frequency	4.65 ± 0.69	0.69 ± 1.37*
Q7, intercourse satisfaction	4.55 ± 0.87	0.88 ± 1.49*
Total mean IIEF-5 score	22.08 ± 3.96	4.33 ± 5.72*

KEY: SHIM = Sexual Health Inventory for Men; IIEF-5 = 5-item (short form) International Index of Erectile Function; RC = radical cystectomy; Q = question.  
Data presented as mean ± SD.  
Wilcoxon rank-sum test used to compare preoperative and postoperative changes across study groups.  
Each IIEF-5 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 the mean of the responses to all 5 domains of IIEF-5.  
\* P < 0.05 after RC vs. baseline.

year or longer), and after the use of sildenafil citrate or any erectile aid for erectile dysfunction (ED). Medical records were obtained and reviewed to assess the baseline medical data and social history, as well as the type of urinary diversion and nerve-sparing surgery. When the operative report did not specify any consideration or protection of the neurovascular bundles, the procedure was deemed a non-nerve-sparing procedure.

The mean level of preoperative sexual activity before surgery was 2.0 ± 1.2 per week. Of these 49 patients, 38 (78%) had undergone orthotopic urinary diversion (Studer pouch), 8 (16%) had undergone ileal conduit diversion, and 3 (6%) had undergone cutaneous continent diversion (Indiana). Only 16 (33%) of the 49 patients had undergone nerve-sparing procedures. Of the 16 patients who had undergone nerve-sparing RC, 6 had pathologic Stage T1, 2 had Stage T2a, and 8 had Stage T2b, and all had negative surgical margins. The mean follow-up interval was 47.6 ± 22.7 months after surgery. Of these 49 patients, 2 developed recurrent cancer. When comorbidities were assessed in the 49 patients, hypertension was found in 35%, diabetes in 6%, and coronary artery disease in 22%.

#### SURVEYS AND DATA ASSESSMENT

Sexual function was assessed at baseline (preoperative), after RC, and after treatment using the abridged 5-item IIEF-5 questionnaire, referred to as the SHIM.<sup>9</sup> This questionnaire was used to define and validate the degree of sexual dysfunction in our surgical population. Specific domains analyzed in the SHIM questionnaire include erection confidence, erection firmness, ability to maintain an erection, maintenance frequency, and intercourse satisfaction. This questionnaire provided us with a comprehensive assessment of baseline, postoperative, and post-treatment sexual function in this population of patients. Responses were scored from 0 to 5. The total SHIM score was calculated by adding responses from all five domains. The mean baseline scores to the questions were calculated and compared with the postoperative scores to assess the change in response.

In addition to the SHIM questionnaire, we asked patients to estimate their approximate frequency of sexual intercourse at baseline, after surgery, and after treatment. Patients' spouses or partners were also asked to rate their level of satisfaction, similar to question 5 of the SHIM.

#### STATISTICAL ANALYSIS

The mean and standard deviation were calculated for all the domains of the SHIM questionnaire. Paired *t* tests were

used to assess changes from baseline. Wilcoxon rank sum tests were used to compare the preoperative and postoperative changes across study groups. Statistical significance was assessed with a two-tailed test at *P* < 0.05. Computations used Statistical Analysis Systems, version 8.1, software (SAS Institute, Cary, NC).

#### RESULTS

At a mean follow-up of 47.6 ± 22.7 months, 42 (86%) of the 49 patients were unable to achieve vaginal penetration after surgery. The mean total SHIM (IIEF-5) score of the 49 patients at baseline was 22.1 ± 4.0. After surgery, the mean total SHIM score for the entire group was 4.33 ± 5.72 (Table I). Of these 49 patients, 7 had erections sufficient for vaginal penetration at a mean of 17.1 ± 4.1 months after surgery. Those 7 patients had a mean total baseline SHIM score of 21.1 ± 4.1 and a mean total postoperative score of 16.6 ± 4.9 at a mean follow-up of 44.4 ± 25.1 months. When analyzing these 7 patients for common denominators to explain their potency, 6 (86%) of the patients had undergone a nerve-sparing procedure. Although this subgroup's mean age of 51.0 ± 10.9 years was lower than the remaining 42 patients' mean age (58.9 ± 8.4 years), the difference was not statistically significant (*P* = 0.055). Additionally, the incidence of comorbid disorders (hypertension, diabetes, coronary artery disease) was similar in both the sexually active and impotent subgroups, with a rate of 43% (3 of 7) and 48% (20 of 42), respectively (*P* = 0.83).

In the other 42 patients who had no potency sufficient for vaginal penetration, 4 were able to achieve erections with an erectile aid or medical therapy (sildenafil citrate). Two patients responded successfully to sildenafil citrate. Two other patients were using erectile aids to achieve erections, one with a vacuum constriction device and one using intracavernosal injection therapy. In

**TABLE II. SHIM (IIEF-5) analysis: treatment with sildenafil citrate and erectile aids**

Treatment Response and Type	Baseline Before RC	After RC	After Treatment
Positive response to sildenafil (n = 2)	24.50 ± 0.71	5.50 ± 0.71*	23.50 ± 2.12 <sup>†</sup>
Negative response to sildenafil (n = 20)	21.90 ± 5.20	1.65 ± 1.50*	1.80 ± 1.68
Positive response to erectile aids (n = 2)	22.50 ± 3.54	1.00 ± 0.00*	23.00 ± 2.83 <sup>†</sup>

Abbreviations as in Table I.

Data presented as mean ± SD.

Wilcoxon rank sum test used to compare preoperative and postoperative changes across study groups.

Each IIEF-5 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 the mean of the responses to all 5 domains of IIEF-5.

\* P < 0.05 after RC vs. baseline.

<sup>†</sup> P < 0.05 after RC vs. after treatment.

**TABLE III. SHIM (IIEF-5) analysis: stratified by type of urinary diversion**

Urinary Diversion	Baseline Before RC	After RC
Orthotopic substitution (n = 38)	21.92 ± 4.32	5.24 ± 6.21* <sup>†</sup>
Ileal conduit (n = 8)	22.63 ± 2.45	1.13 ± 0.33*
Continent cutaneous diversion (n = 3)	22.67 ± 2.31	1.33 ± 0.58*

Abbreviations as in Table I.

Data presented as mean ± SD.

Wilcoxon rank sum test used to compare preoperative and postoperative changes across study groups.

Each IIEF-5 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 the mean of the responses to all 5 domains of IIEF-5.

\* P < 0.05, after RC vs. baseline.

<sup>†</sup> P < 0.05, orthotopic substitution vs. ileal conduit/continent cutaneous.

the 42 patients who were impotent, our data indicated that 22 (52%) attempted sildenafil citrate, with only 2 (9%) having responses sufficient for vaginal penetration (Table II).

We stratified the degree of ED (using SHIM scores) by the type of urinary diversion. The difference in the mean total SHIM score of 5.24 ± 6.21 after orthotopic substitution was statistically significant (P < 0.05) compared with that after ileal conduit (mean total SHIM score 1.13 ± 0.33) and cutaneous continent (mean total SHIM score 1.33 ± 0.58) diversions (Table III). However, this difference was not as clinically significant, because the difference between “almost never or never” does not differ in the SHIM questionnaire from “did not attempt.”

#### COMMENT

The results of this study have important significance in the treatment of bladder cancer. Although RC has focused primarily on cure, recurrence, and continence during the past decade,<sup>2-5</sup> our results suggest that ED is an important complication after this procedure that has not been well recognized. ED was a prevalent problem in our study, occurring in 42 (86%) of 49 sexually active men after RC. These 42 patients were sexually active before surgery, with a mean frequency of 2.0 ± 1.3 times per week and a mean

age of 58.9 ± 8.4 years. Seven (14%) of the 49 patients were naturally potent after surgery, and 6 of those 7 (86%) had undergone a nerve-sparing procedure. Of concern, only 52% of this sexually active series sought treatment for their ED.

This study also points out the important impact of the postoperative treatment of patients with ED. Of the 42 patients with ED after RC, 20 (47%) did not seek treatment. This fact emphasizes the importance of preoperative counseling and earlier aggressive treatment and consultation after surgery. Currently, these patients often have a discussion regarding their ED 12 to 18 months after surgery. This delay in addressing this issue after RC may discourage patients and may explain why many sexually active patients in our study did not seek treatment after RC.

In our series, only 2 (9%) of 22 patients responded to sildenafil citrate as defined by successful vaginal penetration. It is well known that preservation of the neurovascular bundles is vital for the success of sildenafil citrate.<sup>7-9</sup> Sildenafil citrate does not work as a phosphodiesterase type 5 inhibitor when nitric oxide is not released from the neurovascular bundle. The 2 patients who responded to sildenafil citrate had preservation of neurovascular bundles. It is unclear from the operative reports how many of the other 20 patients had undergone nerve-sparing RC. It appears that most

were non-nerve-sparing procedures, explaining our low response rate to sildenafil citrate.

In 1984, Walsh<sup>10</sup> was the first to show that a modified surgical technique (nerve sparing) resulted in the increased postoperative potency of individuals who had undergone radical cystoprostatectomy. Of the 11 patients who had undergone nerve-sparing procedures in this study, 9 (82%) had regained sexual potency after 1 year.<sup>11</sup> In 1990, using a larger sample size, Brendler *et al.*<sup>12</sup> reported that 27 (52%) of 52 patients who had undergone nerve-sparing cystoprostatectomy regained potency after 1 year. Since that landmark study, others have reported similar rates of potency after nerve-sparing RC, ranging from 42% to 71%.<sup>13–17</sup> Preservation of the neurovascular bundles appears to be essential for the return of sexual potency after RC.

The 9 patients in our study who were sexually active after RC (defined by vaginal penetration) had only one common denominator. Eight (89%) of these 9 patients had undergone nerve-preserving RC. Although these 9 patients had a mean age of  $51.0 \pm 10.9$  years, the difference from the remaining 42 patients' mean age ( $58.9 \pm 8.4$  years) was not statistically significant. We also found that the incidence of comorbidity (43%) in these 9 patients was similar to that of the impotent subgroup (48%).

## CONCLUSIONS

Although surgical cure is always the priority, ED will become a more accountable endpoint in the future. Similar to what occurred in surgical prostate cancer,<sup>18–20</sup> better screening and monitoring protocols for bladder cancer will cause stage migration and provide earlier indications for RC. Removing earlier staged disease will make more patients eligible for nerve-sparing procedures. Additionally, as younger patients are diagnosed, the momentum for a "quality-of-life cystectomy" will continue to increase as patients' expectations change. Redefining the future "quality-of-life cystectomy" is in evolution as we continue to perform more orthotopic urinary diversions and consider more patients eligible for neurovascular preservation.

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## EDITORIAL COMMENT

This is a nonrandomized, self-selected group of 49 men (mean age  $58 \pm 9$  years) who underwent RC during a 7-year period at one institution. All men were sexually active before surgery. Only 16 of 49 patients underwent a "nerve-sparing" procedure, and 84% received a continent urinary diversion. The patients were evaluated for sexual function by the SHIM questionnaire preoperatively, 1 year or more after surgery, and after using sildenafil citrate. The mean follow-up was  $48 \pm 23$  months.

Only 9 (18%) of these 49 men were able to achieve erections