

FEMALE SEXUAL DYSFUNCTION AFTER RADICAL CYSTECTOMY: A NEW OUTCOME MEASURE

CRAIG D. ZIPPE, RUPESH RAINA, ASHA D. SHAH, ERIC Z. MASSANYI, ASHOK AGARWAL, JAMES ULCHAKER, STEPHEN JONES, AND ERIC KLEIN

ABSTRACT

Objectives. To assess, in our contemporary radical cystectomy (RC) series, female sexual dysfunction and whether the type of diversion affected the occurrence of sexual dysfunction. Outcome data after RC with and without orthotopic diversion has focused primarily on cure, urethral recurrence, and continence.

Methods. The baseline and follow-up data from 27 sexually active female patients (mean age 54.79 ± 12.7 years) who underwent RC from 1997 to 2002 for transitional cell carcinoma of the bladder (16 with Stage T1-T2 and 11 with Stage T3-T4) were obtained. Thirteen patients were premenopausal before RC. Of the 27 patients, 10 (37%) underwent Studor orthotopic diversion, 7 (26%) Indiana cutaneous diversion, and 10 (37%) ileal conduit diversion. A 10-item version of the self-administered Index of Female Sexual Function questionnaire was used to assess sexual dysfunction. The specific domains analyzed in the Index of Female Sexual Function include the degree of vaginal lubrication, ability to achieve orgasm, degree of pain during intercourse, overall sexual desire and interest, and overall sexual satisfaction, with responses graded on a scale of 1 (almost never, never) to 5 (almost always, always).

Results. With a mean follow-up of 24.2 months (range 15 to 65.1), the total mean baseline Index of Female Sexual Function score decreased from 17.4 ± 7.23 to 10.6 ± 6.62 after RC ($P \leq 0.05$). The most common symptoms reported by the patients included diminished ability or inability to achieve orgasm in 12 (45%), decreased lubrication in 11 (41%), decreased sexual desire in 10 (37%), and dyspareunia in 6 patients (22%). Only 13 (48%) of the 27 patients were able to have successful vaginal intercourse, with 14 (52%) reporting decreased satisfaction in overall sexual life after RC. Eight partners (30%) had a decrease in desire for sexual activity owing to apprehension after cancer diagnosis and treatment. Although the numbers were small, the preliminary data suggested no differences in sexual function between patients undergoing Studor orthotopic diversions and those undergoing Indiana cutaneous diversions.

Conclusions. Sexual dysfunction is a prevalent problem after female RC. The nature of the dysfunction involves multiple domains, including decreased orgasm, decreased lubrication, lack of sexual desire, and dyspareunia. Our early results suggest that the type of continent diversion does not affect sexual function. Surgical modifications such as urethral and vaginal sparing, neurovascular preservation, and tubular vaginal reconstruction sparing may improve female sexual function after RC. UROLOGY 63: 1153-1157, 2004. © 2004 Elsevier Inc.

Outcome measures after radical cystectomy (RC), with or without orthotopic diversion, has focused primarily on cure, urethral recurrence, and continence.¹⁻⁴ However, sexual dysfunction is

a major concern and side effect in many of our younger female patients.^{2,5} During RC, the neurovascular bundles (located on the lateral walls of the vagina) are usually removed or damaged by removal of the bladder, urethra, and anterior vaginal wall.⁵⁻⁸ In addition, significant devascularization of the clitoris often occurs with removal of the distal urethra, affecting subsequent sexual arousal and desire.^{5,6,8}

Therefore, we conducted this clinical study to address sexual dysfunction in a subset of sexually active women undergoing RC. Using a modified Index of Female Sexual Function (IFSF) question-

C. D. Zippe is a member of the speaker's bureau for Pfizer.

From the Glickman Urological Institute and Center for Advanced Research in Human Reproduction, Infertility and Sexual Function, Cleveland Clinic Foundation, Cleveland, Ohio

Reprint requests: Craig D. Zippe, M.D., Glickman Urological Institute, Cleveland Clinic Foundation, 9500 Euclid Avenue, Desk A100, Cleveland, OH 44195

Submitted: August 11, 2003, accepted (with revisions): December 29, 2003

naire,^{9,10} we reported the sexual function data in a contemporary RC series. In this study, we stratified the sexual response by the type of urinary diversion (Studor orthotopic, Indiana cutaneous, or standard ileal conduit diversion) to determine whether vaginal sparing (as performed in the orthotopic diversions) influenced the sexual response.

MATERIAL AND METHODS

STUDY SUBJECTS AND DESIGN

The Cleveland Clinic Institutional Review Board approved this study, and all patients granted their written informed consent. The baseline and follow-up data from 34 sexually active female patients undergoing RC from 1997 to 2002 for transitional cell carcinoma of the bladder (20 with Stage T1-T2 and 14 with T3-T4) were obtained. The study participants were a self-selected, nonrandomized group who underwent RC.

In a multidisciplinary bladder cancer clinic, we requested that all patients with bladder cancer complete the IFSF questionnaire before (baseline) and after RC as a part of their initial and routine follow-up evaluations. The 34 patients who agreed and provided informed consent to participate in the study were initially evaluated with a comprehensive sexual history, physical examination, and pertinent laboratory testing. All 34 patients had completed the IFSF questionnaire in the office before RC (within 1 month of screening) and at a mean interval of 24.2 months after RC during their follow-up visit. Twenty-seven patients (80%) were sexually active (frequency once a month to every 3 days) before RC. The mean age for these patients was 54.79 ± 12.7 years; 13 (38%) were premenopausal before RC. The 7 patients who were not sexually potent before RC were not included in this analysis.

We retrospectively stratified the 27 patients (16 with Stage T1-T2 and 11 with Stage T3-T4) according to the type of urinary diversion they had undergone. Of the 27 patients, 10 (37%) underwent Studor orthotopic diversion, 7 (26%) Indiana cutaneous diversion, and 10 (37%) ileal conduit diversion.

All patients were entered into the database of the Bladder Cancer Registry of the Cleveland Clinic Foundation to ensure appropriate follow-up. The median follow-up for all 27 patients was 24.2 months (range 15 to 65) after RC.

SURVEYS AND DATA ASSESSMENT

Sexual function was assessed at baseline (preoperatively) and after RC using a modified 10-item version of the IFSF questionnaire by Kaplan *et al.*⁹ This modification was necessary to define sexual dysfunction in our surgical population and is clinically useful in an office setting. Currently, no validated, widely accepted questionnaires are available for assessing female sexual function. The IFSF questionnaire by Kaplan *et al.*⁹ is patterned after the International Index of Erectile Function, a 15-question, validated, multidimensional questionnaire used for the assessment of male sexual dysfunction.^{9,10} The specific domains (preoperative versus after RC) analyzed in our modified IFSF questionnaire included pain-free intercourse, degree of vaginal lubrication, overall sexual desire and interest, ability to achieve orgasm, and overall sexual satisfaction. This questionnaire provided us with a comprehensive assessment of the baseline and surgery-related changes for this subgroup of patients. Responses were scored from 0 to 5 (0, no sexual activity; 1, rarely/occasionally; 2, less than one half the time; 3, sometimes/one half the time; 4, more than one half the time; 5, almost always). The responses were stratified by the type of urinary diversion. The total IFSF score was calculated by adding the mean score of all five domains.

The mean baseline scores to the questions were calculated and compared with the final scores to determine the change in response. Test-to-test reliability was performed by computing the correlation between the domain scores and total scores at baseline and at 24.2 months after RC. Test-to-test reliability was high for the degree of vaginal lubrication ($r = 0.76$), degree of pain during intercourse ($r = 0.74$), and ability to achieve orgasm/sexual arousal ($r = 0.71$). The total scale score reliability was also high ($r = 0.70$).

In addition to the modified IFSF questionnaire, we addressed the psychosocial aspect of the women's sexual response.⁹⁻¹³ Patients completed the IFSF questionnaire before (baseline) and at a mean of 24.2 months (range 15 to 65.1) after RC. Supplementary details regarding diagnosis and surgical techniques were taken from the patients' records. We stratified the patients' IFSF responses by the type of urinary diversion (Studor orthotopic, Indiana cutaneous, and standard ileal conduit diversion) to determine whether vaginal sparing (as performed in the orthotopic diversions) influenced the sexual response. All 27 patients completed the IFSF questionnaires.

STATISTICAL ANALYSIS

The mean and standard deviation were calculated for all the domains of the IFSF questionnaire. Paired *t* tests were used to assess the changes from baseline. An analysis of covariance model was fitted for each question. The Wilcoxon rank sum test was used to compare the preoperative to postoperative changes across the study groups (ie, Studor orthotopic diversion, Indiana cutaneous diversion, and ileal conduit diversion). 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

With a mean follow-up of 24.2 months (range 15 to 65.1), the total mean baseline IFSF score decreased from 17.4 ± 7.23 to 10.6 ± 6.62 after RC ($P \leq 0.05$; Table I). The most common symptoms reported by the patients included diminished ability or inability to achieve orgasm in 12 (45%), decreased lubrication in 11 (41%), decreased sexual desire in 10 (37%), and dyspareunia in 6 (22%). The mean scores for the degree of vaginal lubrication (questions 6 and 7) and the ability to achieve orgasm (questions 10 and 11) decreased significantly from 3.3 ± 1.90 and 4.0 ± 1.83 to 1.6 ± 2.01 and 2.2 ± 2.09 , respectively ($P = 0.0098$ and $P = 0.0306$) after RC (Table I). A third domain, pain-free intercourse (questions 4 and 5) dropped from a mean of 3.5 to 2.0 after RC ($P = 0.07$).

The overall baseline IFSF score of the 13 women who were premenopausal was not significantly different statistically than that of the women who were postmenopausal (18.1 ± 8.2 versus 16.6 ± 10.1 , respectively; $P = 0.076$). The only difference between the two groups was the baseline response to the degree of vaginal lubrication (questions 6 and 7), which was higher in the premenopausal group (4.23 versus 3.29 ; $P = 0.004$). However, the changes in the overall IFSF scores and specific domains of the degree of vaginal lubrication (1.89 versus 1.56), ability to achieve orgasm (2.29 versus

TABLE I. IFSF domains: baseline and after radical cystectomy (n = 27)

IFSF Domain	Before Radical Cystectomy	After Radical Cystectomy	P Value
Free of pain during intercourse	3.5 ± 1.99	2.0 ± 2.22	0.0711
Degree of vaginal lubrication	3.3 ± 1.90	1.6 ± 2.01*	0.0098
Overall sexual desire and interest	2.9 ± 1.30	2.1 ± 1.25	0.1262
Ability to achieve orgasm	4.0 ± 1.83	2.2 ± 2.09*	0.0306
Overall sexual satisfaction	3.7 ± 1.23	2.7 ± 1.53	0.0775
Total mean IFSF score	17.4 ± 7.23	10.6 ± 6.62*	0.0067

KEY: IFSF = Index of Female Sexual Function.
Data presented as mean ± SD, unless otherwise noted.
See text for explanation of scale.
* P < 0.05, IFSF domains before and after radical cystectomy using Student's t test.

TABLE II. IFSF domains stratified by type of urinary diversion

IFSF Domain	Ileal Diversion (n = 10)		Studor Pouch (n = 10)		Indiana Pouch (n = 7)	
	Before RC	After RC	Before RC	After RC	Before RC	After RC
Free of pain during intercourse	1.00	0.00	4.33	2.67	4.13	2.50
Degree of vaginal lubrication	2.33	0.00	4.33	1.33	3.25	2.33
Overall sexual desire and interest	2.25	1.00	3.67	2.00	2.88	2.75
Ability to achieve orgasm	2.5	0.00	4.67	2.00	4.13	2.88
Overall sexual satisfaction	2.25	1.75	4.67	2.33	4.00	3.38
Total mean IFSF score	9.34	2.75*	21.67	10.33*	18.39	13.84*

KEY: IFSF = Index of Female Sexual Function; RC = radical cystectomy.
Data presented as mean value; Wilcoxon rank sum test used to compare preoperative-to-postoperative changes across study groups.
* P < 0.05 IFSF domains before and after radical cystectomy.

2.24), and degree of pain during intercourse (2.06 versus 2.09) after RC were no different between the two groups. Similarly, no statistically significant differences were found in either intercourse satisfaction or in the degree of sexual desire after RC.

Only 13 (48%) of the 27 patients were able to have successful vaginal intercourse, with 14 (52%) reporting decreased satisfaction in overall sexual life after RC. Of the 27 patients, 13 (48%) reported a physical inability due to decreased clitoral sensation and vaginal penetration as a result of surgical morbidity. In 8 partners (30%), a decrease occurred in desire for sexual activity owing to apprehension after cancer diagnosis and treatment. When we compared the total mean IFSF scores preoperatively and postoperatively, no statistically significant difference was found between the Indiana (21.67 versus 10.33) and Studor (18.39 versus 13.84) pouches (P = 0.12; Tables II and III). Thus, our early result suggests that preservation of the anterior vaginal wall will not result in improved sexual function after RC.

COMMENT

Our results demonstrated that female sexual dysfunction is a prevalent problem, with 52% of pre-

TABLE III. Total IFSF scores stratified by type of urinary diversion

Diversion Type	Mean Age (yr)	Score Before RC	Score After RC
Ileal diversion (n = 10)	65.75	9.34 ± 4.5	2.75 ± 2.4
Studor pouch (n = 10)	54.75	21.67 ± 6.5	10.33 ± 6.2
Indiana pouch (n = 7)	58.25	18.39 ± 2.3	13.84 ± 4.2

Abbreviations as in Table II.
Data presented as mean ± SD, unless noted otherwise; Wilcoxon rank sum test used to compare preoperative-to-postoperative changes across study groups.

operatively sexually active women becoming dysfunctional after RC. Whether the type of diversion affects sexual function remains to be determined. Our preliminary data suggest no statistically significant difference between the Indiana and Studor pouch diversions. Thus, the benefit in preserving the anterior vaginal wall is still unclear. Recently, surgeons have acknowledged the impact of pelvic surgery on female sexual function by attempting to preserve the vagina and its neurovascular innervation during removal of the bladder.^{8,14-16}

The surgical morbidity of female RC needs to include sexual dysfunction as an outcome measure (just as we discuss urinary continence/hypercontinence), and urologists should be encouraged to attempt neurovascular preservation in appropriate cases in which vaginal preservation is safe. Recognizing subtle refinements in their surgical technique can have a significant impact on the sexual outcomes of female patients. Two domains in our IFSF questionnaire had statistically significant declines in mean scores: the ability to achieve orgasm/sexual arousal and the degree of vaginal lubrication. A third domain, pain free during intercourse, dropped from a mean of 3.5 to 2.0 ($P = 0.07$). No statistically significant differences were found in the IFSF scores between the premenopausal and postmenopausal groups after RC. Our findings are similar to the early findings of Shover and von Eschenbach,¹⁴ that most women experience a significant degree of vaginal dryness, tightness, and pain after RC.

However, both physical and emotional factors, such as a decrease in sexual attractiveness, may influence sexual life after RC and bladder reconstruction surgery.^{11,17,18} In our study, 13 patients (48%) had sexual dysfunction because of a physical inability caused by decreased clitoral sensation and vaginal penetration as a result of surgical morbidity. Also 8 partners (30%) had a decrease in desire for sexual activity owing to apprehension and physical imperfection with urostomy. These psychological and biogenic factors after RC make it more difficult to evaluate female sexual dysfunction.^{11,17-21}

Although the Johns Hopkins group pioneered potency-sparing cystoprostatectomy, potency cannot be achieved in a large percentage of patients.¹ Moreover, preservation of normal sexual function in women has not been the main goal in most studies of neobladders in women. Anatomic dissection has mainly been guided by preservation of the innervation to the sphincteric area to safeguard continence.^{14,18,22} Recently, others have considered sexual function by preserving the vagina as much as possible and taking care to preserve the neurovascular structures, although the uterus was removed.^{7,8} Horenblas *et al.*¹⁵ performed a prospective clinical trial of modified cystectomy for normal sexual function and anatomic urinary tract reconstruction without oncologic concessions. Their report first suggested that preservation of the clitoral vasculature could be achieved with transection of the urethra at the level of the bladder neck and retrograde dissection of the bladder from the anterior vaginal wall. By dissecting close to the vaginal wall no damage is done to the neurovascular vaginal structures or clitoris. All internal genitalia remain in place, and the neobladder is anastomosed

to the intact urethra after creating a hole in the neobladder by everting the mucosa.^{15,16}

Our data suggest that the following surgical modifications may be appropriate in sexually active women: (a) routine preservation of the distal urethra in selected diversions in an effort to preserve the clitoral neurovasculature; (b) preservation of the anterior vaginal wall (as much as possible) to maintain vaginal lubrication and neurovascular innervations; and (c) tubular reconstruction of the vagina (versus posterior flap rotation) to preserve vaginal depth and maintain pain-free intercourse.

Although efforts have been made to improve surgical methods by preserving the vaginal neurovasculature to prevent sexual dysfunction, treatment of sexual dysfunction with oral therapy has not been explored.^{9,12,22,23} The success of oral phosphodiesterase type 5 inhibitor (sildenafil citrate) therapy in men has prompted its use in women, and this may show promise for improving the sexual quality of life in the female population.^{12,23,24} Similar to male penile physiology, nitric oxide-mediated stimulation of clitoral cavernosal smooth muscle increases clitoral blood flow and results in genital engorgement, which is important in female sexual arousal.^{9,12,13,25}

Thus, by improving clitoral sensation and blood flow, sildenafil citrate may subsequently improve vaginal lubrication and sexual satisfaction.^{9,12,25} It is also reasonable to assume that changes in blood flow to both the clitoris and the vagina are mediated in part by the release of nitric oxide.^{9,13,22,25} The role of cyclic guanosine monophosphate-specific phosphodiesterase type 5 in either the clitoris or vagina remains to be determined. Our preliminary data has established a need for more extensive research in the area of female sexual dysfunction after radical pelvic surgery. Clinical research is ongoing to analyze both "newer" surgical modifications and early pharmacologic intervention in an effort to better improve the future quality of life after female cystectomy.

REFERENCES

1. Schlegel PN, and Walsh PC: Neuroanatomical approach to radical cystoprostatectomy with preservation of sexual function. *J Urol* 138: 1402-1406, 1987.
2. Nordstrom GM, and Nyman CR: Male and female sexual function and activity following ileal conduit urinary diversion. *Br J Urol* 70: 33-39, 1992.
3. Hart S, Skinner EC, Meyerowitz BE, *et al*: Quality of life after radical cystectomy for bladder cancer in patients with an ileal conduit, cutaneous or urethral Kock pouch. *J Urol* 162: 777-781, 1999.
4. Santucci RA, Park CH, Mayo ME, *et al*: Continence and urodynamic parameters of continent urinary reservoirs: comparison of gastric, ileal, ileocolic, right colon and sigmoid segments. *Urology* 54: 252-257, 1999.
5. Berman L, Berman J, Felder S, *et al*: Seeking help for sexual function complaints: what gynecologists need to know

- about the female patient's experience. *Fertil Steril* 79: 572–576, 2003.
6. Stenzl A, Colleselli K, Poisel S, *et al*: Rationale and technique of nerve sparing radical cystectomy before an orthotopic neobladder procedure in women. *J Urol* 154: 2044–2049, 1995.
 7. Stenzl A, Colleselli K, Poisel S, *et al*: Anterior exenteration with subsequent ureteroileal urethrostomy in females: anatomy, risk of urethral recurrence, surgical technique and results. *Eur Urol* 33: 18–20, 1998.
 8. Schoenberg M, Hortopan S, Schlossberg L, *et al*: Anatomical anterior exenteration with urethral vaginal preservation: illustrated surgical method. *J Urol* 161: 569–572, 1999.
 9. Kaplan SA, Reis RB, Kohn IJ, *et al*: Safety and efficacy of sildenafil in postmenopausal women with sexual dysfunction. *Urology* 53: 481–486, 1999.
 10. Rosen RC, Riley A, Wagner G, *et al*: The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 49: 822–830, 1997.
 11. Weijmar Schultz WC, Van de Wiel HB, Hahn DE, *et al*: Psychosexual functioning after treatment for gynaecological cancer: an integrative model, review of determinant factors and clinical guidelines. *Int J Gynecol Cancer* 2: 281–290, 1992.
 12. Caruso S, Intelisano G, Lupa L, *et al*: Premenopausal women affected by sexual arousal disorder treated with sildenafil: a double blind, crossover, placebo controlled study. *Br J Obstet Gynecol* 108: 623–628, 2001.
 13. Berman LA, Berman JR, Werbin T, *et al*: The use of the Female Intervention Efficacy Index (FIEI) as an immediate outcome measure of medical intervention to treat female sexual dysfunction. *J Sex Marital Ther* 27: 427–433, 2001.
 14. Shover LR, and von Eschenbach AC: Sexual function and female radical cystectomy: a case series. *J Urol* 134: 465–468, 1985.
 15. Horenblas S, Meinhardt W, Ijzerman W, *et al*: Sexuality preserving cystectomy and neobladder: initial results. *J Urol* 166: 837–840, 2001.
 16. Colombo R, Bertini R, Salonia A, *et al*: Nerve and seminal sparing radical cystectomy with orthotopic urinary diversion for select patients with superficial bladder cancer: an innovative surgical approach. *J Urol* 165: 51–55, 2001.
 17. Althof SE, Turner LA, Levine SB, *et al*: Through the eyes of women: the sexual and psychological responses of women to their partner's treatment with self-injection or external vacuum pump therapy. *J Urol* 147: 1024–1027, 1992.
 18. Rosen RC, Taylor JF, Leiblum SR, *et al*: Prevalence of sexual dysfunction in women: results of a survey study of 329 women in an outpatient gynecological clinic. *J Sex Marital Ther* 19: 171–188, 1993.
 19. Stein JP, Esrig D, Freeman JA, *et al*: Prospective pathologic analysis of female cystectomy specimens: risk factors for orthotopic diversion in women. *Urology* 51: 951–955, 1998.
 20. Goldstein I, Lue TF, Padma-Nathan H, *et al*, for the Sildenafil Study Group: Oral sildenafil in the treatment of erectile dysfunction. *N Engl J Med* 338: 1397–1404, 1998.
 21. NIH Consensus Development Panel on Impotence: NIH Consensus Conference: impotence. *JAMA* 270: 83–90, 1993.
 22. Basson R: Female sexual response: the role of drugs in the management of sexual dysfunction. *J Obstet Gynecol* 98: 350–353, 2001.
 23. Rajfer J, Aronson WJ, Bush PA, *et al*: Nitric oxide as a mediator of relaxation of the corpus cavernosum in response to nonadrenergic, noncholinergic neurotransmission. *N Engl J Med* 326: 90–94, 1992.
 24. Andersson KE, and Wagner G: Physiology of penile erection. *Physiol Rev* 75: 191–236, 1995.
 25. Berman JR, Berman LA, Lin H, *et al*: Effect of sildenafil on subjective and physiologic parameters of the female sexual response in women with sexual arousal disorder. *J Sex Marital Ther* 27: 411–420, 2001.