

Mini-reviews

The truly international authorship every month in the Journal is reflected in the Mini-Review section in this issue. One from the USA, one from Canada, and two from Italy. It is a great pleasure to the Editor that this is so, and I hope also to the readership and to those who make such excellent contributions. The topics covered are female sexual dysfunction after pelvic surgery, zoledronic acid in prostate and renal cancers, intravesical gemcitabine for superficial bladder cancer, and the reduction of patient discomfort during TRUS-guided biopsy of the prostate.

Female sexual dysfunction after pelvic surgery: the impact of surgical modifications

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INTRODUCTION

Female sexual dysfunction (FSD) is a highly prevalent and often underestimated problem in the community. It is an age-related, progressive problem associated with several biological, medical and psychological factors. Few data on FSD come from well-designed, community-based, epidemiological studies.

The National Health Survey (a large community-based study in women aged <60 years) showed that 43% of 1749 women had some form of sexual dysfunction. FSD is certainly not a problem limited to young women; population census data from the USA show that ≈ 10 million American women aged 50–74 years self-reported some form of sexual dysfunction [1]. In a recently conducted international survey, which included 4507 women, 34% of the participants had decreased sexual interest and 19% did not consider sexual intercourse to be pleasurable [2]. FSD includes disorders of sexual desire, arousal and organic or sexual pain associated with self-distress. Sexual dysfunction after pelvic surgery is an important cause of organic dysfunction [3,4].

Pelvic surgery forms an important and underestimated cause of sexual dysfunction [3,4]. Urological surgery, e.g. simple and radical cystectomy (RC) and sling procedures, gynaecological surgery (simple and radical hysterectomy) and colorectal surgery (low anterior, or abdominoperineal, resection, APR) are among the most important causes of FSD. Recently, FSD has become a major quality-of-life issue in patients undergoing pelvic surgery.

Surgical modification by Walsh *et al.* [5] in men opened a new era of nerve-sparing radical prostatectomy, which later followed for cystoprostatectomy, also with encouraging results. Recently, the same principles were applied in the field of female RC, also with considerable success, and state-of-the-art nerve-sparing RC has opened a new era in female RC. No matter what the cause, FSD can compromise a woman's quality of life. In this review we discuss FSD after major pelvic surgery, with special emphasis on the current concepts of surgical modifications and our experience. We also outline the current status of medication for FSD.

FSD AFTER PELVIC SURGERY

AFTER RADICAL CYSTECTOMY

RC in women or anterior exenteration has been the standard treatment for aggressive

superficial bladder cancer or invasive carcinoma [6]. It includes removing the urinary bladder, urethra, uterus, ovaries and anterior vaginal wall. The endpoints of RC are primarily focused on continence and recurrence. Sexual dysfunction after RC may be caused by the trauma or physical and emotional disturbances. Other factors that may affect sexual life and quality of life after RC are the type of urinary diversion or orthotopic bladder substitution, nerve-sparing modification, urethral resection and vaginal-sparing. During RC the neurovascular bundles (located on the lateral walls of the vagina) are usually removed or damaged along with the removal of the bladder, urethra and anterior vaginal wall [4,7,8]. In addition, there is often significant devascularization of the clitoris with removal of the distal urethra, affecting subsequent sexual arousal and desire [4,7,8]. FSD is a major concern of many younger women undergoing pelvic surgery.

The type of urinary diversion has also been implicated hypothetically to influence sexual dysfunction after RC; in the initial series reported by Nordstrom and Nyman [3] five of six patients reported sexual dysfunction after RC with an ileal conduit. The most important reasons for the dysfunction were loss of sexual desire, vaginal dryness and dyspareunia. However, later studies [9,10] showed no significant difference between the type of urinary diversion and sexual dysfunction. Bjerre *et al.* [9] evaluated the sexual profile of women with different types of urinary diversion after RC; 37 patients completed the questionnaire, 17 who had a continent urinary diversion and 20 with an ileal conduit. Data were analysed in 33 patients; there was no significant difference between the types of diversion. The lack of a validated questionnaire, combined with the few patients in each group, may be an important reason for the failure to obtain a significant difference between the types of diversion.

We conducted a study to evaluate FSD after RC with different types of urinary diversions; the baseline and follow-up data were obtained from 34 women who had RC between 1997 and 2002, and who were interested to participate in the study. Of the 34 patients, 27 were sexually active before surgery; of these 27, 10 (37%) had an orthotopic urinary diversion (Studer), seven (26%) a continent cutaneous diversion (Indiana) and 10 (37%) an ileal conduit

diversion. A 10-item version of the self-administered Index of Female Sexual Function questionnaire (IFSFF) was used to assess sexual dysfunction [10]. The specific domains analysed in the IFSFF 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). The total mean (SD) baseline IFSFF score decreased from 17.4 (7.23) to 10.6 (6.62) after RC ($P < 0.05$). 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 six (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. When the IFSFF scores were stratified according to the type of urinary diversion, there was no difference between the scores before and after RC. The few patients in each subgroup may be the reason why the difference was not significant [10].

This study showed that FSD is a prevalent problem after RC; sexual function was shown to be affected in all the domains, including decreased orgasm, decreased lubrication, lack of sexual desire and dyspareunia. The results also showed that the type of urinary diversion did not affect sexual dysfunction. This recent report on the magnitude of FSD after RC, and recent reports on surgical modification, stimulated the use of the 'quality of life cystectomy' in women.

THE CLEVELAND CLINIC FOUNDATION 'QUALITY-OF-LIFE CYSTECTOMY' IN WOMEN

Walsh *et al.* [5] popularized the role of nerve-sparing surgery in men with prostate cancer, methods later also incorporated into RC for men. In limited reports, RC was shown to affect sexual activity in women; as in men. In 1995, Stenzl *et al.* [7] first reported that removing the distal urethra is associated with significant devascularization of the clitoris and thus reduced sexual arousal. They also reported that preserving the urethra was not associated with a greater risk of local recurrence [8]. Burkhard and Studer [11] reported that complete resection of the

cranial two-thirds of the vagina, with the caudal border of resection just below the bladder neck, results in dissection of most autonomic nerves to the urethra and vagina in women. However, if the lateral vaginal walls are left intact, most of the plexus fibres to the urethra may be preserved, with careful dissection of the bladder neck and cranial urethra. They further reported recently that preserving the neurovascular pedicle was associated with a significant improvement in the recovery of erectile function [12]. This pioneering work by Studer *et al.* has made urologists realise the importance of nerve-sparing surgery in female RC, and modify the surgical technique accordingly. Initial reports from Horenblaus *et al.* [13] showed normal vaginal lubrication in all three women who had a nerve-sparing RC with preservation of all internal genitalia.

Our modified technique includes: an infra-umbilical incision (to minimize pain and allow earlier mobilization), neurovascular preservation (careful identification and preservation of bundles on the lateral vaginal wall enhances clitoral sensation), preservation of the anterior vaginal wall (enhances vaginal lubrication), routine hysterectomy avoided (eliminates the risk of vesicovaginal fistula), routine suprapubic tube avoided (to reduce postoperative morbidity/cosmetic scarring), anterior vaginal tubularization preferred rather than a posterior vaginal flap in sexually active women (preserves the depth of the vagina) and subcuticular skin closure (to avoid compromising the body image).

In our centre we retrospectively evaluated the sexual functional outcome in six women who had a nerve-sparing RC with an orthotopic bladder substitution ('quality-of-life' cystectomy) with contemporary non-nerve sparing orthotopic urinary diversion in seven [14]. No patients in the study group received radiotherapy after RC. All patients were evaluated with the Female Sexual Function Index (FSFI) at 6-monthly intervals [15]. The specific domains analysed included pain-free intercourse, degree of vaginal lubrication, overall sexual desire and interest, arousal, ability to achieve orgasm, and overall sexual satisfaction. In the nerve-sparing group, the baseline (preoperative) FSFI score and that at 1 year afterward (24.5 vs 22.3) showed no decline compared with non-nerve sparing group, where there was a marked decline after surgery (25 vs 11) (Table 1). Significant vaginal dryness, lack of arousal and dyspareunia led

FSFI domains	Nerve-sparing (N = 6)		Non-nerve sparing (N = 7)		TABLE 1 <i>The mean FSFI score at baseline and after RC in 13 patients</i>
	before	after	before	after	
Desire	3.3	3	4.2	3	<i>FSFI, Female Sexual Function Index.</i>
Arousal	4.1	3	3.2	1.2	
Lubrication	4.7	4.7	4.8	1.2	
Orgasm	3.2	3.2	4.6	1.2	
Pain	5	4.7	3.6	2.8	
Satisfaction	4.2	3.7	4.6	1.6	
Total mean composite score	24.5	22.3	25	11	

to the discontinuation of sexual intercourse in the latter group. Neurovascular preservation not only improved urinary control after surgery but also improved sexual function compared to the non-nerve sparing group.

FSD AFTER RADICAL CYSTECTOMY AND SIMPLE HYSTERECTOMY FOR TREATING CERVICAL CANCER

Hysterectomy is the most common pelvic surgery in women of all ages; over half a million women undergo hysterectomy for different reasons each year in the USA [16]. Most women were not evaluated for sexual life after hysterectomy; of those who were willing to report their sexual function, 15–37% were shown to have a considerable decrease in their sexual life after surgery [17,18]. The pathophysiology, which has been implicated in FSD after hysterectomy, includes lack of vaginal lubrication and loss of libido. Both these complications are further aggravated by bilateral oophorectomy. Vaginal dryness and a short vaginal vault are also two important factors reported as causes of dyspareunia after surgery.

Quality-of-life issues are becoming significant endpoints in gynaecological surgical patients; these issues have not been reported adequately. The introduction of cervical screening programmes (annual smear test) has led to the early detection of cervical cancer in younger women. This age migration can potentially make sexual function a major postoperative issue of gynaecological surgery. Although reports of sexual function after gynaecological surgery date back to the 1980s, the lack of a standard questionnaire and definitions has produced wide variations in these reports. In a population-based epidemiological study in Sweden, Bergmark *et al.* [19] reported that reduced sexual

satisfaction and dyspareunia were the primary source of symptom-induced distress after treatment for cervical cancer. Recent studies by Jensen *et al.* [20] showed that patients treated with radical hysterectomy and radiotherapy had short-term sexual difficulties, e.g. dyspareunia and vaginal dryness leading to decreased sexual satisfaction. However, some of these problems subsided by 6 months after surgery.

FSD AFTER TREATING OTHER GYNAECOLOGICAL CANCERS

FSD is a common complication after managing ovarian cancer and is similar to that after managing cervical cancer [21]. Multimodal treatments which include hysterectomy, oophorectomy and adjuvant chemotherapy are commonly used in managing ovarian cancer. FSD has been a universal complication after these multimodal treatments. Stewart *et al.* [22] reported that 57% women were treated for ovarian cancer had a decrease in sexual function. Recently, Carmack Taylor *et al.* [21] reported that of 232 patients with ovarian cancer only half were sexually active after treatment. Of these patients 47% reported no or little desire, 80% reported problems with vaginal dryness and 62% reported pain or discomfort during penetration. The reasons for the sexual inactivity included: lack of a partner (44%), lack of interest (39%), physical problems making sex difficult (23%) and fatigue (11%). It is obvious from these two studies that FSD is a significant complication after treatment of ovarian cancer. Sexual rehabilitation should be addressed in these patients, and should also include their partners. Published data on sexual dysfunction after treatment for endometrial and vulval cancer are limited.

There is a clear increase in awareness about the impact of gynaecological cancer surgery

on the sexual function of women. The assessment and treatment of sexual function should become an important part of the standard care of women diagnosed and treated for gynaecological cancers.

Simple hysterectomy is the most common gynaecological surgery, sexual dysfunction afterward has not been widely reported. The scarcity of reports is a major limitation. FSD after hysterectomy is associated with the indication for the hysterectomy and various preoperative conditions such as dyspareunia and dysmenorrhoea. Several studies report that sexual function improved after simple hysterectomy in 30–50% of patients [23–25]. The potential explanation for this improvement includes the relief from preoperative dyspareunia and dysmenorrhoea [23]. The Maryland Women's Health Study showed that women after simple hysterectomy had an improvement in overall sexual functioning with no change in the frequency of orgasm [26]. Dragisic *et al.* [27] reported no change in sexual desire, orgasm frequency, or orgasm after simple hysterectomy. Questions were raised about the impact of the type of hysterectomy (vaginal vs abdominal) on sexual function. However, El-Toukhy *et al.* [28] reported no significant difference in sexual function after abdominal or vaginal simple hysterectomy. Apparently, from published reports, simple hysterectomy has no adverse effects on sexual function. These reports need to be confirmed using validated questionnaires that can stratify the different domains of sexual function, which include orgasm, desire and arousal, pain during the intercourse, lubrication, and satisfaction.

Recently, there has been growing interest among gynaecologists in FSD after pelvic surgery; this increased awareness will lead to the development of better surgical techniques and better information on sexual dysfunction after surgery. The risk and benefits of any pelvic surgery should include accurate information on sexual dysfunction, to obtain fully informed consent. In future, FSD should be routinely discussed in gaining informed consent for gynaecological surgery.

FSD AFTER SURGERY FOR RECTAL CANCER

Genitourinary dysfunction after pelvic surgery is most commonly related to injury of the autonomic pelvic nerves. Rectal cancers have been some of the most important pelvic

cancers causing significant mortality and morbidity. Low anterior and APR are commonly used as curative treatments for rectal cancer; rates of sexual dysfunction after these oncological procedures are 10–60% [29]. These high rates of sexual dysfunction have provoked oncologists to modify their technique. Currently, most surgeons use total mesorectal excision (TME) with preservation of the neurovascular bundle, which has been shown to reduce rates of sexual dysfunction [30]. Enker *et al.* [31] reported that APR, when used in accordance with the principles of TME and autonomic nerve preservation, ensures the greatest likelihood of resecting all regional disease, while preserving both sexual and urinary function. In that study, the authors showed that 57% of patients undergoing APR and 85% undergoing sphincter-preserving surgery were able to maintain their sexual function. In a study by Pocard *et al.* [32], four of seven women were able to achieve orgasm similar to that before surgery, with TME, autonomic nerve preservation and complete intraoperative identification of the nerves. Laparoscopically assisted mesorectal excision is used increasingly; Quah *et al.* [33] reported that sexual dysfunction rates were higher after laparoscopic than open surgery in men, but there was no such difference in women.

It is evident from published reports that sexual dysfunction is a significant problem after radical rectal surgery, and was often under-reported, especially in women. The introduction of screening programmes (fecal occult blood, colonoscopy) even in the colorectal field had allowed these cancers to be detected at an early stage in younger patients, which may increase the importance of quality of life in the future.

Rectal cancers are commonly treated with multimodal treatments, which include neoadjuvant and adjuvant radiation therapy [33]. These treatments, although increasing the cure rate, also increase sexual dysfunction. Mannaerts *et al.* [34] reported that the preoperative ability to have an orgasm had disappeared in half of women who had multimodal treatment. Because of such a high prevalence of FSD after treatment, patients should receive preoperative counselling about treatment-related effects on sexuality.

Standard treatment options for rectal cancer are associated with high rates of sexual

dysfunction. TME has shown some promise in reducing sexual dysfunction. When feasible, TME with autonomic nerve preservation can be used to preserve sexual function.

MEDICAL TREATMENTS FOR FSD

Numerous medications are available for treating FSD, including hormones and vasoactive drugs. However, no single treatment has been shown to be effective.

Currently available treatment options for FSD include oestrogens, androgens, phosphodiesterase inhibitors and dopamine-receptor antagonists. Women with a lack of sexual desire are probably more responsive to androgens, oestrogens and dopamine-receptor antagonists, whereas those with sexual arousal disorder may be more responsive to phosphodiesterase inhibitors and prostaglandins [35]. Oestrogens have been the mainstay for treating FSD; they improve clitoral and vaginal sensitivity and lubrication, and sexual desire [36]. Androgens have been used to treat FSD because of the assumption that FSD is an androgen-deficiency disease. Testosterone increases clitoral sensitivity and sexual arousal [37]. The role of phosphodiesterase-5 inhibitors has not been evaluated as widely in women as it has in men, but some reports suggest that these inhibitors appear to increase clitoral sensitivity, especially in postmenopausal women [38]. Further trials are essential to assess the effectiveness of sildenafil for treating FSD. Multimodal treatments using oestrogens to increase the libido and vaginal lubrication, and phosphodiesterase-5 inhibitors to increase lubrication and arousal, are underway. Currently, phosphodiesterase-5 inhibitors are not FDA approved for FSD treatment.

SUMMARY

FSD is a multifactorial and complex problem of women in the community. The approach to FSD is not the same as in men. FSD is an important aspect of quality of life in women after any pelvic surgery. The importance of nerve-sparing pelvic surgery has been well documented in urology and colorectal surgery, and should soon be integrated into gynaecology and oncology. Education about FSD after this complication should be included in fully informed consent. The

management of FSD should include a psychological and medical evaluation; the medical management of FSD is developing rapidly and the future of this field will be interesting and encouraging. Gynaecologists should play a major role in managing FSD, irrespective of its cause, but further studies are essential for formulating effective treatment strategies.

CONFLICT OF INTEREST

None declared.

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- Abbreviations:** FSD, female sexual dysfunction; IFSF, Index of Female Sexual Function; FSFI, Female Sexual Function Index; RC, radical cystectomy; APR, abdominoperineal resection; TME, total mesorectal excision.