GYNECOLOGY

Does treatment for cervical and vulvar dysplasia impact women's sexual health?

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Human papillomavirus—associated disease represents an immense public health burden worldwide. Persistent human papillomavirus infection can lead to the development of cervical dysplasia and vulvar dysplasia, both of which have been increasing in incidence in women in recent years. Numerous studies have focused on methods for screening and diagnosis of cervical dysplasia, but few have looked at the effects of treatment on women's psychological and sexual health. Even fewer studies have addressed these issues in women with vulvar dysplasia. The aim of this article was to provide a comprehensive review of the existing evidence concerning the impact of therapy for cervical and vulvar precancers on women's sexual function and sexual relationships. We performed a search of the medical literature for the time period up to and including August 2013 on PubMed. The findings from a limited number of studies to date indicate that psychosexual vulnerability increases after diagnosis and treatment of both cervical and vulvar dysplasia. More in-depth research is needed to better understand the effects of different treatment modalities on women's sexual health and relationships during and following treatment.

Key words: cervical intraepithelial neoplasia, dysplasia, human papillomavirus, sexual health, vulvar intraepithelial neoplasia

Human papillomavirus (HPV)—associated disease represents an immense public health burden worldwide. Approximately 80-90% of sexually active men and women will likely acquire HPV infection at least once in their lifetime.[1] HPV is associated with 530,000 new cases of cervical cancer and 270,000 cervical cancer deaths worldwide each year.[2] Although more than 120 types of HPV exist, 40 are known to affect the anogenital tract, with types 16 and 18 responsible for approximately 70% of cervical cancers.

Much is known about HPV virology, epidemiology, clinical manifestations, and prevention strategies including screening programs and prophylactic vaccines. Less is known about the impact of HPV infection on women's psychological and sexual well-being. Studies of the psychological effects of screening and diagnosis have documented that an abnormal Papanicolaou result and the time period before, during, and following colposcopy are associated with anxiety and distress.[3-9]

In addition, patients testing positive for HPV have increased anxiety, distress, general concern,[10] and a significantly worse feeling about their sexual relationships[11] when compared with patients receiving negative test results.

Two small studies have looked at women's experiences in response to a diagnosis of vulvar intraepithelial neoplasia (VIN). One found that women experienced shock and a sensation of losing control of their bodies.[12] Another study found that women being followed up for VIN scored poorly on quality of life and sexual functioning assessments.[13]

Even less is known about the effects of treatment for HPV-associated disease on quality of life, sexual health, and sexual relationships. Most of the available literature is focused on outcomes in patients treated for cervical and vulvar malignancies. However, given the prevalence of HPV and the widespread adoption of HPV testing in screening protocols, the treatment of premalignant HPV-related disease is far more common than the treatment for cancer. The aim of this article was to provide a comprehensive review of the existing evidence concerning the impact of therapy for cervical and vulvar precancers on women's sexual function and sexual relationships.

We conducted a search of the medical literature up to and including August 2013 on PubMed using a number of

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related terms including cervical dysplasia, vulvar dysplasia, human papillomavirus, sexual health, sexual function, psychosexual impact, psychological impact, treatment impact, and quality of life. The search was limited to English literature. We found a total of 6 articles that studied the impact on sexual health after treatment for cervical dysplasia (Table 1) and 5 articles that studied the impact on sexual health after treatment for vulvar dysplasia (Table 2). We excluded 2 pilot studies with a small sample size whose primary aim was not the impact of treatment for cervical dysplasia or vulvar dysplasia on women's sexual health.[12,13]

Effects of treatment for cervical dysplasia on sexual health

Cervical HPV disease is manifested histologically as cervical intraepithelial neoplasia (CIN), which can be low grade (or CIN 1), reflecting productive viral infection that is usually self-limited, or high grade (HGCIN or CIN 2, CIN 3, or CIN 2/3), reflecting a neoplastic transformation that could progress to cancer in a low proportion of cases.

The standard of care is to monitor low-grade CIN until it resolves and to treat HGCIN. Treatment modalities include excisional procedures (cold-knife conization, large loop excision of the transformation zone/loop electrosurgical excision procedure [LLETZ/LEEP], and laser conization) or ablative procedures (cryotherapy and laser ablation).

We identified 6 studies that have looked specifically at the impact of CIN treatment on women's sexual health (Table 1). Four studies assessed the impact of LEEP. Juraskova et al[14] used a qualitative approach and found 3 main themes reported among 21 women treated with LEEP: issues of uncertainty, trust in one's body, and communication.

Following the diagnosis of CIN, women were most concerned about cancer, but in the posttreatment period, their concern evolved to a focus on future reproductive viability. With regard to the theme of communication, the study found that some women indicated an initial distancing from their partner, and women who were single indicated feeling a sense of relief at not being in a relationship while undergoing treatment.

The 3 other studies of the impact of LEEP used questionnaires to examine the domains of sexual function. Hellsten et al[15] used a modified version of a questionnaire first used by Campion et al[16] and later modified by Howells et al[17] to assess the impact of LEEP at 6 months and 2 years of follow-up. The study found a significant decrease in spontaneous interest, frequency of intercourse, and sexual arousal and a significant increase in negative feelings towards sex at 6 months among 45 women who were treated with LEEP compared with 52 women with dysplasia who had not undergone LEEP. At the 2-year follow-up, spontaneous interest and frequency of intercourse remained significantly decreased in the women who had undergone LEEP.

Similar results were found by Serati et al,[18] who used a validated questionnaire, the Female Sexual Function Index (FSFI), which measures 6 sexual domains (desire, arousal, lubrication, orgasm, satisfaction, and pain).[19] This study found that desire was significantly decreased after treatment, whereas the other domains were unaffected. Inna et al[20] used a self-designed questionnaire and found that frequency of sexual intercourse, dysmenorrhea, and dyspareunia after LEEP were not significantly different following treatment. However, overall sexual satisfaction, orgasmic satisfaction, and vaginal elasticity were significantly decreased up to 1 year following LEEP.

Campion et al[16] assessed the psychosexual impact of diagnosis and laser treatment of CIN using a self-designed questionnaire that interrogated the following aspects of sexuality: frequency of spontaneous sexual interest, frequency of intercourse, frequency of adequate vaginal lubrication and sexual arousal with intercourse, frequency of orgasm with intercourse, frequency of dyspareunia, and frequency of negative feelings toward intercourse. Women in the treatment group were treated for CIN with carbon dioxide laser and in the comparison groups were undergoing gynecological care for noncervical disease but had partners who had been diagnosed with a sexually transmitted infection, either condyloma acuminata or nongonococcal urethritis. The authors found that women treated with laser experienced significantly decreased spontaneous sexual interest and frequency of intercourse, decreased vaginal lubrication and sexual arousal, and decreased frequency of orgasm when compared with controls. Women who were treated for CIN also demonstrated a significant increase in negative feelings toward sexual intercourse or toward a regular partner and increased dyspareunia, whereas women in the comparison group did not.

The age range for participants in this study was lower (17-26 years) than in the other studies in the literature (Table 1). This study found a decrease in sexual function among all 6 domains, whereas other studies found significant differences only among desire/spontaneous interest and frequency of intercourse.

One study evaluated the change in sexual function in women 1 year after cold-knife conization for cervical dysplasia.[21] The author conducted face-to-face interviews using a self-designed questionnaire to ask patients about the strength of libido, frequency of orgasm during intercourse, frequency of intercourse, and dyspareunia. No statistically significant differences were found before and after treatment regarding libido, frequency of orgasm, or frequency of intercourse, but there was a statistically significant decrease in the number of women experiencing dyspareunia. Although the results of this study did not follow the overall trends seen in the other studies, this was the only study in which the patients did not complete the questionnaire independently, so interviewer bias cannot be excluded.

Effects of treatment for vulvar dysplasia on sexual health

VIN is an HPV-associated squamous lesion of the vulva that can lead to cancer if left undiagnosed and untreated. Studies show an increasing incidence of VIN, especially among women younger than 50 years of age.[22,23] The recent pronounced rise in incidence may be

TABLE 1
Overview of studies on sexual health in women treated for cervical dysplasia

CIN

Author/year/country	Study design	Study population	Diagnosis	Treatment	Age (mean)	Follow-up time (mean)	Tool implemented	Significant findings/impact on measures of sexual function
Juraskova et al,[14] 2007, Australia	Qualitative	21	CIN 1-3	LLETZ (LEEP)	24-54 (34)	Immediately after treatment and up to 8 mo after treatment	Self-designed semistructured telephone interview	Qualitative findings; see text for results
Hellsten et al,[15] 2008, Sweden	Cross-sectional	97 45 LEEP 52 With dysplasia but did not undergo LEEP	CIN 1 above age 30 y and CIN 2/3 at any age	LEEP	23-49 (27)	At time of LEEP, 6 mo, and 2 y	Psychosexual Questionnaire designed by Howells et al[17]; STAI	At 2 yr follow-up: decrease in spontaneous interest and frequency of intercourse
Campion et al,[16] 1988, United Kingdom	Prospective controlled	105 15 CIN 1 11 CIN 2 25 CIN3 54 Controls	CIN 1-3	Laser	17-26 (23)	Before treatment and 6 mo	Self-designed Questionnaire	At 6 mo follow-up: decrease in spontaneous sexual interest, frequency of intercourse, vaginal lubrication, sexual arousal, and frequency of orgasm; increase in negative feelings toward sexual intercourse and in dyspareunia
Serati et al,[18] 2010, Italy	Cross-sectional	58	CIN 1 persistent and CIN 2/3	LEEP	22-3 (36)	At time of LEEP, and 6 mo	FSFI	At 6 mo follow-up: decrease in desire
Inna et al,[20] 2010, Thailand	Cross-sectional	89	CIN 1-3	LEEP	24-57 (42)	12.1—70.9 wks (29.3)	Self-designed Questionnaire	At up to 1 y follow-up: decrease in overall sexual satisfaction, orgasmic satisfaction, and vaginal elasticity
Kilkku et al,[21] 1982, Finland	Retrospective uncontrolled cohort	64	Dysplasia or carcinoma in situ (HGCIN)	CKC	17-52 (27)	6 wks, 6 mo, and 12 mo	Self-designed Questionnaire	At up to 1 y follow-up: decrease in dyspareunia

CIN, cervical intraepithelial neoplasia; *CKC*, cold-knife conization; *FSFI*, Female Sexual Function Index; *HGCIN*, high grade cervical intraepithelial neoplasia; *LEEP*, loop electrosurgical excision procedure; *LLETZ*, large loop excision of the transformation zone; *STAI*, State-Trait Anxiety Inventory.

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TABLE 2
Overview of studies on sexual health in women treated for vulvar dysplasia

VIN

Author	Study design	Study population	Lesion	Treatment	Age (mean)	Follow-up time (mean)	Tool implemented	Significant findings/impact on measures of sexual function
Narayansingh et al,[32] 2000, United Kingdom	Cross-sectional	5	VIN 3	Local excision and flap repair	30-48 (38)	5—33 mo (18.4 mo)	Modified sexual rating scale questionnaire	At 5-33 mo follow-up: mean sexual rating scale score was 71.8% with scores ranging from 25% to 90%
Andersen et al,[29] 1988, United States	Cross-sectional	84 42 in situ vulvar cancer 42 healthy controls	Vulvar carcinoma in situ (HGVIN)	Laser or chemotherapy (6); Local excision (26); Total vulvectomy (9); radical vulvectomy (1)	31-81 (50)	14 mo to 10 y (5 y)	Derogatis Sexual Experience Scale; self-designed questionnaire: sexual arousability index; profile of mood states; dyadic adjustment scale	At 1-5 yr follow-up: increased inhibition of sexual excitement and orgasm
Thuesen et al,[30] 1992, Denmark	Cross-sectional	18	Vulvar carcinoma in situ (HGVIN)	Local excision	20-55 (41)	3-11 y (8 y)	Self-designed questionnaire	Qualitative findings; see text for results
Likes et al,[31] 2007, United States	Cross-sectional	86 43 VIN 43 healthy controls	VIN (36); vulvar cancer (6); no pathology report availabler (1)	Excision	18-77 (47.3)	At least 6 wks following excision	FSFI and QLQ-C30	At $\geq$6 wks follow-up: decrease in desire and sexual satisfaction
Shylasree et al,[33] 2008, United Kingdom	Cross-sectional	82	VIN 2/3	Data not available	26-81 (48)	Data not available	Self-designed Questionnaire, Hospital Anxiety and Depression Scale, revised sexual rating scale	Qualitative findings; see text for results

HGVIN, high grade vulvar intraepithelial neoplasia; *QLQ-C30*, European Organization for Research and Treatment of Cancer's Quality of Life Questionnaire; *VIN*, vulvar intraepithelial neoplasia.

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associated with increasing rates of HPV infection.[24] The diagnosis of VIN is made by histological evaluation of a vulvar biopsy specimen and then traditionally classified into low-grade (or VIN 1) or high-grade (HGVIN or VIN 2 and 3).

Analogous to CIN lesions, low-grade VIN is considered a manifestation of HPV infection, whereas HGVIN is a premalignant lesion that is usually treated to prevent cancer. In 2004, the International Society for the Study of Vulvovaginal Disease classified VIN into 2 clinically distinct types: a usual type, which is associated with HPV, and a differentiated type, which is not associated with HPV.[25]

Treatment for VIN has traditionally been surgical, but topical imiquimod treatment has also been shown to be efficacious.[26-28] Surgical treatment includes CO_2 laser ablation, wide local excision, and vulvectomy, which is usually used to treat vulvar cancer. In an effort to preserve normal vulvar anatomy and function, medical treatments for VIN have also been investigated. These include topical therapies such as imiquimod, 5-fluorouracil, cidofovir, α-interferon, and nonpharmacological treatments such as photodynamic therapy. The extent of treatment is dependent on the size and location of the VIN lesion and may be limited to a small area or may involve the entire vulva.

The high recurrence rate of VIN of up to 46-70%[29] means that many women undergo multiple rounds of treatment. We identified 5 studies that looked specifically at the impact of treatment for VIN on women's sexual health (Table 2).[30-34] One of these studies[33] will not be discussed in detail because of the fact that it assessed the sexual function of women after local excision and flap repair for VIN, which is no longer a standard treatment for VIN.

The earliest study evaluated 42 patients treated for HGVIN and compared the results of interview data and questionnaires with a group of 42 age-matched women with no gynecological issues.[30] The results showed that compared with healthy women and over time from 1 year after the treatment to the end of follow-up (on average 5 years), women treated for VIN had significantly increased inhibition of sexual excitement (86% at time of follow-up compared with 31% before treatment) and significantly increased inhibition of orgasm (67% at time of follow-up compared with 43% before treatment).

Of note, at the time of follow-up, 79% of the women treated for HGVIN reported being not sexually active, but we were unable to ascertain whether their decreased level of sexual activity was correlated with the other reported changes in sexual function. Of interest as well is that despite increased inhibition of sexual excitement and orgasm, women treated for HGVIN did not report a decrease in desire. The study did not make direct comparisons among the various treatment modalities. Using an assessment via chart review of the magnitude of vulvar disruption from treatment, the authors found that more conservative treatments (less disruption of genital anatomy) were associated with less sexual dysfunction. They also indicated that several women commented on their reluctance to initiate new relationships because of the effects of treatment on their bodies.

In 1992, Thuesen et al[31] retrospectively evaluated the impact of local excision for VIN on patients' sexual function and somatopsychic reactions. Eighteen women under the age of 60 years treated for HGVIN were individually interviewed using a questionnaire designed by the authors. The study found that although all 18 participants reported that the frequency of sexual intercourse before treatment had been acceptable, after treatment 3 women found intercourse to be too frequent and 3 women found it to be too infrequent. Of those who reported too frequent intercourse, 2 experienced dyspareunia and 1 experienced scorching and itching. Of the 3 who reported too infrequent intercourse, 1 reported that her husband had lost interest in her after the operation and 2 reported being fearful of having intercourse because of changes in the width of the vagina following treatment. One woman reported reduced libido following treatment, and several women suffered from dyspareunia after treatment (2 of 16 before vs 6 of 18 after). None of the women reported reduced sexual arousal or orgasmic dysfunction either before or after treatment.

We found only 1 study[32] that used a validated instrument, the FSFI, to assess sexual functioning in women following vulvar excision. This was a cross-sectional study comparing 43 women after vulvar excision for VIN ($n = 36$) or vulvar cancer ($n = 6$) with a healthy age-matched comparison group of 43 women in the assessment of sexual function and quality of life. The study used the European Organization for Research and Treatment of Cancer's Quality of Life Questionnaire, the QLQ-C30. The results found significant differences between the overall FSFI and QLQ-C30 scores between the treatment group and the control group. Specifically, the FSFI domain scores for desire, arousal, orgasm, and satisfaction showed statistically significant mean differences between the groups. In both groups, sexual desire was the most affected area. When a post hoc comparison was undertaken and data for the participants with vulvar cancer ($n = 6$) were removed, leaving a study sample of 36, the physical domains of sexual function (arousal, lubrication, orgasm, and pain) lost statistical significance between the groups, but the psychological domains of sexual function (desire and satisfaction), and the overall FSFI score, remained significantly lower in the treatment group.

Shylasree et al[34] conducted a study that looked both at the effect of demographic, psychological, and disease-related factors on quality of life outcomes in women with VIN 2/3 and at the effect of VIN treatment on women and their partners. This is the only study we found that sought to address partner and relationship issues, although the information was based only on women's responses and did not include a query of partners themselves. Of the 82 study participants, 44 were sexually active.

In the qualitative data analysis, which focused on the effects of treatment for VIN on sexual health, 21 women provided written explanations for their reasons for being sexually inactive and

33 for being sexually unhappy. Common reasons included soreness or pain, fear, self-consciousness, older age, a lack of sex drive, no current partner, and fear of passing on the virus or disease.

Conclusions and future directions

HPV infection and associated lesions are associated with a social stigma. The concerns and anxieties around a new diagnosis have been shown to have a significant impact on women's psychological well-being. However, the extent to which this diagnosis affects women in their existing and new sexual relationships remains to be fully explored. Treatment of vulvar and cervical dysplasia can contribute to a sense of loss of control over one's body and anxiety concerning personal and genital health, can influence body image and self-esteem, and can raise questions of trust and loyalty in sexual partnerships. All of these factors can be detrimental for a woman's emotional, sexual, and overall well-being.

The studies reviewed here on treatment for CIN found that domains of female sexuality such as desire, spontaneous interest, and frequency were statistically lower following treatment for CIN when compared with the levels before treatment.[15,18,20] These studies postulated that the domains significantly affected were psychological in nature, possibly attributed to the anxiety associated with the diagnosis and treatment of CIN. It is not unreasonable to hypothesize that similar psychological components of sexual health are negatively affected in women treated for VIN.

Thus far, only 1 study[32] has used the FSFI in women with VIN, and the results of this study do suggest that the impairment in sexual function following vulvar excision for VIN is psychological in nature. It is also reasonable to hypothesize that some of the effects of treatment might be physiological in nature, such as scarring or pain, but these results have not been found in the studies to date.

Overall, the studies of sexual impact from the treatment for CIN and VIN have found that women do not return to their pretreatment sexual function. The studies are limited by the fact that, for the most part, they have not used validated sexual function questionnaires, they have had small sample sizes, and they have not assessed partner dynamics directly. In addition, only 1 study,[29] to our knowledge, was able to draw associations between the extent of treatment and the impact on sexual health, and no studies compared the impact of different treatment modalities for VIN or CIN on women's sexual health.

A recent study[35] has advanced the field by validating a new questionnaire to assess the burden of VIN in women by assessing symptoms, diagnosis, treatment and follow-up, including questions on sexual health; this will be a useful tool for use in future research.

We would advocate that future research address issues pertaining to the sexual health of women following treatment for CIN and VIN. These include assessing the impact of different treatment modalities on sexual function, assessing how treatment affects women in their willingness to initiate new sexual relationships, exploring issues of partner trust and dynamics as women undergo treatment, and looking at the impact of guilt and changes in body image on a woman's sexual health.

These knowledge gaps could be studied using a modified version of the questionnaire validated by Lockhart et al,[35] which has already been shown to have good reliability and validity among women with VIN, as one component of in-depth interviews with women who have undergone treatment for CIN or VIN. In addition, it will be important for future research to elicit patient ideas regarding how to mitigate the effects of treatment. The findings from such a qualitative study could then be applied to a multisite prospective study of interventions to decrease the sexual impact of treatment.

We believe that better understanding of the impact of CIN and VIN treatment will allow the development of a patient-centered approach to the optimization of management for these conditions.

Clinicians should continue to educate their patients about the link between HPV and CIN/VIN, the risk of progression to cancer, and the need for treatment for HGCIN and HGVIN. Despite the limited amount of information about the sexual effects of treatment for HPV-related precancerous lesions, it may be prudent for clinicians to counsel their patients about the possibility of sexual side effects of these treatments. Clinicians should also take into consideration the effects of scarring and disruption of genital anatomy when planning treatment of precancerous lesions.

In conclusion, based on the limited literature currently available, treatment for cervical and vulvar dysplasia appears to have a negative impact on sexual health. More research is needed for providers to be better equipped to counsel patients about the outcomes and risks of different treatment modalities. In addition, better understanding of the effects of treatment on sexual health will help to generate ideas for interventions to mitigate these effects. ■

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