



Full length article

Do different treatment strategies influence women's level of psychosexual distress? Observational cohort study of women with premalignant HPV-associated genital lesions



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ABSTRACT

Objective: To examine the impact of different treatment strategies - surgical treatment or watchful waiting- on sexual activity, psychosocial distress, and fear of progression in women with Human Papillomavirus (HPV)-associated premalignant genital lesions.

Study design: Observational cohort study of women diagnosed with HPV-associated premalignant lesions of the cervix, vagina or vulva. Patients were stratified into two groups depending on the severity of their premalignancy: surgical treatment or watchful waiting. Validated patient administered questionnaires, i.e. Fear of Progression questionnaire (FoP-Q), Cervical Dysplasia Distress Questionnaire (CDDQ), and Sexual Activity Questionnaire (SAQ) were completed after clinical evaluation (baseline), at 6- and 12-months follow-ups.

Results: 209 women treated with surgery (N = 125) were compared with women who were monitored in regular intervals (N=82). During an observational period of 12 months there were no significant differences in fear of progression, psychosocial distress, and sexual activity ($p > 0.05$). The level of concerns and anxiety about the future, and fear of progression were present, mostly at baseline. While there was a small increase of tension from visit to visit in both groups, patients generally were able to cope with their clinical situation quite well.

Conclusions: Fear of progression, psychosocial distress and sexual activity in women with precancerous HPV- associated premalignant genital lesions seem to be independent from type of treatment. Both treatment strategies may be applied without major psychological sequelae, as long as adequate information is provided.

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Introduction

Persistent genital Human Papilloma Virus (HPV)-infection may last for several years and have a considerable psychological impact [1–6]. Cervical cancer screening programs have paid little considerations to psychosocial factors [7–9] although adverse psychological reactions are common in women diagnosed with precancerous gynecological lesions. Previous research has focused on screening programs and the psychological impact of an abnormal smear or HPV-diagnosis. HPV testing itself may cause concerns, especially in younger women, in women with a higher risk of cervical cancer and in those who are reporting that they did not understand the meaning of test results [2–4]. A positive HPV

diagnosis seems to trigger several negative feelings and reduce sexual desire [5,10]. Being diagnosed with an abnormal smear may have a negative impact on mental health for up to three months follow-up [11,12].

However, psychological issues in women diagnosed with dysplasia after a positive screening result have not been sufficiently considered in the scientific literature. We conducted an observational study of 209 women diagnosed with HPV-related premalignant lesions of the cervix, vagina or vulva. Psychosexual distress and fear of progression were found to be common at the time of diagnosis [13,14]. In the present prospective one-year follow-up study we examined how different management strategies influence women's anxiety and sexuality over time. We hypothesized that the period of watchful waiting between the diagnosis and confirmation of regression or need for treatment may be associated with increased psychosocial distress.

The aim of this study was to compare psychosocial distress, fear of progression and sexual activity in women diagnosed with

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precancerous gynecological lesions depending on the type of treatment, i.e. surgical treatment versus watchful waiting.

Materials and methods

This is an observational cohort study of women diagnosed with premalignant HPV-associated lesions of the cervix, vagina or vulva. Women were recruited from a university-based colposcopy clinic after referral for evaluation for suspect precancerous genital lesions. After initial clinical evaluation, including cytology, HPV testing and colposcopy guided biopsy, further clinical management was discussed with the patient. According to the Austrian colposcopic guidelines [15], women with histologically confirmed high grade-lesions (Cervical Intraepithelial Neoplasia (CIN) 2/3) of the cervix, vagina or vulva were offered surgical treatment, i.e. excision/conisation or laser vaporation. In women with a low risk profile (younger age, short duration of HPV infection and, histological intermediate risk, i.e. CIN2) conservative management, i.e. watchful waiting, was discussed and decided according to patient's preference. In patients with histological confirmed low-grade lesions (CIN1, Vaginal Intraepithelial Neoplasia (VAIN) 1 or Vulvar Intraepithelial Neoplasia (VIN) 1) or inconclusive test results conservative management with regular control visits was recommended. Test results and decisions on further management were explained to all study participants.

At baseline participants were asked to complete the following validated questionnaires: the Fear of Progression Questionnaire (FoP-Q), the Sexual Activity Questionnaire (SAQ) and Cervical Dysplasia Distress Questionnaire (CDDQ). For the 6- and 12-months follow-up assessments, the same questionnaires were mailed to the participants including a prepaid return envelope. To improve the response rate they received a reminder letter a few weeks later.

The SAQ measures the impact of treatment on sexual functioning and is structured in three sections: The first section assesses whether women are sexually active (3 items); the second section explores reasons for sexual inactivity. The third section on sexual functioning is intended for sexual active women only, and includes 10 questions concerning pleasure (6 items), discomfort (2 items), habit and tiredness [16]. Higher SAQ scores indicate higher levels of pleasure and frequency, and lower levels of discomfort. The FoP-Q assesses patient's fears regarding disease progression (43 items) and includes 4 subscales: affective reactions, anxiety triggers and expression of anxiety, partner or family related

concerns, work-related worries and loss of autonomy, and a total coping score. Higher scores indicate higher levels of anxiety and better coping [17]. The CDDQ was used to assess women's perception of diagnostic procedures with 17 items and three subscales: 'tension and discomfort', 'embarrassment' during a gynaecological examination, and concerns of 'sexual and reproductive consequences' [18]. Higher scores indicate higher psychosocial distress. Scores were calculated according to the questionnaire manuals. In addition, two open ended questions were used to assess women's source of information regarding their illness and their satisfaction with the level of information received. A detailed description of qualitative data was published elsewhere [13].

Statistical analysis

The intention-to-treat analysis was limited to patients who completed all three questionnaires and when no changes in their primary type of treatment were made.

Demographic and clinical data were analyzed using descriptive statistics. Means and standard deviations were used to describe quantitative characteristics. Chi2-tests were used for baseline analysis between groups; ANOVA tests for differences between patient groups over time. A non-parametric test was used (Mann Whitney U-Test) for not normally distributed with unequal variances. A p-value of ≤ 0.05 was regarded statistically significant. For statistical analysis the SPSS 24 (IBM-SPSS Statistics for Windows 24. Armonk, NY) was used.

Results

Two-hundred and nine patients consented to participate and filled in the questionnaires at baseline; 167 completed the 6-months follow-up, and 92 the 12-months follow up. Twenty-one patients (10%), were excluded due to change in treatment modality (i.e. from conservative to surgical treatment), resulting in 92 women (48 with primary surgical treatment and 44 with conservative watch and wait management) (see Fig. 1). Mean age was 38 years (SD ± 14 years), 93% were Caucasians and 74% had completed secondary or tertiary level of education. The majority of women (79%) were living in a partnership, 48% had at least one child and 56% had a desire for further children. No statistically significant differences in sociodemographic data were found between the two groups ($p < 0.05$). Women were diagnosed with

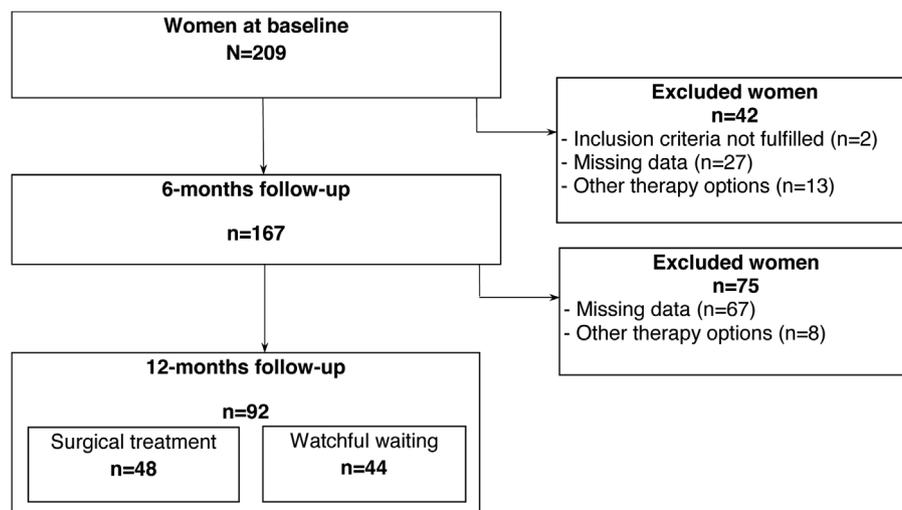


Fig. 1. Flow chart for patient selection and data analysis.

Table 1
Demographic and clinical characteristics by study treatment group.

		Surgery group N = 48	Watchful waiting group N = 44
Age		39 (± 14)	37 (± 14)
Nationality	Austria	45 (52%)	41 (48%)
	Other	3 (3%)	3 (3%)
Living situation	Alone	9 (60%)	6 (40%)
	With partner/family	30 (52%)	28 (48%)
	With partner/family without joining household together	8 (53%)	7 (47%)
	Other	1 (25%)	3 (75%)
Education level	Compulsory school	17 (35%)	7 (16%)
	Secondary 2nd stage	12 (25%)	12 (27%)
	High-school	10 (21%)	18 (41%)
Employment	Higher (university)	9 (19%)	7 (16%)
	yes	34 (48%)	37 (52%)
Children	no	14 (67%)	7 (33%)
	yes	27 (56%)	21 (44%)
Desire for child	no	21 (48%)	23 (52%)
	yes	14 (39%)	22 (61%)
Current diagnosis	no	30 (58%)	22 (42%)
	Cervix	31 (65%)	42 (95%)
	CIN1/ abnormal PAP smears	2	35
	CIN2	4	6
	CIN3/ AIS	25	1
	Vagina	6 (13%)	2 (5%)
	VAIN1	0	2
	VAIN2	0	0
	VAIN3	6	0
	Vulva	11 (23%)	0
Pre-treatment	VIN2	2	0
	VIN3	9	0
	yes	11 (48%)	12 (52%)
no	37 (54%)	32 (46%)	

Data are number (percent) or mean (\pm SD).

precancerous lesions of the cervix (79%), the vagina (9%) and the vulva (12%). The detailed clinical diagnoses per treatment group are shown in Table 1. All women with high-grade lesions grade 3, i.e. CIN3, VAIN3 and VIN3 received surgical treatment, except one woman who refused primary surgery. Women with low-grade lesions were usually managed conservatively, except in cases with additional risk factors.

Fear of progression

Fear of progression was not statistically significant different between the surgical treatment group and the watchful waiting

Table 2
Fear of progression questionnaire (FoP-Q).

FoP subscales	Affective reactions*	Partnership/family*	Work	Loss of autonomy	Total score
Baseline	1.4 \pm 0.7 (92)	1.3 \pm 0.8 (92)	0.8 \pm 0.8 (92)	0.6 \pm 0.7 (92)	1.0 \pm 0.6 (92)
6 months Follow-up	1.3 \pm 0.6 (90)	1.2 \pm 0.9 (90)	0.7 \pm 0.7 (89)	0.6 \pm 0.6 (90)	0.9 \pm 0.6 (90)
12 months Follow-up	1.2 \pm 0.6 (86)	1.1 \pm 0.8 (86)	0.6 \pm 0.6 (85)	0.5 \pm 0.6 (87)	0.8 \pm 0.6 (87)
Difference between study groups**	Z = -0.927 p = 0.35	Z = -1.376 p = 0.17	Z = -0.91 p = 0.93	Z = -0.568 p = 0.57	Z = -1.232 p = 0.22

Data are mean \pm standard deviation (numbers).

* Higher scores indicate higher level of fear. Scores range from 1 to 5, except the total score (5 to 20).

** Mann-Whitney U-Test.

group ($p > 0.05$). The FoP-Q mean scores were low in both groups, indicating a low level of fear. The mean scores slightly decreased from baseline to 12-months follow-up in all subscales (affective reactions, partnership/family, work, loss of autonomy). The total coping scores were 2.7 (± 0.7) at baseline and 2.6 (± 0.6) at 6- and 12-months follow-up ($p = 0.89$) (see Table 2). This means that women in both groups coped moderately well with their situation. The coping scores were 2.7 (± 0.7) at baseline and 2.6 (± 0.6) at 6- and 12-months follow-up ($p = 0.89$).

Sexual activity

In the surgical treatment group 86% and in the watchful waiting group 74% of the participants were sexually active. The subscale scores of the SAQ were not statistically significant different between the surgical treatment group and the watchful waiting group ($p > 0.05$). Patients in both groups experienced low sexual discomfort during intercourse. Mean scores of the single item on tiredness were low, between 0.6 (± 0.7) and 0.9 (± 1.0) and were not significantly different between patient groups ($p = 0.35$). The scores remained stable during the 6- and 12-months follow-up visits (see Table 3).

Psychosocial distress

Psychosocial distress measured by the CDDQ did not statistically significant differ between the surgical treatment group and the watchful waiting group ($p > 0.05$) (see Table 4). Concerns about sexual and reproductive consequences were consistently low from baseline to 6- and 12-months follow-up visits. Tension and discomfort and embarrassment during a gynecologic examination increased slightly over time.

Information

About 80% of women reported having been informed about their disease by their treating physicians and more than half retrieved information from the internet, with most women accessing more than one source of information. The information sources did not statistically significant differ between the surgical treatment group and the watchful waiting group ($p > 0.05$). The majority of patients in both groups were satisfied (48%) or very satisfied (18%) with the level of the information received.

Comment

In this prospective study we assessed fear of progression, psychosocial distress and sexual activity in women with HPV-associated premalignant genital lesions over a period of 12 months. In our study population these variables remained stable over time and did not significantly differ between patients with primary surgical treatment and patients with conservative treatment who were monitored in regular intervals. These results indicate that the objective severity of disease (i.e. high-grade versus low-grade precancerous lesions) does not influence the degree of patients' distress. The findings also contradict the hypothesis that the period of watchful waiting between initial diagnosis and confirmation of regression may be associated with increased distress.

According to current European and American guidelines [15,19] two different management strategies (i.e. immediate surgical treatment or watchful waiting), may be applied to women with HPV-associated high grade-genital lesions. Especially in younger women with intermediate histological risk (CIN2) conservative management with watchful waiting up to 24 months seems to be a safe option [20–22]. In a retrospective chart review of 154 women younger than 24 years, regression rates of 75% for CIN2 and of 22%

Table 3
Sexual activity questionnaire (SAQ).

	Sexual pleasure [*]	Sexual discomfort [*]	Sexual habit [*]
Baseline	12.5 ± 4.8 (69)	4.9 ± 1.3 (69)	0.9 ± 0.6 (69)
6 months Follow-up	12.0 ± 4.4 (73)	4.9 ± 1.4 (73)	0.9 ± 0.7 (72)
12 months Follow-up	12.3 ± 3.8 (72)	5.0 ± 0.6 (72)	0.9 ± 0.6 (71)
Difference between study groups ^{**}	Z = -0.531, p = 0.60	Z = -0.988, p = 0.32	Z = -0.168, p = 0.89

Data are mean ± standard deviation, numbers.

^{*} Pleasure score ranges from 0 to 18, with low scores representing low pleasure. Discomfort score ranges from 0 to 6, with low scores representing great discomfort. Habit scores ranges 0–3, with low scores representing low frequency.

^{**} Mann-Whitney U-Test.

Table 4
Cervical Dysplasia Distress Questionnaire (CDDQ).

CDDQ subscales	Tension and discomfort [*]	Embarrassment [*]	Sexual and reproductive consequences [*]
Baseline	1.1 ± 0.7 (91)	0.5 ± 0.6 (91)	0.8 ± 0.6 (91)
6-months Follow-up	1.2 ± 0.7 (91)	0.6 ± 0.7 (91)	0.7 ± 0.6 (86)
12-months Follow-up	1.3 ± 0.7 (88)	0.6 ± 0.7 (88)	0.7 ± 0.6 (86)
Difference between study groups ^{**}	Z = -1.67, p = 0.87	Z = -0.866, p = 0.39	Z = -1.023, p = 0.31

Data are mean ± standard deviation, numbers.

^{*} Higher scores indicate higher levels of distress. Scores range from 0 to 3.

^{**} Mann-Whitney U-Test.

for CIN3 lesions were found. Median time to regression was 10.8 months which warrants watchful waiting for up to 24 months after diagnosis. During this time period HPV infection and associated genital lesion may regress, persist or progress [20]. In women with persistent or progressing lesion a change to surgical treatment was recommended in our study.

In a recent case-control study, women with cervical dysplasia were found to have reduced sexual function, body image and quality of life. However, similar to our results, further management, i.e. conization or observation, did little influence psychosexual impairment [23]. Our finding, that anxiety is a common initial response after diagnosis, is in accordance with previous studies. In a Chinese cohort of women, state of anxiety, cervical cancer worry, and psychosocial burden were high after notification of a high-risk HPV test result but decreased over time [24]. In the prospective TOMBOLA study women with low-grade cytologic abnormalities were likely to experience psychosocial distress after colposcopy and related procedures, even when the colposcopy was found to be normal [25]. However, anxiety, depression and other long-term psychosocial sequelae seem to be independent from applied management strategy, i.e. cytological surveillance versus immediate referral for colposcopy [26,27].

The present study provides new and valuable information about psychological issues in women with cervical dysplasia. While most recent studies have investigated the psychological impact of screening tests [5,10–12,14,28] or further cytologic or colposcopic surveillance [24–27,29], the impact of different management strategies in women with diagnosed genital dysplasia has received little attention.

A considerable strength of our study is the prospective assessment of three psychological dimensions by validated questionnaires: fear of progression, psychosocial distress, and sexual activity. Our data refers to women who were treated as intended at baseline and who completed questionnaires at all three time points.

For the interpretation of our results it needs to be considered that patients were excluded from the analysis when their treatment modality was changed. In women with persistent or progressing lesion a change from conservative to surgical treatment was recommended. The study findings are limited by the rather low response rate of 44%. The drop-out analysis showed that non-responders were significantly younger than patients who completed all questionnaires. However, no differences in questionnaire data were found between these groups. The generalizability of the results may be limited by the fact that study participants were mostly Caucasian, and well-educated.

Most patients in this study felt well-informed about their condition and treatment options. It is known, that good knowledge of HPV correlates with less anxiety, concern and perceived risk of developing cancer [30]. Clinicians play an important role in providing information, but also in moderating the effects of an abnormal test result through the manner and mode in which the information is delivered [31]. Acknowledgment of patients' disease-associated concerns and treatment expectations is essential for a stable physician–patient relationship, women's psychological wellbeing and patient compliance [5,32,33].

In women with HPV-related premalignant cervical lesions both management strategies, i.e. immediate treatment or watchful waiting, may be applied without major psychological sequelae as long adequate information is provided. In most cases decision about treatment modality is determined by clinical diagnosis, i.e. high- or low-grade lesion. In some cases, choice of treatment may depend on patients' personal circumstances, preference and additional risk factors. When discussing potential treatment options with the patient, doctors should not only consider medical factors, but also individual concerns and potential psychological burdens.

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