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Full length article

Should men whose female partners have cervical high grade intraepithelial lesion (HSIL) be screened?

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ABSTRACT

Objective: The subject of screening for genital HPV lesions in the male partner of women with cervical high-grade squamous intraepithelial lesions (HSIL) remains a topic of discussion. The present study evaluated the prevalence of penile high-grade squamous intraepithelial lesion (HSIL) clinical lesions in 196 men whose female partners had been diagnosed with cervical low-grade and high-grade intraepithelial lesions (LSIL, HSIL) in Ile-de-France.
Methods: In cases involving couples where the female partner had been diagnosed with a cervical LSIL or HSIL lesion, the male partner underwent examination using the peniscopy method. The presence of clinical identified HPV lesions was confirmed by biopsy proven histological analysis.
Results: The mean age of the 196 couples was 33.4 years for women and 35.6 years for men. Among the 196 women, 125 (64 %) had cervical LSIL and 71 (36 %) had cervical HSIL detected by colposcopy and confirmed by histology. Among 196 men, 65 (33 %) HPV lesions were identified and confirmed by histology. Of these, 44/196 (22 %) were penile LSIL and 21/196 (11 %) were penile HSIL. The risk of penile HSIL increased twofold (Fisher test 1.9) if the female partner had cervical HSIL (11/71, 15.5 %) versus cervical LSIL (10/125, 8 %).
Conclusion: A man with a partner who has cervical HSIL is twice as likely to have penile HSIL than if his partner has LSIL cervical. This suggests that peniscopy should be offered to this population. It could avoid the persistence or recurrence of cervical HSIL of their partner.

Introduction

Anogenital human papillomavirus (HPV) infection is currently the most common sexually transmitted infection. It is estimated that there is 85 % of women and 90 % of men getting HPVs by age 45 [1].

Although women bear a disproportionate burden of HPV infection, men are also affected by the virus. A study in 2022 identified 657,317 HPV-related cancer cases, of which 264,019 (40.2 %) were in men [2]. While awaiting efficient male vaccination, men whose female partner has a cervical lesion should be screened clinically or virologically to reduce the risk of recurrence/persistence of the cervical lesion and the development of a high-grade lesion in men. The incidence of penile intraepithelial lesion has doubled over the past 20 years, and an incidence rate in 2019 that is 2.37 times higher than in 2000 [3].

In couples where the woman has cervical HPV infection, the prevalence of HPV infection in the man depends on whether the screening is clinical or virological. Peniscopy detects clinical HPV lesions in 20–60 % of cases and genital smears with HPV genotyping in 2–80 % of cases [4–7]. However, the presence of biopsy-proven HPV lesions in men and HPV genotyping in men are two different approaches to prevention.

We know that HPV infection can resolve spontaneously without intervention, and positive genotyping does not indicate the need for immediate treatment of the patient or his sexual partners. However, asymptomatic HPV lesions in men are thought to be an important source of ongoing transmission to female partners, and HPV lesions in men could increase the risk of cervical cancer [8].

Currently, HPV screening of male partners whose female partners have HSIL is not a core component of prevention protocols. However, cross-infection between couples is more likely than in other situations to lead to persistent HPV infection, increasing the risk of developing cervical HSIL [9]. The aim of this prospective study is to investigate the concordance between histological HPV lesions in men and cervical LSIL or HSIL in their female partners. It will provide an overview of the current situation to propose HPV screening and prevention in men and new ideas for the joint health of heterosexual couples.

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Patients and methods

Between February 2022 and December 2023, 196 women were diagnosed with 125 histologically confirmed cervical LSIL and 71 HSIL in the Operative Colposcopy Center. All male partners of the 196 female partners underwent peniscopy using a colposcope (Zeiss 150 FC) with a 5 % acetic acid test combined with meatoscopy to look for lesions of the urethral meatus. HPV-induced lesions can be diagnosed by the clinical criteria of maculopapular acetowhite, pigmented, leukoplastic or even erythroplastic and verrucous lesions.[10] All HPV lesions suspected by peniscopy were biopsied and embedded in 10 % buffered formalin. Histology was performed by the same pathologist at the CerbaPath laboratory (CB). Histological diagnoses were defined as low-grade squamous intraepithelial lesions (LSIL), or high-grade squamous intraepithelial lesions (HSIL), according to the Lower Anogenital Squamous Terminology (LAST).[11] Fisher test was used for data analysis.

Results

The mean age of the women was 33.4 years [24–61 years] and that of the men 35.6 years [28–63 years]. In our male population, HPV identified lesions by peniscopy were histologically proven in 65/196 (33 %) of the cases. These lesions were completely asymptomatic, single or not very extensive, acid-white, pigmented or weakly erythroplastic (Figs. 1, 2, 3). In 8/131 (6 %) men without HPV identified lesions, genital dermatosis (lichen sclerosus, psoriasiform or lichenoid lesions, aspecific balanitis) was diagnosed clinically without biopsy. Male HPV lesions were located in the balanopreputial region in 56/65 (86 %), the foreskin in 4/65 (6 %) and the urethra in 5/65 (8 %). Among the HPV 65 biopsy proven penile lesions 38/125 (30 %) were diagnosed in men of which the female partner has LSIL and 27/71 (38 %) were diagnosed in men of which the female partner has HSIL. Histological analysis showed penile LSIL in 44/65 (68 %) of cases and penile HSIL in 21/65 (32 %). Peniscopy detected penile LSIL in 28 (22 %) and HSIL in 10 (8 %) of 125 women with cervical LSIL. Peniscopy detected penile LSIL in 16 (22.5 %) and HSIL in 11 (15.5 %) of the 71 women with cervical HSIL (Table 1).

Discussion

Genital HPV infection is a common sexually transmitted infection, and its prevalence in genital specimens is estimated to be 35 % in the general population.[12] In addition, several studies have shown HPV transmission rates of 5–100 % per sexual act, with a median of 40 %, and Grabowski's series described a 2-year incidence of 10 % in couples for 37 different genotypes [13,14]. Also, the likelihood of infecting a negative partner was greater if the partner was persistently infected at 6 months [15].

Fig. 1.

Fig. 2.

The series by Wissing et al showed a prevalence of HPV infection between 53 % and 81 % in men whose partner was infected with genotypes 6, 11, 16, 18, 31, 42 and 51, but did not specify the presence or absence of clinical lesions [16]. Similarly, Skoulalkis et al described a prevalence of at least one HPV genotype in 49 % of asymptomatic men whose partner had cervical lesions of any grade [17]. Reiter's *meta*-analysis found concordance for different HPV genotypes in 25 % of couples [18]. Similarly, Martin-Ezquerra et al and Lopez-Diez et al described concordant HPV-induced lesions in 10 % of men whose partner had CIN [19,20]. Other studies of genital HPV genotyping have found concordance between 16 % and 25 % of couples [21,22].

In our series, 33 % of men whose partners had cervical intraepithelial lesion had clinical HPV lesions. This suggests an association between the presence of cervical intraepithelial lesion and clinical HPV lesions in their male partners. Our clinical results are similar to other studies that have looked at HPV. The overall prevalence of genital HPV infection was 31 % in a *meta*-analysis by L. Bruni [23]. This study provides a general estimate of the prevalence of HPV in men, regardless of the status of their partners. In addition, the prevalence of penile intraepithelial lesion increases by 8 % if the partner has cervical HSIL. This also suggests that the presence of HSIL in women increases the risk of HPV lesions in their partners.

This study found that male partners of women with cervical HSIL were twice as likely to have a penile HPV lesion than male partners of women with cervical LSIL. The association of high-grade lesions is evident in both men and women, particularly in the case of women, as the incidence of penile intraepithelial lesion has doubled over a 20-year period [3]. This cross-infection between partners often leads to persistent HPV infection and increases the likelihood of developing high-grade cervical and penile lesions [24].

Furthermore, our study showed that men were twice as likely to have

Fig. 3.

Table 1
HVP lesion histology among couples.

Female Histological Cervical Lesions		Males Histological Biopsy Lesions		Males Normal
		Penile LSIL	Penile HSIL	No Biopsy
Cervical LSIL	125	28 (22.4 %)	10 (8 %)	87 (69.6 %)
Cervical HSIL	71	16 (22.5 %)	11 (15.5 %)	44 (62 %)
Total patients	196	44	21	131

Fisher's Exact Test p-value: 0.2845 OR: 1.9051 to 95% [0.5888; 6.2921].

or develop HSIL in the penis when their partner had HSIL in the cervix. This cross-infection between partners often leads to persistent HPV infection and increases the likelihood of developing high-grade cervical and penile lesions [25]. Clinical screening for HPV lesions in the male partner is important in the context of preventing the risk of recurrence of cervical HPV lesions [26]. Especially since the positive predictive values of peniscopy and histopathology are between 83 % and 92 % in men whose female partner has a cervical HPV lesion [27].

These men are significantly affected by HPV infection, as evidenced by the development of high-grade lesions. The present study argues for extending HPV screening and treatment efforts for men.

However, a bias that needs to be considered is the fact that this study was performed in a single institution (CCO). Multi-centric studies with a larger number of cases should be performed to confirm this correlation between penile HSIL and cervical HSIL. To determine whether including men in screening improves protection for women and reduces the risk of associated cancers, scientific research into modelling and implementation is required.

Nevertheless, couples should be offered clinical penile screening for HSIL, as HPV transmission is a common problem until male vaccination coverage is effective (26 % of boys and 55 % of girls are vaccinated in France) [28].

In a couple, a man whose female partner has cervical HSIL is twice as likely to have penile HSIL as if his partner had cervical LSIL. These results highlight the importance of screening for HPV lesions in men as well as women to reduce the transmission and complications associated with this viral infection. Vaccination remains the most effective preventive measure against HPV infection and associated health problems in men.

CRediT authorship contribution statement

Olivier Aynaud: Writing – original draft, Methodology, Investigation, Conceptualization. **Bernard Huynh:** Validation, Resources. **Christine Bergeron:** Validation, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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