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The society for lower genital tract disorders since 1964

A correction was published in January 2017 for this title. Click here to view the correction.

COMMITTEE OPINION

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(Replaces Committee Opinion Number 509, November 2011)

Committee on Gynecologic Practice
American Society for Colposcopy and Cervical Pathology

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice and the American Society for Colposcopy and Cervical Pathology (ASCCP) in collaboration with committee member Oluwatosin Goje, MD, and ASCCP members and experts Jason Reutter, MD, Herschel Lawson, MD, and Colleen Stockdale, MD, MS.

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Management of Vulvar Intraepithelial Neoplasia

ABSTRACT: Vulvar intraepithelial neoplasia (VIN) is an increasingly common problem, particularly among women in their 40s. Although spontaneous regression has been reported, VIN should be considered a premalignant condition. Immunization with the quadrivalent or 9-valent human papillomavirus vaccine, which is effective against human papillomavirus genotypes 6, 11, 16, and 18, and 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively, has been shown to decrease the risk of vulvar high-grade squamous intraepithelial lesion (HSIL) (VIN usual type) and should be recommended for girls aged 11–12 years with catch-up through age 26 years if not vaccinated in the target age. There are no screening strategies for the prevention of vulvar cancer through early detection of vulvar HSIL (VIN usual type). Detection is limited to visual assessment with confirmation by histopathology when needed. Treatment is recommended for all women with vulvar HSIL (VIN usual type). Because of the potential for occult invasion, wide local excision should be performed if cancer is suspected, even if biopsies show vulvar HSIL. When occult invasion is not a concern, vulvar HSIL (VIN usual type) can be treated with excision, laser ablation, or topical imiquimod (off-label use). Given the relatively slow rate of progression, women with a complete response to therapy and no new lesions at follow-up visits scheduled 6 months and 12 months after initial treatment should be monitored by visual inspection of the vulva annually thereafter.

Recommendations and Conclusions

The American College of Obstetricians and Gynecologists (the College) and the American Society for Colposcopy and Cervical Pathology make the following recommendations and conclusions:

- Immunization with the quadrivalent or 9-valent human papillomavirus (HPV) vaccine, which is effective against HPV genotypes 6, 11, 16, and 18, and 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively, has been shown to decrease the risk of vulvar high-grade squamous intraepithelial lesions (HSIL) (also known as vulvar intraepithelial neoplasia [VIN usual type]) and should be recommended for girls aged 11–12 years with catch-up through age 26 years if not vaccinated in the target age.
- Cigarette smoking is strongly associated with vulvar HSIL (VIN usual type), and cessation should be encouraged.
- There are no screening strategies for the prevention of vulvar cancer through early detection of vulvar HSIL (VIN usual type).
- Detection is limited to visual assessment with confirmation by histopathology when needed.
- Biopsy is indicated for visible lesions for which definitive diagnosis cannot be made on clinical grounds, possible malignancy, visible lesions with presumed clinical diagnosis that is not responding to usual therapy, lesions with atypical vascular patterns, or stable lesions that rapidly change in color, border, or size.

- Biopsy should be performed in postmenopausal women with apparent genital warts and in women of all ages with suspected condyloma in whom topical therapies have failed.
- Treatment is recommended for all women with vulvar HSIL (VIN usual type). Because of the potential for occult invasion, wide local excision should be performed if cancer is suspected, even if biopsies show vulvar HSIL.
- When occult invasion is not a concern, vulvar HSIL (VIN usual type) can be treated with excision, laser ablation, or topical imiquimod (off-label use).
- Women with vulvar HSIL (VIN usual type) are at risk of recurrent disease and vulvar cancer throughout their lifetimes.
- Women with a complete response to therapy and no new lesions at follow-up visits scheduled 6 months and 12 months after initial treatment should be monitored by visual inspection of the vulva annually thereafter.

Scope of the Problem

Vulvar intraepithelial neoplasia (VIN) is an increasingly common problem, particularly among women in their 40s. Data from the U.S. Surveillance, Epidemiology, and End Results program demonstrate that VIN incidence increased more than fourfold between 1973 and 2000 (1). Although spontaneous regression has been reported, VIN should be considered a premalignant condition, as shown by a case series of 405 New Zealand women with VIN (2). Sixty-three (16%) women received no treatment, 10 of whom experienced progression to invasive cancer (2). Although cancer regression has been reported, especially among women in whom cancer was diagnosed during pregnancy (3), the risk of progression to cancer has been documented in treated and untreated patients, and prognostic factors are not sufficiently reliable to select women for treatment. Occult invasive cancer has been reported in 3% of women undergoing surgery for VIN, although two thirds of cases of invasive cancer in women receiving surgical treatment for VIN are superficial (3). The focus of this Committee Opinion is the management of usual type VIN, which was renamed in 2015 by the International Society for the Study of Vulvovaginal Disease (ISSVD) as high-grade squamous intraepithelial lesions of the vulva (vulvar HSIL) (4).

Classification

Traditionally, squamous VIN was classified into three grades, analogous to the three-grade cervical intraepithelial neoplasia classification. In 2004, ISSVD replaced the previous three-grade classification system with a single-grade system, in which only high-grade disease is classified as VIN (5). In that system, VIN is subdivided into usual type VIN (including warty, basaloid, and mixed VIN) and differentiated VIN. Usual type VIN commonly is associated with carcinogenic genotypes of HPV and other HPV persistence risk factors, such as cigarette smoking and immunocompromised status, whereas differentiated VIN usually is not associated with HPV and is more often associated with vulvar dermatologic conditions, such as lichen sclerosus. Differentiated VIN associated with lichen sclerosus is more likely to be associated with a squamous cell carcinoma of the vulva than usual type VIN. Furthermore, it has a higher recurrence rate (6) and decreased disease-specific survival from invasive squamous cell carcinoma (7).

The rationale for changing the terminology in 2015 was to unify the nomenclature of HPV-associated squamous lesions of the lower genital tract. The ISSVD recommends the terms low-grade squamous intraepithelial lesion of the vulva (vulvar LSIL) and high-grade squamous intraepithelial lesion of the vulva (vulvar HSIL) for histopathologic diagnoses of productive HPV infections, which includes external genital warts and precancer, respectively. The 2015 terminology is similar to the World Health Organization's classification and to the Lower Anogenital Tract Squamous Terminology (commonly known as the LAST Project) classification that is used by the American Society for Colposcopy and Cervical Pathology and has been adopted by the College (8). Based on the 2015 ISSVD terminology of vulvar squamous intraepithelial lesions (4), usual type VIN is now classified as vulvar HSIL, and differentiated VIN remains the same. Flat lesions associated with basal atypia and koilocytic changes (formerly termed VIN 1) are considered LSIL (condyloma or HPV effect) in the current 2015 ISSVD classification system (4). Other intraepithelial vulvar neoplasms, such as Paget disease and melanoma in situ, are rare (see Table 1).

Prevention

Immunization with the quadrivalent or 9-valent HPV vaccine, which is effective against HPV genotypes 6, 11, 16, and 18, and 6, 11, 16, 18, 31, 33, 45, 52, and 58, respectively, has been shown to decrease the risk of vulvar HSIL (VIN usual type) and should be recommended for girls aged 11–12 years with catch-up through age 26 years if not vaccinated in the target age (9, 10). The bivalent HPV vaccine (subtype 16, 18) has not been studied for vulvar HSIL (VIN usual type) prevention. Cigarette smoking is strongly associated with vulvar HSIL (VIN usual type), and cessation should be encouraged. Although cigarette smoking has been identified as a risk factor for vulvar HSIL (2), there was no reported association between vulvar HSIL and cigarette smoking in studies that specifically addressed recurrence with regard to smoking status (11–13). Differentiated VIN may be associated with vulvar dermatoses, and treatment of vulvar dermatologic disorders (especially of lichen sclerosus) reduces the risk of cancer (14).

Table 1. 2015 International Society for the Study of Vulvovaginal Disease Terminology of Vulvar Squamous Intraepithelial Lesions and 2004 Terminology ⇦

2015 Terminology	2004 Terminology
Low-grade squamous intraepithelial lesion of the vulva (vulvar LSIL, flat condyloma, or HPV effect)	Condyloma, HPV effect*
High-grade squamous intraepithelial lesion of the vulvar (vulvar HSIL, VIN usual type)	Usual-type VIN (subdivided): a. VIN, warty type b. VIN, basaloid type c. VIN, mixed (warty or basaloid) type
Differentiated type VIN	Differentiated type VIN

Abbreviations: HPV, human papillomavirus; VIN, vulvar intraepithelial neoplasia.

*Sideri M, Jones RW, Wilkinson EJ, Preti M, Heller DS, Scurry J, et al. Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD Vulvar Oncology Subcommittee. J Reprod Med 2005;50:807–10.

Data from Bornstein J, Bogliatto F, Haefner HK, et al. The 2015 International Society for the Study of Vulvovaginal Disease (ISSVD) Terminology of Vulvar Squamous Intraepithelial Lesions. Obstet Gynecol 2016;127(2):264–8.

Diagnosis

There are no screening strategies for the prevention of vulvar cancer through early detection of vulvar HSIL (VIN usual type). Detection is limited to visual assessment with confirmation by histopathology when needed. The appearance of vulvar HSIL (VIN usual type) can vary. Most women have visible lesions that are elevated, but flat lesions occur. Color can vary from white to gray or from red to brown to black. Biopsy is indicated for visible lesions for which definitive diagnosis cannot be made on clinical grounds, possible malignancy, visible lesions with presumed clinical diagnosis that is not responding to usual therapy, lesions with atypical vascular patterns, or stable lesions that rapidly change in color, border, or size. Expert opinion is divided regarding the need for biopsy of all warty lesions, but biopsy should be performed in postmenopausal women with apparent genital warts and in women of all ages with suspected condyloma in whom topical therapies have failed. Although information regarding the evaluation of women with immunocompromised conditions and HPV-related disease is limited, human immunodeficiency virus (HIV)-seropositive patients and patients on immunosuppression after organ transplant may need biopsy of lesions when the level of suspicion is lower. Colposcopy, or other forms of magnification of the vulva, can be useful in determining the extent of disease if lesions are not visible or not clearly demarcated in women with persistent focal vulvar pruritus and pain with no gross lesions, and women who remain symptomatic despite appropriate treatment for presumed vulvo-vaginitis. It should be performed after applying 3–5% acetic acid to the vulva for several minutes using soaked gauze pads. Keratinization requires longer acetic acid application for effect and often renders typical colposcopic grading criteria useless. Although toluidine blue testing often is cited for use in the assessment of vulvar HSIL (VIN usual type), this method is used infrequently and rarely beneficial in the diagnosis of vulvar HSIL (VIN usual type).

Treatment

Treatment is recommended for all women with vulvar HSIL (VIN usual type). Because of the potential for occult invasion, wide local excision should be performed if cancer is suspected, even if biopsies show vulvar HSIL. When occult invasion is not a concern, vulvar HSIL (VIN usual type) can be treated with excision, laser ablation, or topical imiquimod (off-label use).

Surgical Therapy

Wide local excision is the preferred initial intervention to obtain a specimen for pathologic analysis for women in whom invasive cancer cannot be adequately ruled out from their clinical or pathologic findings, despite a biopsy diagnosis of only vulvar HSIL (VIN usual type). The excision should include gross margins of 0.5–1 cm around tissue with visible disease, but may be altered to avoid injury to the clitoris, urethra, anus, or other critical structures. Women with lesions in critical areas should be referred to a specialist to avoid impaired psycho–sexual function. Women with clear margins in the excised tissue specimens have a lower, although still significant, risk of recurrence compared with women with involved margins (12). Wide local excision is also acceptable for women in whom cancer is not suspected. Skinning vulvectomy, which removes all vulvar skin, is rarely needed, although it may be useful for cases of confluent multifocal lesions, which can occur in women who are immunocompromised.

Laser Ablation

Laser ablation is acceptable for the treatment of vulvar HSIL (VIN usual type) when cancer is not suspected. It

can be used for single, multifocal, or confluent lesions, although the risk of recurrence may be higher than with excision (15, 16). Appropriate power density (750–1,250 W/cm^2) is critical to avoid deep coagulation injury. Colposcopy facilitates delineation of lesion margins, and use of a micromanipulator or a hand piece with a depth gauge allows application of high-power density without inadvertent defocusing. As with excision, a 0.5–1 cm margin of normal-appearing skin should be treated. In contrast to its application to genital warts, when superficial ablation is acceptable, laser treatment of vulvar HSIL (VIN usual type) requires destruction of cells through the entire thickness of the epithelium. In hair-bearing areas, laser procedures must ablate hair follicles, which can contain vulvar HSIL (VIN usual type) and extend into the subcutaneous fat for 3 mm or more. Consequently, large vulvar HSIL (VIN usual type) lesions over hair-bearing areas may be preferentially treated with surgical excision. Ablation over skin that does not bear hair should extend through the dermis (up to 2 mm).

Medical Therapy

Randomized controlled trials have shown that the application of topical imiquimod 5% is effective for the treatment of vulvar HSIL (VIN usual type) (17, 18), although it is not approved by the U.S. Food and Drug Administration for this purpose. Published regimens include three times weekly application to affected areas for 12–20 weeks, with colposcopic assessment at 4–6-week intervals during treatment. Residual lesions require surgical treatment. Erythema and vulvar pain may limit use. Experience with imiquimod in immunosuppressed patients is limited. Because it is believed to act through local immunomodulators, it may have decreased effectiveness in women who are immunocompromised. Photodynamic therapy has been effective in some trials, but requires specialized equipment and training (19). Topical cidofovir cream and 5-fluorouracil creams have been tested in clinical trials with varying degrees of efficacy (20–22).

Surveillance

Recurrence rates after treatment range from 9% to 50% with all treatment regimens and are higher with positive excision margins (2, 3, 12, 19), and lower in surgically treated patients (23). Higher recurrence rates also are seen with multiple lesions (24). Follow up has been limited in most studies, and women with vulvar HSIL (VIN usual type) are at risk of recurrent disease and vulvar cancer throughout their lifetimes. The value of vulvar self-examination and serial office visits in the detection of recurrence has not been proved, but both appear prudent. Given the relatively slow rate of progression, women with a complete response to therapy and no new lesions at follow-up visits scheduled 6 months and 12 months after initial treatment should be monitored by visual inspection of the vulva annually thereafter.

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CORRECTION

In "Committee Opinion No. 675: Management of Vulvar Intraepithelial Neoplasia" from the American College of Obstetricians and Gynecologists and the American Society for Colposcopy and Cervical Pathology, there is an error on page 2 in the first full paragraph, under "Scope of the Problem." In the fifth sentence, the phrase reading "Although cancer regression has been reported, especially among women in whom cancer was diagnosed during pregnancy (3)..." is incorrect and should read "Although VIN regression has been reported, especially among women in whom VIN was diagnosed during pregnancy (3)..." The full, corrected sentence is as follows: "Although VIN regression has been reported, especially among women in whom VIN was diagnosed during pregnancy (3), the risk of progression to cancer has been documented in treated and untreated patients, and prognostic factors are not sufficiently reliable to select women for treatment."

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