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CAP/ASCCP Lower Anogenital Squamous Terminology for HPV-Associated Lesions

Summary of Consensus Recommendations

Squamous Intraepithelial Lesions

Recommendation:

1. A unified histopathological nomenclature with a single set of diagnostic terms is recommended for all HPV-associated preinvasive squamous lesions of the lower anogenital tract (LAT).
2. A 2-tiered nomenclature is recommended for noninvasive HPV-associated squamous proliferations of the LAT, which may be further qualified with the appropriate –IN terminology.
–IN refers to the generic intraepithelial neoplasia terminology, without specifying the location. For a specific location, the appropriate complete term should be used. Thus for an –IN 3 lesion: cervix = CIN 3, vagina = VaIN 3, vulva = VIN 3, anus = AIN 3, perianus = PAIN 3, and penis = PeIN 3
3. The recommended terminology for HPV-associated squamous lesions of the LAT is *low-grade squamous intraepithelial lesion (LSIL)* and *high-grade squamous intraepithelial lesion (HSIL)*, which may be further classified by the applicable –IN subcategorization.

Biomarkers in HPV-Associated Lower Anogenital Squamous Lesions

Recommendation:

1. p16 IHC *is recommended* when the H&E morphologic differential diagnosis is between precancer (–IN 2 or –IN 3) and a mimic of precancer (e.g., processes known to be not related to neoplastic risk such as immature squamous metaplasia, atrophy, reparative epithelial changes, tangential cutting).
Strong and diffuse block positive p16 results support a categorization of precancerous disease.
2. If the pathologist is entertaining an H&E morphologic interpretation of –IN 2 (under the old terminology, which is a biologically equivocal lesion falling between the morphologic changes of HPV infection [low-grade lesion] and precancer), p16 IHC *is recommended* to help clarify the situation. Strong and diffuse block positive p16 results support a categorization of precancer. Negative or non-block positive staining strongly favors an interpretation of low-grade disease or a non-HPV associated pathology.
3. p16 *is recommended* for use as an adjudication tool for cases in which there is a professional disagreement in histologic specimen interpretation, with the caveat that the differential diagnosis includes a precancerous lesion (–IN 2 or –IN 3).
4. WG4 *recommends against* the use of p16 IHC as a routine adjunct to histologic assessment of biopsy specimens with morphologic interpretations of negative, –IN 1, and –IN 3.

SPECIAL CIRCUMSTANCE

- 4a. p16 IHC *is recommended* as an adjunct to morphologic assessment for biopsy specimens interpreted as ≤ –IN 1 that are at high risk for missed high-grade disease, which is defined as a prior cytologic interpretation of HSIL, ASC-H, ASC-US/HPV16+, or AGC (NOS).
Any identified p16-positive area must meet H&E morphologic criteria for a high-grade lesion to be reinterpreted as such.

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Summary of Consensus Recommendations

Superficially Invasive Squamous Cell Carcinomas (SISCCA)

SISCCA Recommendation:

- The term *superficially invasive squamous cell carcinoma (SISCCA)* is recommended for minimally invasive squamous cell carcinoma of the LAT that has been completely excised and is potentially amenable to conservative surgical therapy.
Note: Lymph-vascular invasion (LVI) and pattern of invasion are not part of the definition of SISCCA, with the exception of penile carcinoma.
- For cases of invasive squamous carcinoma *with positive biopsy/resection margins*, the pathology report should state whether: The examined invasive tumor exceeds the dimensions for a SISCCA (defined below)
OR
The examined invasive tumor component is less than or equal to the dimensions for a SISCCA and conclude that the tumor is "At least a superficially invasive squamous carcinoma."
- In cases of SISCCA, the following parameters should be included in the pathology report:
The presence or absence of LVI.
The presence, number, and size of independent multifocal carcinomas (after excluding the possibility of a single carcinoma).

SISCCA Site-Specific Recommendation

Comments

	Mucosal	
4.	CERVIX	SISCCA of the cervix is defined as an invasive squamous carcinoma that: Is not a grossly visible lesion, AND Has an invasive depth of ≤ 3 mm from the basement membrane of the point of origin, AND Has a horizontal spread of ≤ 7 mm in maximal extent, AND Has been completely excised.
5.	VAGINA	No recommendation is offered for early invasive squamous carcinoma of the vagina. Owing to the rarity of primary SCC of the vagina, there are insufficient data to define early invasive squamous carcinoma in the vagina.
6.	ANAL CANAL	The suggested definition of SISCCA of the anal canal is an invasive squamous carcinoma that: Has an invasive depth of ≤ 3 mm from the basement membrane of the point of origin, AND Has a horizontal spread of ≤ 7 mm in maximal extent, AND Has been completely excised.
	Cutaneous	
7.	VULVA	Vulvar SISCCA is defined as an AJCC T1a (FIGO IA) vulvar cancer. No change in the current definition of T1a vulvar cancer is recommended. Current AJCC definition of T1a vulvar carcinoma: Tumor ≤ 2 cm in size, confined to the vulva or perineum AND Stromal invasion of ≤ 1 mm. Note: The depth of invasion is defined as the measurement of the tumor from the epithelial-stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.
8.	PENIS	Penile SISCCA is defined as an AJCC T1a. No change in the current definition of T1a penile cancer is recommended. Current AJCC definition of T1a penile carcinoma: Tumor that invades only the subepithelial connective tissue, AND No LVI AND Is not poorly differentiated (i.e., grade 3-4).
9.	SCROTUM	No recommendation is offered for early invasive squamous carcinoma of the scrotum. Owing to the rarity of primary SCC of the scrotum, there is insufficient literature to make a recommendation regarding the current AJCC staging of early scrotal cancers.
10.	PERIANUS	The suggested definition for SISCCA of the perianus is an invasive squamous carcinoma that: Has an invasive depth of ≤ 3 mm from the basement membrane of the point of origin, AND Has a horizontal spread of ≤ 7 mm in maximal extent, AND Has been completely excised.