COLLEGE of AMERICAN PATHOLOGISTS

Human Papillomavirus Testing in Head and Neck Carcinomas Guideline Update

Statements and Strengths of Recommendations

SUMMARY OF RECOMMENDATIONS

Guideline Statement	Strength of Recommendation
1. Pathologists should perform HR-HPV testing on all patients with newly diagnosed OPSCC, including all histologic subtypes. This testing may be performed on the primary tumor or on a regional lymph node metastasis when the clinical findings are consistent with an oropharyngeal primary.	Strong Recommendation
2. For oropharyngeal tissue specimens (ie, non-cytology), including regional lymph nodes with metastatic SCC and clinical findings consistent with an oropharyngeal primary, pathologists should perform HR-HPV testing by surrogate marker p16 IHC. In certain scenarios HPV-specific testing should be performed: a) in geographic regions with a low prevalence of HR-HPV-associated OPSCC; b) when p16 immunostaining is equivocal (50%-70% staining or when staining is extensive but weak); c) when there is a discrepancy between p16 staining and morphology; d) for large, multisite tumors overlapping the oropharynx; e) when specimens are from a non-tonsillar, non-base of tongue oropharyngeal site; and f) when required by clinical trials. Additional HPV-specific testing may be done at the discretion of the pathologist and/or treating clinician.	Strong Recommendation
3. For tissue specimens, when p16 IHC is indicated, pathologists should report it as positive (and as a surrogate for HR-HPV) when there is at least 70% nuclear and cytoplasmic expression with at least moderate to strong intensity.	Strong Recommendation
4. Pathologists should routinely perform HR-HPV testing on sinonasal SCC.	Conditional Recommendation
5. When testing a sinonasal SCC specimen for HR-HPV, pathologists should test directly for transcriptionally-active HR-HPV (RNA-ISH); positivity for the surrogate marker p16 IHC may be used to screen tumors for confirmatory HPV-specific testing.	Conditional Recommendation
6. Pathologists should routinely perform HR-HPV testing on patients with metastatic SCC of unknown primary in a cervical lymph node.	Strong Recommendation
7. For tissue specimens (ie, non-cytology) from patients presenting with metastatic SCC of unknown primary in a cervical lymph node, pathologists should perform HPV-specific testing or surrogate marker p16 IHC, followed by HPV-specific testing for p16 positive tumors. An explanatory note on the significance of a positive HPV result is recommended.	Conditional Recommendation

8. Pathologists should not routinely perform HR-HPV testing on patients with primary oral cavity, laryngeal, nasopharyngeal, or hypopharyngeal SCCs of the head and neck for prognostic purposes. *Note:* HR-HPV testing in nasopharyngeal SCCs can be used at the discretion of the pathologist and/or treating clinician.	Strong Recommendation
9. Pathologists should not routinely perform HR-HPV testing on patients with non-squamous carcinomas of the head and neck for prognostic purposes. Note: HR-HPV testing is used in certain diagnostic settings (eg, HPV-related multiphenotypic sinonasal carcinoma) and/or for establishing primary site.	Good Practice Statement
10. Pathologists should perform HR-HPV testing on head and neck FNA of nodal SCC samples from all patients with: (a) clinical findings of an oropharyngeal or sinonasal primary or (b) metastatic SCC of unknown primary.	Conditional Recommendations
11. For FNA specimens, pathologists should perform HPV-specific testing. *Note:* In selected circumstances p16 IHC can be performed instead of HPV-specific testing. If the result of HR-HPV testing on the FNA sample is negative, testing should be performed on tissue if it becomes available.	Strong Recommendation
12. For HPV specific testing, pathologists should use tests that exhibit optimal performance characteristics, such as RNA-ISH or DNA PCR; and have adequate coverage of non-HPV16 high-risk types. DNA-ISH is not recommended.	Strong Recommendation
13. Pathologists should not routinely perform low-risk HPV testing on patients with head and neck carcinomas.	Good Practice Statement
14. Pathologists should not repeat HPV testing on patients with locally recurrent, regionally recurrent, or persistent tumor if primary tumor HR-HPV status has already been established. If initial HR-HPV status was never assessed or results are unknown, testing is recommended. HPV testing may be performed on a case-by-case basis for diagnostic purposes if there is uncertainty regarding whether the tumor in question is a recurrence or a new primary SCC.	Good Practice Statement
15. Pathologists should not routinely perform HR-HPV testing on patients with distant metastases if primary tumor HR-HPV status has been established. HR-HPV testing may be performed on a case-by-case basis for diagnostic purposes if there is uncertainty regarding whether the tumor in question is a metastasis or a new primary SCC. A positive p16 IHC result, in this setting, should be confirmed with an HPV-specific test.	Good Practice Statement
16. Pathologists should not provide a tumor grade or differentiation status for HPV-associated OPSCCs.	Good Practice Statement

The term *HR-HPV* used in this chart refers to any of the HPV-specific tests and/or to the surrogate marker p16.
Abbreviations: HPV, human papillomavirus; HR-HPV, high-risk human papillomavirus; IHC, immunochemistry; ISH, in situ hybridization; OPSCC, oropharyngeal squamous cell carcinoma; PCR, polymerase chain reaction; SCC, squamous cell carcinoma; FNA, fine needle aspirations.

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