

The Role of HPV in Oropharyngeal Cancer: Diagnosis, Treatment, and Prognosis

Shodiyev Anvar Erkinovich

Samarkand State Medical University, Department of Otorhinolaryngology No. 2, PhD

Bo'riyev Shaxzod Saydullo o'g'li

2nd year resident of the Department of Otorhinolaryngology No. 2, Samarkand State Medical University

Abstract: Human papillomavirus (HPV) has emerged as a major etiological factor in a subset of oropharyngeal squamous cell carcinomas (OPSCC), particularly affecting younger, non-smoking individuals. This article explores the virology of HPV, its oncogenic mechanisms, and its distinct epidemiological and clinical features in oropharyngeal cancer. We provide an extensive review of diagnostic approaches, current treatment paradigms including surgery, radiotherapy, and immunotherapy, and explore the evolving landscape of prognosis and surveillance. This multidisciplinary synthesis aims to inform ENT specialists, oncologists, and researchers on the changing profile of oropharyngeal cancer in the HPV era.

Key points: HPV, oropharyngeal cancer, OPSCC, biomarkers, p16, immunotherapy, de-escalation therapy, radiotherapy, ENT oncology.

Introduction

Oropharyngeal squamous cell carcinoma (OPSCC) represents a growing subset of head and neck cancers, with a significant shift in its etiological profile over the past few decades. Traditionally associated with alcohol and tobacco use, OPSCC is now increasingly linked to infection with high-risk types of human papillomavirus (HPV), particularly HPV-16. The HPV-positive phenotype of OPSCC exhibits distinct molecular and clinical characteristics, including a better prognosis and response to therapy. This epidemiological transition underscores the urgent need to adapt diagnostic, therapeutic, and prognostic strategies to the unique features of HPV-associated disease.

This article explores the current understanding of HPV-driven oropharyngeal cancers, with a focus on the underlying virology, diagnostic biomarkers (particularly p16 overexpression), current therapeutic strategies, treatment de-escalation trials, and prognostic implications. We also review the role of vaccination in prevention and its future potential in shaping the epidemiology of OPSCC.

Materials and Methods

This review integrates data from systematic literature searches conducted in PubMed, Scopus, and Web of Science databases from January 2000 to March 2025. Keywords used included: “HPV oropharyngeal cancer,” “HPV-16 OPSCC,” “p16 biomarker,” “HPV vaccination and head and neck cancer,” “de-escalation radiotherapy,” and “immunotherapy in HPV+ OPSCC.” Clinical guidelines from the National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and World Health Organization (WHO) were also referenced.

Inclusion criteria:

- a. Peer-reviewed original articles
- b. Meta-analyses and systematic reviews
- c. Clinical trial data
- d. Publications in English

Exclusion criteria:

- a. Non-peer-reviewed materials
- b. Case reports without generalizable data
- c. Studies focusing on non-oro-pharyngeal HPV cancers

Results

Epidemiology and Risk Factors

The incidence of HPV-associated OPSCC has risen significantly, particularly in North America and Europe. Studies report a doubling of HPV-positive OPSCC cases over the past two decades, now comprising over 70% of all oropharyngeal cancer cases in some populations. Unlike traditional OPSCC, HPV-positive cases are more common in younger, Caucasian, non-smoking males with higher socioeconomic status.

Virology and Pathogenesis

HPV infects the basal layer of mucosal epithelium via microabrasions. Among the high-risk types, HPV-16 is the most prevalent in OPSCC. Once inside the cell, the virus integrates into the host genome, disrupting cellular regulation via the E6 and E7 oncoproteins. E6 promotes degradation of p53, while E7 inactivates retinoblastoma protein (pRb), leading to unchecked cellular proliferation and evasion of apoptosis.

Diagnostic Biomarkers

p16 Immunohistochemistry: p16 is a cyclin-dependent kinase inhibitor overexpressed in HPV-positive tumors due to pRb inactivation. It is used as a surrogate marker and is widely recommended in clinical practice.

HPV DNA/RNA Detection: In situ hybridization (ISH) and polymerase chain reaction (PCR) techniques are used to detect high-risk HPV genotypes.

Next-Generation Sequencing (NGS): Increasingly used in research settings to profile viral integration sites and mutational signatures.

Staging and Classification

In recognition of the different behavior of HPV-positive tumors, the 8th edition of the AJCC staging system introduced separate staging criteria for HPV-mediated OPSCC. These tumors often present with smaller primary lesions but more extensive nodal involvement, yet carry a significantly better prognosis.

Treatment Strategies

Surgical Approaches: Transoral robotic surgery (TORS) and transoral laser microsurgery (TLM) offer minimally invasive options with reduced morbidity. Suitable for T1–T2 tumors with limited nodal disease.

Radiotherapy and Chemoradiation: Standard of care remains high-dose intensity-modulated radiotherapy (IMRT) with or without concurrent cisplatin. However, concerns about long-term toxicity have fueled interest in de-escalation.

De-escalation Trials: Studies such as ECOG 3311 and PATHOS explore whether reduced intensity of therapy can maintain high cure rates while minimizing long-term side effects.

Immunotherapy: Immune checkpoint inhibitors (e.g., nivolumab, pembrolizumab) are approved for recurrent/metastatic settings, with ongoing trials evaluating their role in first-line treatment and adjuvant settings.

Vaccination and Prevention: HPV vaccination (Gardasil 9) has been shown to prevent high-risk HPV infections and is expected to reduce future OPSCC incidence.

Prognostic Implications

HPV-positive OPSCC is associated with improved survival rates — 3-year survival exceeds 80% compared to ~60% for HPV-negative disease. Favorable prognostic factors include non-smoking status, younger age, and limited tumor burden. The presence of HPV is now a critical stratification factor in clinical trials and treatment decisions.

Discussion

The rise of HPV-positive oropharyngeal cancer represents both a clinical challenge and a therapeutic opportunity. Improved outcomes in this subgroup support the ongoing exploration of treatment de-intensification strategies, though careful patient selection is critical. The use of p16 as a surrogate marker, while convenient, does not fully capture the complexity of viral oncogenesis, and further refinement of diagnostic tools is needed.

The integration of immunotherapy and targeted therapy into earlier lines of treatment may further improve outcomes. However, the most impactful strategy remains prevention. Widespread HPV vaccination, especially in male populations, could dramatically reduce the incidence of this malignancy over the coming decades.

Despite better survival, HPV-positive OPSCC patients often experience treatment-related morbidity, including dysphagia, xerostomia, and psychosocial distress. Thus, long-term survivorship care and quality-of-life considerations must be central in treatment planning.

Conclusion

HPV-positive oropharyngeal cancer is now a dominant clinical entity with distinct characteristics and improved prognosis. Accurate diagnosis through p16 testing and HPV DNA/RNA detection, tailored therapy with potential for de-escalation, and robust prevention through vaccination are pillars of modern management. Future research must refine risk stratification and personalize therapy, while global health efforts must ensure equitable vaccine access to stem the rising tide of HPV-related malignancy.

References:

1. Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol*. 2011;29(32):4294-4301.
2. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med*. 2010;363(1):24-35.
3. Gillison ML, Trotti AM, Harris J, et al. Radiotherapy plus cetuximab or cisplatin in HPV-positive oropharyngeal cancer (NRG Oncology RTOG 1016): a randomised, multicentre, non-inferiority trial. *Lancet*. 2019;393(10166):40-50.
4. Fakhry C, Westra WH, Li S, et al. Improved survival of patients with HPV-positive head and neck squamous cell carcinoma in a prospective clinical trial. *J Natl Cancer Inst*. 2008;100(4):261-269.
5. Ашуров, З. Ш., & Усербаева, Р. К. (2022). Влияние тревожности и депрессии у матерей на эффективность воспитания подростков, основанного на технике повышения осознанности (mindfulness).

6. Maqsd, M. (2024). Significance of Diagnosis of Nystagmus in Miner's Disease. EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE, 4(2), 214-217.
7. Расулова, К. А., & Насретдинова, М. Т. (2022). ҲАЛҚУМДАГИ ЗАМБУРУҒЛИ ЗАРАРЛАНИШНИНГ САМАРАЛИ ДАВОЛАНИШИНИ БАҲОЛАШ. Биология ва тиббиёт муаммолари,(2), 135.
8. Rasulova, K. (2023). TREATMENT AND PREVENTION OF FUNGAL RHINITIS AND ALLERGIC RHINITIS. Science and innovation, 2(D10), 150-154.
9. Abdurashidov Asilbek Abdurashidovich , R. K. A. qizi ., (2024). MODERN INTERPRETATION OF THE ORIGIN AND TREATMENT OF SYMPTOMS OF LARYNGITIS . International Journal of Integrative and Modern Medicine, 2(3), 49–52. Retrieved from <https://medicaljournals.eu/index.php/IJIMM/article/view/201>
10. Насретдинова, М., Хайитов, А., & Салимова, Ш. (2016). Совершенствование диагностики различных форм грибковых риносинуситов. Журнал вестник врача, 1(4), 28-32.
11. Хайитов, А. А., Хушвакова, Н. Ж., & Насретдинова, М. Т. (2017). Диагностика показателей ключевых цитокинов у больных с острым бактериальным риносинуситом. In Инновационные технологии в медицине детского возраста Северо-Кавказского федерального округа (pp. 93-95).
12. Khayitov, A. A., Nasretdinova, M. T., Ziyadullayev, S. X., & Shadiev, A. E. (2021). Immunological parameters in patients with chronic cystic sinusitis. Annals of the Romanian Society for Cell Biology, 25(1), 152-157.
13. Raupova, K., Nasretdinova, M. T., Normuradov, N. A., & Rakhimov, J. H. (2024). TEMPORAL CHARACTERISTICS OF THE ACOUSTIC REFLEXES OF THE INTRA-AURAL MUSCLES IN " NOISE " WORKERS WITH NORMAL HEARING AS WELL AS WITH INITIAL AND PRONOUNCED HEARING IMPAIRMENT. Ethiopian International Journal of Multidisciplinary Research, 11(04), 447-450.
14. Бекмуратов, М. А., Насретдинова, М. Т., Хатамов, Ж. А., & Рустамова, Э. И. (2024). Показатели ЭЭГ и РЭГ у рабочих с различной степенью профессиональной тугоухости. Otorhinolaryngology Eastern Europe, 538.
15. Насретдинова, М. Т., Нурова, Г. У., Хайитов, А. А., & Шодиева, М. Б. (2023). ОЦЕНКА КЛИНИЧЕСКОЙ ЭФФЕКТИВНОСТИ РАДИОВОЛНОВОЙ ХИРУРГИИ У ПАЦИЕНТОВ С ВАЗОМОТОРНЫМ РИНИТОМ. Miasto Przyszłości, 37, 62-72.
16. Насретдинова, М. Т., Нормирова, Н. Н., Шадиёв, А. Э., & Нормуратов, Н. А. (2023). КОХЛЕОВЕСТИБУЛЯР КАСАЛЛИКЛАРИ БЎЛГАН БЕМОРЛАРДА ВЕСТИБУЛЯР ФУНКЦИЯНИ УРГАНИШ. ЖУРНАЛ СТОМАТОЛОГИИ И КРАНИОФАЦИАЛЬНЫХ ИССЛЕДОВАНИЙ, 4(3).
17. Nasretdinova, M. T., & Normuradov, N. A. (2023). Study of occupational stress in employees of medical and preventive institutions. Science and Education, 4(8), 52-56.
18. Расулова, К. А., & Насретдинова, М. Т. (2022). ҲАЛҚУМДАГИ ЗАМБУРУҒЛИ ЗАРАРЛАНИШНИНГ САМАРАЛИ ДАВОЛАНИШИНИ БАҲОЛАШ. Биология ва тиббиёт муаммолари,(2), 135.
19. Taxsinovna, N. M., Musinovna, R. K., Boyarovich, Y. A., & AM, Y. (2024). On the dynamics of the functional state of the vestibular analyzer in patients with cervical osteochondrosis with vertebral artery syndrome. Innovation in the Modern Education System, 5(41), 417-422.
20. Taxsinovna, N. M., Musinovna, R. K., Rahmatullayevich, N. O., & Mirsayid, L. (2024). STATE OF THE PROTECTIVE FUNCTION OF THE ACOUSTIC REFLEX IN WORKERS OF NOISE OCCUPATIONS WITH LESIONS OF CORTICAL AND SUBCORTICAL

PARTS OF THE AUDITORY ANALYZER. INNOVATION IN THE MODERN EDUCATION SYSTEM, 5(41), 423-427.

21. Taxsinovna, N. M., Musinovna, R. K., Abruyevich, K. J., Maftuna, M., & Ibragimovna, R. E. T. (2024). DIAGNOSTIC INFORMATIVITY OF THE DRUGS USED TO REVEAL INTRALABYRINTHINE HYDROPS ACCORDING TO THE DATA OF AUDIOLOGIC AND BIOCHEMICAL STUDIES. INNOVATIVE ACHIEVEMENTS IN SCIENCE 2024, 3(29), 112-117.
22. Raupova, K., Nasretdinova, M. T., Normuradov, N. A., & Rakhimov, J. H. (2024). TEMPORAL CHARACTERISTICS OF THE ACOUSTIC REFLEXES OF THE INTRA-AURAL MUSCLES IN " NOISE" WORKERS WITH NORMAL HEARING AS WELL AS WITH INITIAL AND PRONOUNCED HEARING IMPAIRMENT. Ethiopian International Journal of Multidisciplinary Research, 11(04), 447-450.
23. Xatamov, J. A., Xayitov, A. A., Boltayev, A. E., & Davronov, U. F. (2023). Comprehensive diagnosis and treatment of chronic purulent otitis media with complications. World Bulletin of Public Health, 28, 73-75.
24. Taxsinovna, N. M., Abruevich, X. J., Adxamovich, X. A., & Farmonkulovich, D. U. (2023). Tactics of Treatment of Recurrent Purulent Otitis in Children. Texas Journal of Multidisciplinary Studies, 26, 21-23.