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Letter to the editor

Clinical validation of the Salivary HPV DNA assessment and its link to the locoregional disease burden in advanced HPV associated oropharyngeal cancer

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To the Editor,

A study conducted by Hanna et al on the Salivary HPV DNA assessment and its link to the locoregional disease burden in advanced HPV associated oropharyngeal cancer" made a good read [1]. We read with great interest and envision its contribution to the field of cancer monitoring and prognosis. However, we do have a a few concerns in the study.

Saliva as a surrogate marker for HPV infection

One of the primary concern is that saliva has a mixture of components that can be influenced by multiple variables, including diet, ethnicity, time, site of collection and comorbidities, which can lead sufficient to heterogeneity between patient parameters to invalidate the results. Due to this, the use of saliva as a surrogate marker for HPV infection is still at its infancy. Hanna and colleagues need to discuss this limitation in detail and also highlight their study's robustness in the face of this limitation if the results of this study are to be clinically applicable [2].

Validated High-Risk HPV strains

The authors also choose to use a predefined set of validated High-Risk HPV strains, i.e. HPV-16, 18, 31, 33, and 45 as the index to test their study's hypothesis. However, the rationale behind selecting these particular HPV strains has not been sufficiently discussed in this study. It is important to note that HR-HPV is observed in only about 5% of overall cancers, which narrows down the clinical utility of using this particular HPV as the measurement index [3]. Furthermore, the study could have also addressed the increased risk that patients with primary HPV-HNSCC face, with regards to developing further HPV-related malignancies in the same or other mucosal sites [4].

Other possible prognostic factors for oropharyngeal and associated cancers

Additionally, we would also like to highlight other possible prognostic factors for oropharyngeal and associated cancers, instead of salivary HPV from the oral cavity, where the likelihood of contamination is high.

Hallmarks of cancerous microenvironment

The micro-tears in the oral mucosa during deep kissing provides a viable route for the HPV to reside in the tonsillar crypts [5]. A study of Saliva samples (viral load) when taken from the tonsillar crypts in this subset of patients is warranted which may help to highlight the presence of ongoing HPV infection. Furthermore, the microenvironment of a cancerous tumour is an amalgamation of malignant cells enveloped by immune cells, with inflammation being one of the hallmarks of said microenvironment [6,7]. Therefore, tracing the depletion of immune cells in saliva can also be a potential marker as cellular lysis of immune cells increases with cancer proliferation.

Variable soluble products as a possible marker in lieu of salivary HPV

We may even consider salivary surveillance tracing the phagocytic activities of the innate system that secretes variable soluble products such oxygen metabolites, chemokines, and cytokines (tumor necrosis factor-alpha [TNF-α], IL-1, IL-6) and their correlation with the tumour burden as a possible marker in lieu of salivary HPV [8,9].

All statements made here are in service to the furtherance of scientific discussion and research. We hope that these points are construed by the authors and that they will serve to benefit other researchers working in this field of oncology.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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Availability of data and materials

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Competing interests

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Authors' contributions

RJ predominantly conceived this review and led the development of the letter to the editor. Both RJ and CK wrote the first draft of the letter, and SS and MRM critically revised and edited successive drafts of the manuscript. All authors read and approved the final version of the manuscript.

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