



Letter to the editor

Comment on, “Survival for HPV-positive oropharyngeal squamous cell carcinoma with surgical versus non-surgical treatment approach: A systematic review and meta-analysis”


Dear Editor,

The systematic review and meta-analysis conducted by Sinha et al. titled, “Survival for HPV-positive oropharyngeal squamous cell carcinoma with surgical versus non-surgical treatment approach: A systematic review and meta-analysis”, published in the journal Oral Oncology in November of 2018, presents a thorough statistical and literary analysis of previously published studies and pre-existing data [1]. However, after detailed examination of Sinha et al.’s study, we have found a few core concerns that require elaboration and discussion.

Surgical treatments in the management of HPV-positive Oropharyngeal Squamous Cell Carcinoma (OPSCC)

A primary matter is regarding the hypothesis that forms the basis of this study. The authors state that the study is intended to compare and contrast the survival rates between the surgically and non-surgically treated cohorts of patients suffering from HPV-positive Oropharyngeal Squamous Cell Carcinoma (OPSCC). So we may presume that this study is intended to have clinical utility and inform clinical decision making. However, in the clinical sphere, surgical treatments (Surgical techniques such as minimally invasive transoral surgery, transoral laser microsurgery and transoral robotic surgery) are already the treatment method of choice for HPV-positive HNSCC, as it is a well-known clinical fact that the treatment modality of surgery has better clinical outcomes, both, in terms of survival as well as quality of life. Therefore, the rationale behind this study needs further elaboration and justification [2,3].

Patients survival endpoints

Another major limitation of this study is the survival endpoint based on which the meta-analysis has been conducted. The study conducted by Sinha et al. has only analysed the end-point of Overall Survival (OS). While the end-point of OS is considered standard for survival analysis, the inclusion of Disease Free Survival (DFS) and Progression Free Survival (PFS), help to present a comprehensive picture of patient survival and should be considered, particularly for treatment in OPSCC [4–6]. We would also like to note, that if analysis of DFS and DSS was not possible due to a lack of relevant data, it is imperative that the authors specify this in their study and clearly detail it as one of the limitations of the study.

Risk factors

It may also benefit the authors to elaborate on and discuss the risk factors that affect survival in OSCC. Though Sinha et al. have included HPV as a risk factor and have performed analysis comparing HPV + and HPV – cohorts, other risk pathological risk factors like perineural invasion could also be discussed [7].

<https://doi.org/10.1016/j.oraloncology.2018.12.019>

Received 4 December 2018; Received in revised form 12 December 2018; Accepted 16 December 2018

Available online 19 December 2018

1368-8375/ © 2018 Elsevier Ltd. All rights reserved.

Meta-regression

Additionally, we would like to suggest that rather than limiting the statistical analysis to subgroup analysis, the authors may benefit from including meta-regression analysis into their study as it will serve to further enrich the results and improve the quality of the statistical analysis [8].

We believe that the study conducted by Sinha et al. is rich in data and is a valuable addition to the existing pool of research on the subject. By rectifying the concerns presented, and considering the suggestions, this study should be able to act as a valuable information source for other researchers in the same field, while also having applicability in the clinical sphere.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors confirmed that they have no competing interests.

Funding

Any external source did not fund this study.

Authors’ contributions

RJ is primarily conceived of this critical review and led the development of the letter to the editor. Both RJ and CK wrote the first draft of the letter, and critically revised and edited successive drafts of the manuscript. RJ, and CK, read and approved the final version of the manuscript.

Acknowledgements

Not applicable.

References

- [1] Sinha Parul, Karadaghy Omar A, Doering Michelle M, Tuuli Methodius G, Jackson Ryan S, Haughey Bruce H. Survival for HPV-positive oropharyngeal squamous cell carcinoma with surgical versus non-surgical treatment approach: a systematic review and meta-analysis. *Oral Oncol.* 2018;86:121–31.
- [2] Baliga Sujith, Kabarriti Rafi, Jiang Julie, Mehta Vikas, Guha Chandan, Kalnicki Shalom, et al. Utilization of Transoral Robotic Surgery (TORS) in patients with Oropharyngeal Squamous Cell Carcinoma and its impact on survival and use of chemotherapy. *Oral Oncol.* 2018;86:75–80.
- [3] Park Young Min, Kim Hye Ryun, Cho Byoung Chul, Keum Ki Chang, Cho Nam Hoon, Kim Se-Heon. Transoral robotic surgery-based therapy in patients with stage III-IV oropharyngeal squamous cell carcinoma. *Oral Oncol.* 2017;75:16–21.
- [4] Cheng CS, Chang YM. Clinical implication of discrepancy between overall survival and disease-specific survival rate in oral cavity squamous cell carcinoma. *Int. J. Oral Maxillofac. Surg.* 2017;46:118. <https://doi.org/10.1016/j.ijom.2017.02.415>.
- [5] Korn Ronald L, Crowley John J. Overview: progression-free survival as an endpoint in clinical trials with solid tumors. *Clin. Cancer Res.: Official J. Am. Assoc. Cancer Res.* 2013;19(10):2607–12. <https://doi.org/10.1158/1078-0432.CCR-12-2934>.
- [6] Burke HB. Overall survival vs disease-specific survival. *JAMA Oncology* 2018;4(4):586. <https://doi.org/10.1001/jamaoncol.2016.6786>.
- [7] Saidak Zuzana, Clatot Florian, Chatelain Denis, Galmiche Antoine. A gene expression profile associated with perineural invasion identifies a subset of HNSCC at risk of post-surgical recurrence. *Oral Oncol.* 2018;86:53–60.
- [8] Thompson Simon G, Higgins Julian PT. How should meta-regression analyses be undertaken and interpreted? *Stat. Med.* 2002;21(11):1559–73.

Rama Jayaraj*

*College of Health and Human Sciences, Charles Darwin University,
Ellengowan Drive, Casuarina, Northern Territory 0909, Australia
E-mail address: Rama.Jayaraj@cdu.edu.au.*

Chellan Kumarasamy
*University of Adelaide, North Terrace Campus, Adelaide, South Australia
5005, Australia*

* Corresponding author.