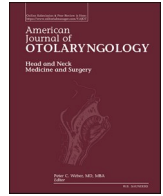


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# American Journal of Otolaryngology–Head and Neck Medicine and Surgery

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## Reply to the commentary on “Impact of time-to-surgery on survival and quality of life in oral cancer”

Dear Editor,

We would like to thank Zhu et al. [1] for their interest in our study entitled “Impact of time-to-surgery on survival and quality of life in oral cancer” [2] and for their thoughtful comments.

First, we would like to clarify the statistical issue raised by the authors. In our study, the analysis reported in Table 3 was explicitly designed as a univariate analysis aimed at exploring the association between each single prognostic factor and survival outcomes (overall survival and disease-free survival). Therefore, the commonly cited “rule of 10 events per variable” does not apply in this context, as it is primarily relevant for multivariable regression models, where overfitting and model instability may occur due to an excessive number of covariates relative to the number of events.

In univariate Cox regression, each model includes only one predictor at a time, and thus the number of covariates is not cumulative. Consequently, the concern regarding the need for approximately 280 events to support our analyses is methodologically inappropriate. Our approach is consistent with standard practice in exploratory survival analyses and is commonly adopted in clinical retrospective studies with limited sample sizes.

Moreover, we clearly acknowledged in the Discussion section the limited number of events and explicitly stated that a multivariate analysis was not performed due to the low number of disease-free survival events, precisely to avoid inappropriate model overfitting.

Regarding the potential impact of COVID-19, we would like to emphasize that all patients included in our cohort were treated between 2008 and 2015, as clearly reported in the Methods section. Therefore, the COVID-19 pandemic could not have influenced either time-to-surgery, survival outcomes, or quality of life in our study population.

Finally, we appreciate the authors' interest in our work and their recognition of its clinical relevance. We agree that larger prospective studies are needed to further clarify the complex relationship between treatment delay, survival, and quality of life in patients with oral squamous cell carcinoma.

### Consent from all authors

All authors reviewed this manuscript and agreed to submit this manuscript.

### CRediT authorship contribution statement

**Giancarlo Tirelli:** Conceptualization, Writing – original draft, Writing – review & editing. **Margherita Tofanelli:** Data curation. **Paolo Boscolo-Rizzo:** Conceptualization, Writing – original draft.

### Ethical approval

Not applicable.

### Funding information

The authors declare that they have no financial or personal relationships with individuals or organizations that could inappropriately influence their work.

### Declaration of competing interest

The authors have no conflicts of interest to declare.

### Acknowledgment

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### References

- [1] Zhu Z, Zhu Y, Ge Y. Commentary on “Impact of time-to-surgery on survival and quality of life in oral cancer”. *Am J Otolaryngol* 2024;45:104443. <https://doi.org/10.1016/j.amjoto.2024.104443>.
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