Letter to the editor

Key approaches to interpret the findings of a meta-analysis on role of chemotherapy in 5000 patients with head and neck cancer treated by curative surgery

To the Editor,

Dauzier and colleagues have recently published a paper in the journal Oral Oncology investigating chemotherapy in Head and Neck Cancer (HNC) patients treated using curative surgery [1]. This study was conducted as a subgroup analysis of a larger meta-analysis pertaining to HNC in over 5000 patients. Although the study conducted by Dauzier et al. has its merits, we believe that a few suggestions could serve to improve the quality of the study as well as address few issues.

Inoperable and unresectable tumours

There is a distinct difference between inoperable and unresectable tumours. Involvement of great vessels of the neck and tumour encroachment into the anatomic structures that are ready conduits to the skull base causing a R2 resection are often categorised as unresectable irrespective of the skill of the surgeon. Inoperable tumours is a subjective term and can vary amongst patients depending on the performance status of the individual, comorbidities, skill and armamentarium of the surgeon. Induction chemotherapy has failed to shrink the tumour uniformly due to the pseudopod shape of the tumour and are often used in inoperable and unresectable tumours with no promising results [2].

The status of the margin remains the same despite induction chemotherapy with an added concern of an additional toxicity, however concurrent chemotherapy when preceded by the surgical intervention have a better locoregional control and overall survival. The malignant cells get cleared microscopically by physical and chemical treatment.

Multiple care for loco-regionally advanced HNC malignancies

Chemotherapy in combination with radiation has emerged as a standard of care for loco-regionally advanced HNC malignancies. Unresectable, locally advanced tumours have a poor prognosis and CCRT has demonstrated improvement in 5-year overall survival rates (of 6.5%) and lower local failure rates (of 9.3%) as compared to radiation therapy alone, while also allowing for organ preservation strategies. In metastatic disease, palliative chemotherapy remains the only option and provides meaningful overall and progression-free survival benefit in patients. Latest advances in immunotherapy with checkpoint inhibitors like nivolumab and pembrolizumab have also cemented the way for better prognosis in this subset of patients [3].

Random-effects model of meta-analysis

The primary issue with the study conducted by Dauzier et al. is its use of the fixed-effects model for conducting the meta-analysis. Considering the large sample size of 5000 patients, and the likelihood of variance in the trails from person to person, as well as the moderate heterogeneity ($I^2 = 35\%$), the random-effects model of meta-analysis is more suitable for conducting an appropriate meta-analysis. The application of the fixed-effects model here is a limitation of the study and needs to be highlighted [4].

Publication bias assessment

Furthermore, Dauzier and colleagues have used a singular database (MACH-NC) as the source of all data presented in this study. A single source of data may lead to possible biases within the study, which need to be accounted for. The authors have not mentioned any steps taken in order to ensure minimization of bias, within their study. Additionally, they have not conducted a publication bias assessment, which helps indicate any biases in the reporting of the original trials. We highly recommend that publication bias assessment be considered [5].

Assessment of the heterogeneity in the meta-analysis

Finally, we also recommend that the Tau^2 as well as the Cochran-Q to also be considered, as statistical measures so as to assess the heterogeneity in the meta-analysis. Although the I^2 statistic is widely used as a measure of heterogeneity, it presents cases where its applicability and reliability can be called to question. Having multiple methods of assessing heterogeneity should increase the reliability of the measurement of this parameter [4,6].

We hope that the authors, as well as future researchers, contemplate these points when piloting a systematic-review or meta-analysis.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Authors' contributions

RJ contributed to the conceptualisation, design and development of the Letter to the Editor and review by revising different versions. RJ,

MRM, SSM, CK, SSS, AG and SB provided input into the study design, and drafting the manuscript. All authors have read and approved the final version of the manuscript.

Declaration of Competing Interest

The authors confirmed that they have no competing interests.

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