



Micro-metastasis and isolated tumour cells: the span between elective neck dissection versus neck observation in early oral cancer

Anand Subash¹ · Abhijeet Singh² · Piyush Sinha³

Received: 7 May 2020 / Accepted: 20 May 2020 / Published online: 28 May 2020
© Springer-Verlag GmbH Germany, part of Springer Nature 2020

Abstract

Early oral squamous cell carcinoma (SCC) has a propensity for lymph-node metastasis. To address or not to address the neck electively during the ablative surgery has been an ongoing debate. In recent years, some practice-changing trial and systematic reviews have emerged and put to rest the discussion of elective neck dissection versus neck observation. Today elective neck is not a mere staging procedure. It has a definitive survival advantage, but the pathological basis of this advantage has not been elaborated. Understanding this could help answer some of the critical aspects of tumour spread.

Keywords Neck dissection · Oral cancer · Metastasis · Lymph node

To intervene or observe the neck has been an ongoing debate in early oral cancer. We read with interest the Systematic Reviews and Meta-analysis by Ibrahim et al. Their work includes some of the landmark practice-changing trials [1].

The meta-analysis includes both retrospective and prospective studies that have compared the outcomes of elective neck dissection against neck observation in early oral cancers. D’Cruz et al. [2] in a retrospective study in 2009 noted that an elective neck dissection (END) did not impact disease-free survival (DFS) or overall survival (OS) and emphasised on the need for a prospective randomised-controlled trial (RCT). The results of their RCT, the Mumbai trial [3], contradicted their earlier findings, highlighting the strength of a prospective RCT.

Evidence today is building up suggesting a significant survival benefit with elective neck dissection in early oral malignancy. Randomised trials, like the Mumbai trial [3]

and SEND trial [4] have sent out a strong message highlighting the impact of an END.

It was interesting to note that in the Mumbai trial [3], the patients in the observation arm had higher staged nodal recurrences, and only a few of them salvageable, with a dismal outcome. A key finding that was overlooked in this trial was the pattern of DFS as represented in the Kaplan–Meier graphs. The patients in observation arm if not recurred in the 1st year were less likely to recur. Another rivetting finding in the Mumbai trial was the comparable overall survival when the true negatives in the END arm were compared to the true negatives of the observation arm. This key finding underplays the beneficial role of END in these cases. This can be essential learning for the future and may behold answers to why an elective neck dissection is not a mere staging procedure.

All these studies and analysis have looked at the pathological nodal positivity, and none have looked beyond the conventional histopathological evaluation. The roles of micro-metastasis (MM) and isolated tumour cells (ITC) have not been evaluated in any study. The impact of MM and ITC has not been established till now [5]. Still, the presence of these in the nodes or the concept of “tumour in transit” could be the missing link as to why END offers DFS benefit in clinically N0 oral cancers. This concept is also supported by an exciting yet unavowed finding in the Mumbai Trial and SEND trial that the chances of patients developing a distant metastasis were similar in the intervention and the observation arm.

This comment refers to the article available online at <https://doi.org/10.1007/s00405-020-05866-3>.

✉ Anand Subash
dranandsubash@gmail.com

¹ Department of Head and Neck Surgical Oncology, HCG Cancer Centre, HCG Towers, P. Kalinga Rao Road, Sampangi Ram Nagar, Bangalore, Karnataka 560024, India

² Department of Surgical Oncology, AIIMS, Rishikesh, India

³ Department of Head and Neck Surgical Oncology, Medanta Hospital, Lucknow, India

The current diagnostics are not capable of accurately identifying a MM or ITC preoperatively. Specific micro-sectioning and IHC staining of nodes can only detect these subtle changes which have just started in the lymph node. For studies looking at the role of sentinel lymph-node biopsy in early oral cancer, this may behold an unexplored arena. We believe that future trials should try and address this aspect of the disease biology. We may, indeed, be using the wrong metric, yet getting the measures right.

Compliance with ethical standards

Conflict of interest No conflict of interest amongst authors and all authors have contributed towards the article. There are no financial affiliations, and the authors have nothing to disclose.

References

1. Ibrahim SA, Ahmed ANA, Elmersy HA, Darahem IMH (2020) Elective neck dissection in T1/T2 oral squamous cell carcinoma with N0 neck: essential or not? A systematic review and meta-analysis. *Eur Arch Otorhinolaryngol*. <https://doi.org/10.1007/s00405-020-05866-3> (published online ahead of print, 2020 Feb 25)
2. D’Cruz AK, Siddachari RC, Walvekar RR et al (2009) Elective neck dissection for the management of the N0 neck in early cancer of the oral tongue: need for a randomized controlled trial. *Head Neck* 31(5):618–624. <https://doi.org/10.1002/hed.20988>
3. D’Cruz AK, Vaish R, Kapre N, Dandekar M, Gupta S, Hawaldar R et al (2015) Elective versus therapeutic neck dissection in node-negative oral cancer. *N Engl J Med* 373(6):521–529
4. Hutchinson IL, Ridout F, Cheung S, Shah N, Hardee P, Surwald C et al (2019) Nationwide randomised trial evaluating elective neck dissection for early stage oral cancer (SEND study) with meta-analysis and concurrent real-world cohort. *Br J Cancer* 121(10):827–836
5. Majumdar KS, Rao VUS, Prasad R, Ramaswamy V, Sinha P, Subash A (2020) Incidence of micrometastasis and isolated tumour cells in clinicopathologically node-negative head and neck squamous cell carcinoma. *J Maxillofac Oral Surg* 19(1):131–135. <https://doi.org/10.1007/s12663-019-01239-4>

Publisher’s Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.