

Re: adjuvant radiation in early oral cancers with isolated perineural invasion

Sir,

We commend Rajappa et al for their recent study on the impact of perineural invasion,¹ which has been discussed only scantily in the past. There has been a lack of prospective randomised studies either for or against adjuvant treatment in early oral cancers with singular adverse histopathological features (perineural invasion, lymphovascular invasion, the worst pattern of invasion, and the grade of tumour). Young patients with early oral cancers have a good prognosis, but there is an inclination towards overtreatment (with a limited armamentarium) at the cost of added toxicity.

The widespread neural network, which enables tumour cells to spread extensively along its course, has always prompted clinicians to be aggressive and overtreat malignancies with perineural invasion. The nerves have a limited neural network, which reduces the importance of perineural invasion in contrast to large calibre nerves.

Rajappa et al considered perineural invasion to be a clinically homogeneous entity, but it has diverse histopathological features. The extent, site of invasion (multifocal, intratumoural, or extratumoural), type of nerve involved, and distance from the tumour can influence the biology of the lesion and the subsequent course of the disease. The use of molecular markers to confirm the presence of perineural invasion (considering the subjectivity involved in the interpretation of perineural invasion) is important.

The authors have cherry-picked cases of perineural invasion that have not consistently been independently prognostic, and may be observed in the heterogeneous subsites of the cavity. The tongue is notorious as a site of locoregional recurrence because of its frail anatomical barriers, and dense lymphovascular network. The presence of perineural invasion alone at an early stage can exacerbate the biology, and can influence the need for adjuvant treatment.

The tissues in subsites of the oral cavity have their own genetic signatures. Yu et al observed the presence of microRNA-21 that promotes perineural invasion and can influence overall survival,² which is also governed by many other factors such as coexisting diseases and socioeconomic factors.³ Rajappa et al could have collated these factors to strengthen their argument.

They discussed the impact of adjuvant radiation on overall survival, but the endpoints of disease-free survival and disease-specific survival are more accurate.⁴ A hazard ratio to trace the oncological outcome should have been assessed. The American Statistical Association have stated that p values are “commonly misused and misinterpreted”, and are significant contributors to the current problems with reproducibility in scientific publications.⁵ Perineural invasion often indicates

an advanced tumour or aggressive biology. Correlation is not synonymous with causation and, while Rajappa et al have gleaned a significant correlation, it remains unknown if perineural invasion is the driver or a bystander. Further prospective studies would solve this quandary.

Conflict of interest

We have no conflicts of interest.

Ethics statement/confirmation of patient's permission

Not required.

Reference

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