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LETTER TO THE EDITOR

Do not omit the grade of malignancy when correlating the lobar location of diffuse gliomas and the risk of preoperative epileptic seizures

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To the Editor,

We enjoyed reading the recent paper by Zhang et al., published in Neurosurgical Review, entitled 'Correlation between glioma location and preoperative seizures: a systematic review and meta-analysis' [1]. The authors are to be congratulated for this effort, which confirms that glioma location—as defined on a lobar basis—has an impact on the risk of epileptic seizures at the time of diagnosis in patients with diffuse gliomas (grades II, III, and IV gliomas according to the World Health Organisation).

The authors acknowledge that the risk of glioma-related seizures varies relative to the World Health Organisation grade of malignancy (from 60 to 100% for grade II, 50–60% for grade III, and 25–50% for grade IV gliomas) [2]. However, we wonder why the authors did not stratify their analysis according to the WHO grade of malignancy? The grade of malignancy, which directly correlates with the risk of glioma-related seizures, is a confounder that should be incorporated in the present meta-analysis, which comprises grades II, III, and IV gliomas. Indeed, it is known that the WHO grade of malignancy varies with tumour location [3]: grade IV gliomas are reported more frequently in the parieto-temporo-occipital junction, which may account for the observed lower risk of preoperative seizure in occipital lobe gliomas (OR = 0.53, 95% CI = 0.32–0.88, $p = 0.014$), and grade II gliomas are reported more frequently in frontal and insular lobes, which may account for the observed higher risk of preoperative seizure in frontal lobe gliomas (OR = 1.51, 95% CI = 1.09–2.09, $p = 0.013$). This is a main limitation of this important study. As an illustration, one out the 16 studies incorporated in the present meta-analysis, which contributes to 34.9% of patients (1509/4323), included only grade II gliomas [2]. This may account for the reported high heterogeneity of the risk of preoperative seizure, as stated by the authors, and particularly for frontal lobe location.

An explanation of the links between glioma location, glioma grade of malignancy, and risk of preoperative seizure may lie in the complexity of the glioma-related epileptogenic mechanisms, which are multifactorial and intermixed, and in the location of the epileptogenic foci, which are often close to the glioma core [4–6]. The glioma characteristics (including the grade of malignancy and the molecular status) may account for varying glioma-related epileptogenic factors and the glioma location may account for varying brain-related epileptogenic factors. As a consequence, the risk of preoperative seizure, resulting from the intermix between glioma and the brain, justify to study altogether the glioma grade of malignancy and the glioma location when assessing the risk of seizures in diffuse gliomas.

To help the readers get a better idea of the contribution of the above discussed parameters, we strongly encourage the authors to add the glioma grade stratification to the present meta-analysis in order to refine and strengthen their conclusions.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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