

Peer Review File

Article information: <https://dx.doi.org/10.21037/tcr-21-798>

Reviewer A

Well written and well analyzed. Discussion and conclusion sections were well addressed; however, it appears that the total number of patients with high grade (2 and 3 combined=47, 22%) are just too small to draw a conclusion that only brain invasion, bone invasion and tumor location (no skull base) can effectively predict the preoperative pathological grading of patients with meningioma, not peritumoral edema or tumor size >3 cm or even necrosis per se.

As acknowledged by the authors, small number of patients, especially high grades (47 patients) probably would not give enough statistical power to draw a conclusion confidentially as grade 2 and Grade 3 could even look much differently on prep scan. The treatment recommendation for Grade 2 and 3 can be much different as most of the grade 2 patients who had a near fess total resection with low mitotic index can be watched while grade 3 usually requires radiation following surgery.

Suggestions/comments

It would be helpful to provide little more information on how to treat these high grades rather than staring "passive" on line 62 since we still provide active treatments such as radiation, chemotherapy, molecular targeted therapies and clinical trial drugs for high grades with fairly good outcome and prolonged survival.

Reply: Thank you for your professional comments sincerely. In accordance with your suggestions, in the revised manuscript, we have made the correction.

Changes in the text: we have modified our text as advised (see Page 4, line 8-10)

If possible, please provide the number of grade 2 and 3 separately as they can appear differently that could affect the overall analysis and the outcome of the study.

Reply: Thank you for your professional comments sincerely. In patients with high-grade meningiomas, there were 40 patients in grade 2 and 7 patients in grade 3. Separate analysis of each high-grade type may make the results not very reliable. Therefore, we only analyzed the predictors of high-grade meningiomas.

Also, in conclusion, it would be helpful for the readers to understand which location would exhibit a better predictive effect (skull based vs non skull based) as brain invasion and bone invasion were already mentioned.

Reply: Thank you for your professional comments, in the revised manuscript, we have made the correction.

Changes in the text: we have modified our text as advised (see Page 12, line 20)

Reviewer B

Peng et al. constructed a predictive nomogram of meningioma WHO grade based on radiological characteristics of 215 patients. They include three variables in their model, namely tumour size, location and "brain invasion".

Concerns/suggestions:

1. In the introduction, page 3, line 62, the authors state that high grade lesions make further treatments very passive. I'm not entirely sure what the authors are trying to state here but further treatments may be required for high grade lesions.

Reply 1: Thank you for your professional comments sincerely. The "passive" meant to express a forced response, which is not quite accurate. In accordance with your suggestions, in the revised manuscript, we have made the corrections.

Changes in the text: we have modified our text as advised (see Page 4, line 8-10)

2. In the introduction, page 3, line 65, the authors state that imaging differentiation is the most commonly used diagnostic method. Pathological grading remains the gold standard for meningiomas and to direct further treatment. The statement should be revised.

Reply 2: Thank you for your professional comments, in the revised manuscript, we have made the correction.

Changes in the text: we have modified our text as advised (see Page 4, line 13-14)

3. Under the methods section, page 4, lines 84-86, the number of patients meeting the eligibility criteria is in the results section and does not require repeating in the methods.

Reply 3: Thank you for your professional comments. In accordance with your suggestion, in the revised manuscript, we have removed the duplicates in the methods.

4. Under data collection, page 4, the authors should revise their use of the term "brain invasion". Brain invasion is a phenomenon observed histologically and not radiologically. I believe the authors here are referring to the absence of a clear CSF cleft between the meningioma and peri-tumour region, which is not a surrogate marker for brain invasion <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6267603/>. If the authors are referring to the absence of the CSF cleft, then please refer to it as such.

Reply 4: Thank you for your professional comments. It is a great help for us to revise our manuscript with your suggestion. Just as you said, "brain invasion" as a pathological observation result cannot be used as a radiological indicator, and it lacks corresponding imaging features. The imaging observation between the tumor and the brain interface cannot be determined as a "brain invasion", so we revised the definition to express it more accurately and specifically.

Changes in the text: we have modified our text as advised (see Page 5, line 22/ Page 6, line 1-3).

5. Also under data collection, why is T2 hyperintensity thought of as tumour necrosis?

Reply 5: Thank you for your professional comments. The tumor's central necrosis due to ischemia and other reasons forms a cyst. The cyst signal on the T1-weighted image is lower than the tumor parenchymal signal, slightly higher than the cerebrospinal fluid signal, and the T2-weighted signal is very high, which is significantly higher than the tumor parenchyma. On the enhanced MRI scan, the tumor parenchyma was enhanced, but the cystic part was not enhanced. The appearance of T2 non-enhancing high signal in the tumor can be regarded as obvious tumor necrosis.

6. Under discussion, page 6, the authors start their discussion by referring to a

nomogram to predict recurrence by Nassiri et al. Some atypical and anaplastic meningiomas behave in an indolent manner, similar to grade 1 meningiomas and therefore the nomogram presented by Nassiri is of value. Their nomogram is also based on DNA methylation of tumour tissue and not radiological features. If the authors intend to compare the two, they should discuss the added value of their nomogram.

Reply 6: Thank you for your professional comments sincerely. In accordance with your suggestions, in the revised manuscript, we did a comparison and analyzed the added value.

Changes in the text: we have modified our text as advised (see Page 9, line 2-11)

7. Throughout the discussion, the authors ought to tone down the reliability of their nomogram. It's yet to be externally validated and therefore I'd be careful to recommend its use in larger sample, such as described in page 7, line 173

Reply 7: Thank you for your professional comments sincerely. In accordance with your suggestions, in the revised manuscript, we tone down the reliability of the nomogram in the discussion.

Changes in the text: we have modified our text as advised (see Page 9, line 21-22/ Page 10, line 1)