Prognostic Factors for Meningioma Growth: A Meta-Analysis

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Background & Research Objectives

Meningiomas are the most common brain tumor (Fig. 1). However, their growth rate is difficult to predict as previous literature has shown inconsistent relationships with multiple tumor and patient characteristics.

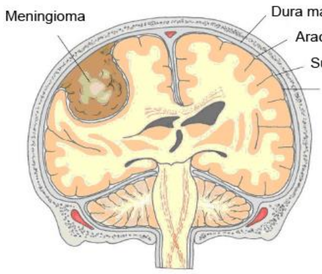

Figure 1 Diagram of the meninges of the brain and a meningioma, which form between the dura mater and arachnoid mater, although they can break through the pia mater into the brain. Indicates the shifts in brain physiology as a result of tissue displacement.[1]

What are the best prognostic factors for meningioma growth?

- Conduct a literature review and synthesize existing hypotheses for relationships between factors and meningioma growth rate.
- Perform a meta-analysis for each factor using data gathered from selected studies.

Study Selection

1,439 articles identified in Google Scholar

→ **1,400 excluded:**
17 non-English articles
1,302 not relevant (from titles/abstracts)
55 included treatments
26 had sample size of <10

39 retrieved for detailed evaluation

→ **21 excluded:**
20 insufficient data for determining odds ratio and standard error
1 supplementary figure with necessary data not accessible

18 studies for the final analysis

Figure 2 Flowchart for selection of studies.

Forest Plots

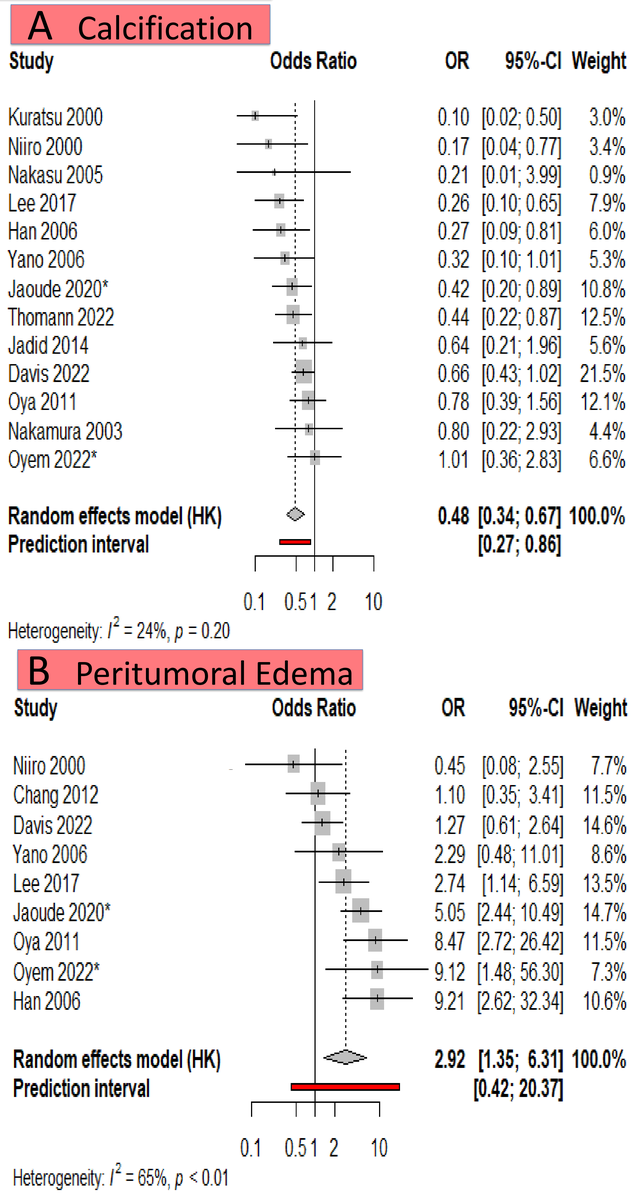

Figure 3 Meta-analysis of the association between meningioma growth on serial imaging and tumor characteristics. In each panel, each study is represented by a grey box (weight of the study) and black line (dash = odds ratio and length = 95% CI). The diamond at the bottom is the pooled effect with the length representing its 95% CI. The vertical line above the 1 is a reference, which indicates where there is no effect.[2] The red line depicts the range in which the point estimate of 95% of future studies will fall, assuming a normal distribution.[3] (A) Indicates a significant negative correlation between the presence of calcification and tumor growth rate, (B) Indicates a significant positive correlation between the presence of peritumoral edema and tumor growth rate. g: Hedge's g, SE: standard error, OR: Odds ratio, CI: confidence interval. (*) Indicates studies with Neurofibromatosis type 2 data.

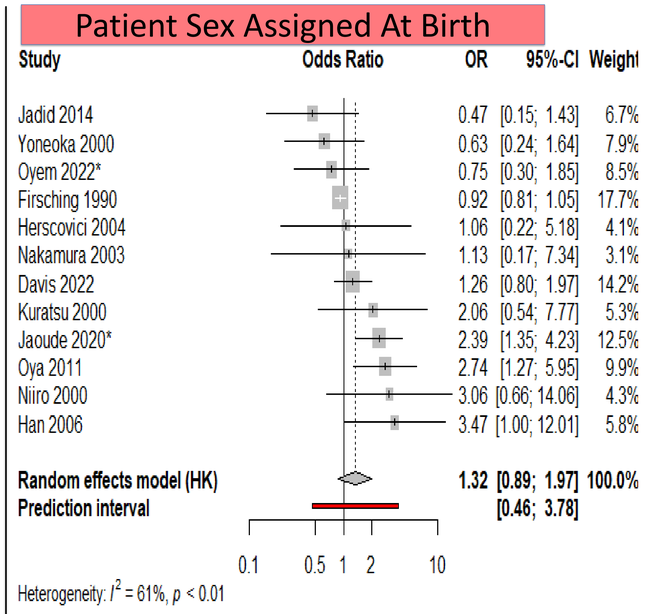

Figure 4 Meta-analysis of the association between meningioma growth on serial imaging and the patient characteristics. This forest plot functions the same as described in Fig. 3. This plot indicates an insignificant positive correlation between male sex and tumor growth rate. g: Hedge's g, SE: standard error, OR: Odds ratio, CI: confidence interval. (*) Indicates studies with Neurofibromatosis type 2 data.

Prognostic Factor Correlations

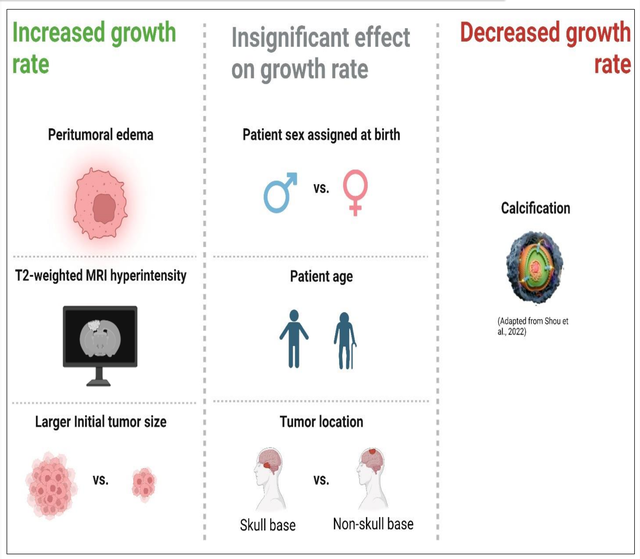

Figure 5 Illustrated results from this study's meta-analyses. Relative strength of correlations with meningioma growth are rank ordered for each section with the strongest correlations at the top (Created with BioRender.com).

Publication Bias

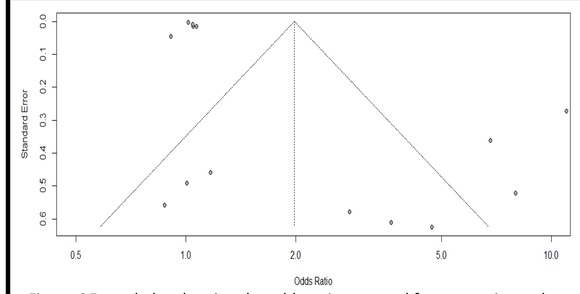

Figure 6 Funnel plot showing the odds ratio reported for tumor size and growth rate as related to the standard error, which indicates the statistical power of the study. A right-handed skew is demonstrated, which shows that studies reporting a negative association between tumor size and growth rate are rarely reported. Publication bias is likely (Egger's test: p = 0.0257).

- Egger's test[4] was performed to test for funnel plot asymmetry and found initial tumor size vs. tumor growth rate to be the only meta-analysis with significant results indicating a possibility of publication bias.

Important Implications

- Peritumoral edema was the strongest predictor of meningioma progression.
- Calcification was the strongest predictor for meningioma non-progression.
- Sex assigned at birth was not found to be a significant predictor of growth rate, despite many studies reporting a connection.[5,6]
- **Suggests a need for restructuring the treatment planning process and moving from patient characteristics (**sex and age**) to radiological characteristics (**peritumoral edema, hyperintensity, tumor size, and calcification).

Future Research

- Utilize a standard measuring tool (e.g., volumetric analysis) and a standard definition/threshold for growth (e.g., 2cm^3/year). [7]
- Perform multivariate meta-analysis to rank each factor against the others and elucidate any interactions between.[2]
- Create a formula for meningioma growth prediction[8] using validated coefficients from meta-analyses like this one
- Develop treatment strategies based on calcification[9,10] and peritumoral edema[11] given their strength as predictors

References

[1] Matsumae, M. (2008). Understanding the tumor. Clinical Study. *Medical Friend Co. Ltd.*, *29*(14). http://neurosurgery.med.u-tokai.ac.jp/en/patients/meningioma/index.html, [2] Harrer, M., Cuijpers, P., Furukawa, T. A., & Ebert, D. D. (2021). *Doing Meta-Analysis with R: A Hands-On Guide*. Boca Raton, FL and London: Chapmann & Hall/CRC Press. https://bookdown.org/MathiasHarrer/Doing_Meta_Analysis_in_R/metareg.html, [3] Borenstien, M., Hedges, L., Higgins, J. P., & Rothstein, H. (2009). Converting among effect sizes. In *Introduction to meta-analysis*. John Wiley & Sons. https://www.meta-analysis.com/downloads/Meta-analysis%20Converting%20among%20effect%20sizes.pdf, [4] Egger, M., Davey Smith, G., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ (Clinical Research Ed.)*, *315*(7109), 629–634. https://doi.org/10.1136/bmj.315.7109.629, [5] Jaoude, S. A., Peyre, M., Degos, V., Goutagny, S., Parfait, B., & Kalamarides, M. (2020). Validation of a scoring system to evaluate the risk of rapid growth of intracranial meningiomas in neurofibromatosis type 2 patients. *Journal of Neurosurgery*, *134*(5), 1377–1385. https://doi.org/10.3171/2020.3.JNS192382, [6] Oya, S., Kim, S.-H., Sade, B., & Lee, J. H. (2011). The natural history of intracranial meningiomas: Clinical article. *Journal of Neurosurgery*, *114*(5), 1250–1256. https://doi.org/10.3171/2010.12.JNS101623, [7] Haidich, A. B. (2010). Meta-analysis in medical research. *Hippokratia*, *14*(Suppl 1), 29–37., [8] Lee, E. J., Kim, J. H., Park, E. S., Kim, Y.-H., Lee, J. K., Hong, S. H., Cho, Y. H., & Kim, C. J. (2017). A novel weighted scoring system for estimating the risk of rapid growth in untreated intracranial meningiomas. *Journal of Neurosurgery*, *127*(5), 971–980. https://doi.org/10.3171/2016.9.JNS161669, [9] Shou, H., Wu, J., Tang, N., & Wang, B. (2022). Calcification-Based Cancer Diagnosis and Therapy. *ChemMedChem*, *17*(4), e202100339. https://doi.org/10.1002/cmdc.202100339, [10] Zhao, R., Wang, B., Yang, X., Xiao, Y., Wang, X., Shao, C., & Tang, R. (2016). A Drug-Free Tumor Therapy Strategy: Cancer-Cell-Targeting Calcification. *Angewandte Chemie International Edition*, *55*(17), 5225–5229. https://doi.org/10.1002/anie.201601364, [11] Dietrich, J., Rao, K., Pastorino, S., & Kesari, S. (2011). Corticosteroids in brain cancer patients: Benefits and pitfalls. *Expert Review of Clinical Pharmacology*, *4*(2), 233–242. https://doi.org/10.1586/ecp.11.1'