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# ‘Meningiomics’ – an integration of data on the patient, tumour, extent of resection and molecular pathology to optimise the management and follow-up for meningiomas

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Champeaux and colleagues report on the outcomes from a single institution study of 505 patients with WHO grade I cranial meningiomas that underwent treatment between 2003 and 2017. During the median follow up period of 6.2 years (IQR: 2.8-9.5) 74 patients had meningioma recurrence or a meningioma-related death, whilst 84 patients died from other causes. The median age at death was 71.7 years (IQR: 59.6-78.6), and eight patients died within one month of surgery, and 29 within a year. Twenty-five patients had early recurrence requiring re-operating at a median 1.3 years (IQR: 0.2-2.6) after the first surgery. Eleven patients had progression to grade II or III meningioma. The authors performed a competing risks analysis, which takes into consideration that when death occurs due to other causes (e.g. myocardial infarction) it prevents the observation of the events of interest – namely meningioma recurrence or meningioma-related death. Based on analysis of their data the absolute risk of WHO grade I meningioma recurrence or death is 16.2% at 5 years and 24.4% at 10 years. As expected the factors for meningioma-related death or progression were venous sinus invasion, subtotal resection (defined as Simpson grade 4-5), and growth of residual tumour. The authors comment that this data can be used to rationalise follow-up and propose that when gross total resection (Simpson grade 1-3) is achieved, imaging surveillance for three years for convexity meningioma and 6 years for all other locations is required. When a subtotal resection is performed then eight years imaging follow-up is sufficient if there is no evidence of meningioma progression.

This study highlights several important points when considering the management for patients with grade I meningioma. Firstly, not all grade I meningioma behave in a ‘benign’ manner and early occurrence and progression can occur. These so-called clinical aggressive meningiomas (CAMs) can’t be readily identified using the current WHO classification, however, DNA methylation [9] and molecular profiling [10] may help to identify them in the future and allow us to predict recurrence risk [6]. This would ensure patients are considered for adjuvant radiotherapy to reduce the risk of recurrence, but until these molecular features are validated in external data sets and become embedded in routine practice follow-up imaging is still required to monitor for early recurrence.

Secondly, the optimum frequency and duration of imaging follow-up required for meningioma is not defined. The patterns of recurrence in meningioma tend to fall in to three categories: early within two years of surgery, intermediate between three and ten years, and late ten years after surgery. Many recent studies report follow-up of approximately five years [2] and authors choose a time period to reflect ‘modern’ neurosurgery. This suggests that studies including patients operated in the 1990s lack validity and this is not the case – after all microneurosurgery was developed in the 1960s and has been in widespread use for meningioma surgery over the last 40 years [4]. Data from studies with 25 years of follow-up show that late meningioma recurrence can occur, especially in patients with subtotal resection [7]. The proposal by Champeaux et al., to discontinue follow-up in subtotal resection of meningioma even when there is no evidence of growth of the residual by eight years, is not fully supported by their data. In addition, there is limited published literature on the natural history and growth rates of residual meningioma. Recent guidelines from the European Association for Neuro-Oncology advise continued follow-up long-term with no recommendation to discontinue surveillance due to the late risk of recurrence for all meningiomas [3]. Nevertheless, it should be possible to optimise the frequency of follow-up and annual surveillance MRI is not necessarily required for all meningiomas and all patients. Neurosurgeons should take into consideration the patient’s age and co-morbidities as these may be competing risks for meningioma recurrence and the need for further treatment, which may make long-term MRI surveillance follow up futile. Data from the English National Cancer Registry on surgically treated meningioma shows that only 66% of patients aged 70-79 years survive for 5 years, which falls to 49% in patients aged >80 years [1], and this is particularly relevant since meningiomas are more common with advancing age.

Thirdly, the use of a competing risk analysis is appropriate in meningioma when there is a high risk that the event of interest (meningioma recurrence or meningioma-related death) will not observed due to the high prevalence of over events, that is, death due to other causes. Indeed this is the rationale behind current phase III atypical meningioma trials excluding patients with co-existing solid cancers [5] since the event of interest is recurrence.

The current management of meningioma relies on practicing evidence based medicine, which integrates the best available evidence with individual clinician expertise [8]. Only by improving the evidence-base can we improve outcomes for more patients. The future of meningioma management will include a more personalised approach to treatment and follow-up that integrates data about patient co-morbidities, meningioma location and extent of resection, WHO grade and molecular pathology. This so called ‘meningiomics’ approach is essential to improve the short, medium and long-term outcomes for patients with cranial meningioma.

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