Meningioma and radiotherapy

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For the majority of patients presenting with a meningioma, the lesion is benign and a surgical cure is obtained by means of gross-total resection. In contrast to benign meningiomas, atypical and anaplastic meningiomas are associated with shorter overall and progression-free survival. Recurrence is seen in 29%--52% of cases with atypical meningiomas and 50%--94% of anaplastic meningiomas. Due to this high recurrence rate, many of these tumors are also treated with adjuvant radiotherapy. However, results have been difficult to interpret, as some studies suggest benefit for adjuvant radiation therapy while others conclude that gross-total resection is more predictive of survival. These studies have been limited by the rarity of nonbenign meningiomas, making accumulation of a large sample size difficult. Thus, it is challenging to define whether the standard of care for nonbenign meningiomas should include adjuvant radiotherapy. In “Does adjuvant external-beam radiotherapy improve outcomes for nonbenign meningiomas? A Surveillance, Epidemiology, and End Results (SEER)–based analysis,” Stessin and colleagues attempt to address this uncertainty by performing a retrospective analysis of patients with WHO Grade II or III meningiomas. They conducted this study by utilizing the SEER database. Although well intentioned, this study does present inherent limitations because of the nature of the database. The SEER database is a collection of population-based cancer incidence and survival data compiled by the National Cancer Institute. It is a comprehensive database that includes approximately 26% of the US population and is comparable to the US population with regard to racial diversity, poverty level, and education level. There is oversight of the registries to ensure accurate data reporting. However, there are many details of each clinical case that are not reported. For instance, cancers can be included in the database without a histological diagnosis (that is, with clinical and radiological diagnoses only), and only the first course of treatment is coded in detail. If a patient receives surgery and adjuvant radiation for a diagnosed meningioma, that is recorded. Yet, if they later receive additional external-beam radiation therapy (EBRT) or surgery for a tumor recurrence, that information is not available. The timing and dose of radiation treatment are also not included in the database, nor are medical comorbidities. Additionally, follow-up information is limited to patient survival at last follow-up; there is no recording of quality-of-life measures or performance scores.

Despite these limitations, there are some types of analysis that can be successfully compiled from the SEER database. Recently, Cahill and Claus explored survival metrics in patients with benign meningiomas. In 6737 patients with a histologically confirmed diagnosis of WHO Grade I meningioma, they demonstrated a 3-year survival rate of 92.4%. Among those patients treated with surgery, the 3-year survival rate was 93.4% versus 88.3% in those who received no treatment or only underwent biopsy. Although this study can accurately determine the overall survival for patients with benign meningioma, caution must be exercised in concluding that surgery is better than no treatment. Those patients who did not receive surgery may have been older, had medical comorbidities, or had tumor close to eloquent brain or in areas that would be difficult to resect. As has been noted by others, this type of selection bias plays a large role and can be difficult to control for with the limited data set available in national registries, making conclusions about treatment efficacy difficult. Many note that national registries are good for epidemiological data, yet caution about making conclusions regarding adjuvant treatments.

Stessin and colleagues attempt to answer a more ambitious question than that addressed by Cahill and Claus. Their study identifies 657 patients between 1988 and 2007 who had histologically confirmed nonbenign meningiomas, 244 of whom were treated with adjuvant EBRT. Many of the patients had nonbenign meningiomas of unknown grade. When these patients were removed from the data set, only 134 patients were left. Furthermore, the WHO definition for classifying meningiomas changed with the 2000 and 2007 editions. It has been shown that the new WHO classification shows a more pronounced stratification in prognosis between Grade II and Grade III meningiomas and is therefore more appropriate. Therefore Stessin and colleagues further narrowed their sample size by including only the patients in the database from 2001 through 2008, resulting in a mere 82 patients...
remaining for analysis. This was too small a number from which to expect significant differences. The only finding from their analysis is that of a decreased survival in patients who received EBRT. However, this conclusion has to be viewed with much caution. The only data set with enough patients to yield significance was the initial group with 657 patients (which includes those with unknown grade and those treated before 2000). In this cohort of 657 patients, there were numerous differences between patients who received EBRT and those that did not. As the authors summarize in Table 1, there were more patients with Grade III meningiomas in the group receiving EBRT, and the group without EBRT had older patients and more patients with unknown tumor grades. This dissimilarity between the groups exemplifies the treatment selection bias that is difficult to statistically control for in retrospective studies.

To the authors’ credit, they acknowledge the limitations of the SEER database. The most damaging is the aforementioned lack of tumor grade and possible misdiagnosis from the pre-2000 WHO classification. Lumping the two disparate groups of Grade II and Grade III meningiomas and including patients with unknown pathological grade is a concern. It is unfortunate that large databases such as SEER do not allow for independent central review of histology. The ability to confirm tumor grade for the available cases could have made a difference in this study’s outcomes. As the authors acknowledge, there are many other missing variables that preclude drawing conclusions about the efficacy of EBRT for nonbenign meningiomas from this study. The extent of tumor resection is not clarified: the SEER database only records gross-total or subtotal resection. Simpson grading, which has become the standard for describing meningioma resection, is not included. Patient comorbidities and Karnofsky Performance Status scores are not available. Lastly, the radiation dose and timing information is inaccessible. In an analysis designed to determine the efficacy of radiation treatment, it is crucial to include dosing of radiation. Conclusions cannot be drawn from a study in which an unknown quantity of patients may have received a suboptimal radiation dose. All of these data points are ones that would be helpful to constitute a multivariate analysis, and their absence significantly alters the impact of the results. Additional concerns relate to the small sample sizes and missing data that limit the statistical analysis. The authors recognize this, and this can provide a note of caution. Again, the SEER database, and other national registry databases are optimized for incidence and basic epidemiological data. There are too many missing variables in the SEER database to allow conclusions about treatment efficacy. Additionally, the nature of observational data is that there is an inherent selection bias. This bias is difficult to overcome, especially with limited information. Studies using national databases should be read with caution and with the goal of answering specific questions within the spectrum of the indices available in the database. The randomized controlled trial (RCT) is still the gold standard for determining treatment efficacy. Prospective RCTs are difficult in neurosurgery and are subject to different types of bias. However, the ability to have similar treatment groups from the outset of the study, and the ability to collect all possible variables needed for multivariate analysis makes the RCT superior, even if the sample size is small. Stessin and colleagues provide a well-intentioned analysis, which clearly identified an area of clinical equipoise. However, a more rigorous study design is needed to answer the question of the efficacy of adjuvant radiotherapy for nonbenign meningiomas. (http://thejns.org/doi/abs/10.3171/2012.2.JNS12182)

Disclosure

The authors report no conflict of interest.

References