LETTER TO THE EDITOR

Response to “Reply to ‘Survival analysis for apparent diffusion coefficient measures in children with embryonal brain tumors,’ by Grech-Sollars et al”

Dear Editor,

We would like to thank Dr Korgun Koral, Dr Daniel C. Bowers, and Dr Robert Timmerman for their thoughts on our publication1 and would like to take the opportunity to respond to their comments.

The main issue brought up is that of heterogeneity. Although we understand the concern expressed on this point, it is important to keep in mind that heterogeneity amongst the patient cohort would generally be expected to mask the effects of interest, rather than enhance them. For example, the lower survival in medulloblastoma patients having metastasis at presentation may be masked by including other tumor types, such as supratentorial primitive neuroectodermal tumors, where conflicting evidence exists as to whether there is a relationship between metastasis at presentation and survival. In a similar way, one would expect the relationship between survival and the apparent transient coefficient in tumor (ATCT) to be masked by cohort heterogeneity, if it is dependent on tumor type. Therefore, the fact that ATCT was significant across embryonal tumor types actually makes a stronger case for it to be considered as a measure of prognosis in addition to currently used variables.

Although different tumor subtypes have different prognoses, this does not imply that ATCT cannot be a useful indicator of longer survival across all of them. Since there was no evidence in our data to suggest that patients with one or another tumor type did not fit the general pattern, the results may be said to broadly apply in all cases. By contrast, restricting the analysis to a very homogeneous sample severely restricts the generalizability of the conclusions that can be drawn. With that said, having separately analyzed the medulloblastoma patient group, we do recommend examining the ATCT by medulloblastoma subgroups in order to examine the predictive value of the ATCT compared with histological and molecular classifications.

We also note that currently the presence of leptomeningeal metastasis and extent of tumor resection affect survival significantly, with specific treatment recommendations carried out based on these variables. In our study, both have been included and analyzed. Our results have shown ATCT to be a stronger indicator of survival than either of these 2 variables.

We acknowledge that the rising incidence of atypical teratoid/rhabdoid tumors in young children is a factor that may contribute to the lower survival in children with embryonal brain tumors younger than 3 years of age. That said, age is a factor considered in determining treatment options for medulloblastoma patients,2 and our study showed that the difference in survival by age is also reflected in this subgroup of embryonal brain tumors.

In conclusion, far from undermining our results, cohort heterogeneity reinforces the strength of ATCT as a biomarker of survival across a range of embryonal tumor types. Nonetheless, further analysis on larger patient groups of a more homogeneous nature would aid in identifying those groups in which it would be most beneficial to incorporate ATCT as part of clinical trials and as a biomarker of survival.

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References