Quantifying the burden of primary central nervous system malignancy

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The burden of central nervous system (CNS) tumors is manifest to neuro-oncologists and requires little supporting evidence or quantification. However, malignant primary CNS tumors comprise <2% of all cancers and must compete with many more common cancers for both public health resource allocation and research funding. Do standard incidence rates and mortality figures adequately capture the global impact of CNS tumors? Put differently, is the death of an 85-year-old man from prostate cancer different from that of a 35-year-old parent and breadwinner with a glioblastoma from a societal perspective?

One method to try assessing societal burden is through “years of potential life lost” (YPLL). YPLL is a calculated figure that represents the average expected time a person would have lived in the absence of a premature disease-related death. By combining mortality with the age at death, YPLL provides information complementary to standard mortality rates and begins to credit the notion that age at death has personal, social, and economic importance. The calculation of YPLL for a given individual is quite simple: YPLL is determined by subtracting the (premature) age of death from disease from the predicted longevity based upon life table estimates, factoring in year of birth, sex, and race/ethnicity. Median YPLL can be calculated across a population of patients with a specific diagnosis, as can a total YPLL that takes into account both the incidence of a disease and its impact upon premature death.

In this issue of Neuro-Oncology, Rouse et al sought to capture the health burden of adult CNS tumors by estimating median YPLL and comparing it with the YPLL of the 4 most common adult cancers (prostate, female breast, lung, and colorectal) as well as pancreatic and ovarian cancer (chosen for their high mortality rates). Focusing on calendar year 2010, they used death certificate attribution of cause of death to as-sign deaths from neuro-oncological tumors to the categories of malignant brain tumor, malignant nonbrain (presumably mostly spinal) tumors, and nonmalignant CNS tumors; the same methodology was used to determine deaths from the other cancers of interest. Longevity estimates were based upon life tables from the Centers for Disease Control and Prevention.

Emphasizing the relevance of CNS tumors among younger cancer patients, this study found that malignant brain tumors were the leading cause of cancer deaths among the included cancers for both males and females aged 20–39 years, as well as for males aged 40–59 years. For females aged 40–59 years, malignant brain tumors closely followed breast cancer as the leading cause of death. Of the cancers studied, malignant brain tumors had the lowest mean age at death for both sexes (63 in men and 66 in women).

Overall, CNS tumors accounted for 6.6% of total YPLL of the tumors under study in men and 4.3% in women; total YPLL from CNS tumors actually exceeded that from prostate cancer despite the latter’s high incidence. At the level of the individual patient, malignant CNS tumors had the highest YPLL of ~20 years, with the runners-up in women being breast cancer (19 years) and in men, pancreatic cancer (15 years). The mean YPLL for the other common cancers in adults ranged from 14 to 18 years. In contrast, another study found the corresponding figure for prostate cancer to be <2 years. Are these results credible, and if so, what are their implications? The study bases cause of death on death certificates, an approach that has been shown to be reliable for CNS tumors and other cancers. The YPLL results for non-CNS tumors are plausible based upon other studies; for example, YPLL was 15.9 for male cancer deaths in 2004 in the United States. These results are concordant with those from a United Kingdom study based upon the East Anglican Cancer Registry in 2002 examining YPLL from 17 tumor types including CNS tumors, which reported an almost identical YPLL of 20.1 for CNS tumors. This British study also demonstrated that CNS tumors have the highest ratio of total years of life lost to the overall number of deaths, reflecting the tendency of these tumors to affect younger patients and be rapidly lethal. The authors of the current manuscript have also recently reported elsewhere that in children (younger than aged 20 years), CNS tumors are the largest cause of total years of life lost due to cancer (31%).

Rouse et al did not attempt to address the question of whether brain tumor research or care is relatively underfunded. The aforementioned British study computed the ratio of total

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years of life lost for common tumor types to total research funding for that cancer from the National Research Council Institute. By this metric, CNS tumors were relatively underfunded, receiving slightly less than half of average cancer funding per year of life lost. Lung, pancreatic, gastric, uterine, and esophageal cancer were even more underfunded, while leukemia received disproportionate funding with 13 times as much funding per YLL than CNS tumors. Admittedly, acquiring similar and reliable figures in the United States might be challenging, and to some extent cancer research is undergoing a shift to a mechanistic underpinning approach that crosses organ site boundaries.

Further refinements to the analysis by Rouse et al might include inclusion of more tumor types that can affect younger patients (eg, hematologic malignancies) as well as breaking CNS malignant tumors into tumor subtypes, as these authors did in their corresponding study of pediatric tumors. Some researchers have extended YPLL determination to estimate the cost of lost productivity for a tumor type, and such assessments for CNS tumors would likely highlight the disproportionate number of patients with CNS tumors (and their caregivers) who exit the work force prematurely because of their diagnosis or treatment-related toxicity. While numbers alone cannot capture the magnitude of the personal and societal loss from brain tumors, they might emphasize the critical need for additional investment into research to improve the outcome from these devastating malignancies.

References
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