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How well are we doing in caring for the patient with primary malignant brain tumor? Are we measuring the outcomes that truly matter? A commentary

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Neurologists, neurosurgeons, and neurooncologists have traditionally measured clinical information about the patient that includes descriptions of mortality, morbidity, time to progression, survival time, magnetic resonance imaging data, and laboratory evaluations. These measurements have been referred to as intermediate health outcomes. They are a reflection of what is happening to the patient but do not provide a direct measurement of total impact on the patient. This paper describes the traditional means of approaching patients with malignant brain tumor. A philosophical shift to a more functional alternative approach is offered. This emphasis on functional assessment and quality of life will help to focus not only on the disease but rather on the total impact of various treatment options on the patient.

Key Words * malignant brain tumor * quality of life * functional assessment * outcomes * patient management

Unlike any other form of malignant disease, primary malignant brain tumor can potentially interfere with all spheres of a patient's life, including intellectual, cognitive, and physical function, and result in a state of ongoing compromised quality of life that frequently overwhelms the providing physician. As a foundation of management, therefore, the provider may break the patient's complaints into the biological facts of the disorder, falling back on the biomedical model of treatment. It is certainly easier to assess the number of seizures, the extent of headache, the toxicity of treatment, the change in size of the lesion on magnetic resonance imaging, and potential experimental protocols than to evaluate the patient's quality of life. There is a consensus in the neurooncological community regarding what constitutes standard of care that begins with establishing an accurate diagnosis as essential to any future treatment plan. This may be performed as a needle biopsy or part of a surgical strategy that consists of debulking and removing the maximum tumor tissue possible without inflicting increased postoperative deficit. This is generally followed by radiotherapy depending on the grade of tumor. Following completion of radiotherapy, chemotherapy is an option for treating more aggressive tumor types. Patients are then followed through their potential disease-free interval to such time that recurrence is established. At this time a second procedure and/or standard chemotherapy are promoted as preliminary requirements to experimental

options. Despite the implementation of many of these different options, good palliative care remains the final responsibility of the providing physician.

I often think that we who take care of patients with brain tumors are in a terrible bind: based on patient outcomes, we have made no dramatic progress over the last 25 years in our management of patients with this challenging disease. Notwithstanding the extraordinary technological advances including more precise imaging, stereotactic technique, image-guided surgery, direct instillation of chemotherapeutic agents into the brain, and gene therapy, the basic pathology has remained impervious to our attempts to neutralize it.

Often a dichotomy between patient expectation and our realistic capabilities exists. A number of centers in the country market their superior ability and expertise in the overall management of malignant primary tumors through promotion of different experimental protocols. Patients frequently interpret these approaches with excessive optimism and view their participation as an "end all, magical treatment" alternative to death. I propose that whether we are delivering recognized, standard care or performing clinical research through experimental protocols, our present data lacks the quality of information that allows meaningful interpretation of outcomes in this patient population. This was well documented in recent review by Steele, et al.,[8] who attempted to categorize the content and role of the routine follow-up visit for primary malignant gliomas and assess the effectiveness of such a follow-up visit in detecting tumor recurrence. All visits to the outpatient clinic of the Medical Oncology Clinic at St. Bartholomew's Hospital in London were retrospectively reviewed for 14 patients with glioblastomas multiforme and 22 patients with anaplastic astrocytomas. Detailed clinical activities at each routine follow-up visit were grouped according to adjustment of medications, detailed discussion with the patient or family, investigations ordered, and results of any consultations obtained. A prospective study was performed during a 6-month period on another 29 visits (16 patients with glioblastoma multiforme and eight with anaplastic astrocytoma). A survey instrument, based on the retrospective review analysis, was completed at the end of every visit either by the conducting physician or an observer of the consultation. This survey categorized the details of the visit.

In the retrospective group, the areas of clinical activity were the adjustment of steroid medication (44%), issues surrounding employment and leisure activities (14%), driving (6%), brain scan results (17%), ordering of neuroimaging (53%), and referral to rehabilitation services (11%). Prior to clinical confirmation in all 36 cases, the patient, relative, or caregiver first noted the symptoms of recurrence. In the prospective group, 20 patients remained clinically stable and four patients developed recurrent disease. Twenty-eight percent of visits dealt with the clinical activity including general physical examination; 100% dealt with the neurological examination; 35% with alterations in medication; 39% with ordering of scans; 4% other investigations; and 100% dealt with clinical and psychosocial factors. Ninety-three percent of outpatient clinical activity was directly tumor related. The results of this study demonstrated that the content of the average neurooncology visit makes determination of specific meaningful outcomes very challenging at best.

Outcome Subtypes

Outcomes can be divided into four different subtypes:[10] process outcomes, clinical outcomes, quality of life measures, and economic analyses.

Process Outcomes. Process outcomes are used to examine operational issues. An example would be the time expended from check in to the Emergency Department to completion of a computerized tomography

scan for a stroke patient considered for thrombolysis. Also included in this category are utilization measures and differences in health care delivery known as "small area variation" in health services research. These outcomes are often used to examine questions of system processing.

Clinical Outcomes. Clinical outcomes reflect clinical information about the patient and include data such as descriptions of mortality and morbidity rates, magnetic resonance imaging data, and laboratory evaluations. Eddy[4] refers to these measurements as intermediate health outcomes, which reflect what is happening to the patient but do not provide a direct measurement of the total impact on the patient. Historically, in neurooncology we have measured clinical outcomes, the most common of which include total survival time, time to progression, or impact as measured by neuroimaging (a scan showing either resolution, decrease in the size of the lesion, no change in lesion size, or interval enlargement). Neurological examination of the patient to determine clinical function has also been used. This examination does not assess neurological function. An alternative to the neurological examination, the the National Institutes of Health Stroke Scale,[2] has become popular in evaluating stroke patients. A formal evaluation tool such as this must have the characteristics that define an appropriate measurement instrument. Such an appropriate tool must discriminate, predict, and evaluate change[5] and provide a methodological framework for assessing health indices.

Quality of Life Outcomes. Quality of life outcomes are used to assess the direct impact of the intervention on the patient, referred to by Eddy[4] as the "Health Outcome." Neurooncology has led the way with the widespread use of the Karnofsky Performance Scale (KPS) (Table 1), which has been shown to be reliable and valid as an outcome measure of functional status.[6,7]

TABLE 1 KARNOFSKY PERFORMANCE STATUS INDEX		
Index	General Category	Specific Criteria
100	able to carry on normal activity - no special need	normally no evidence of disease
90		normal activity; minor signs or symptoms or disease
80		normal activity w/effort; some signs or symptoms of disease
70	unable to work; able to live at home & care for most personal needs; varying amount of assistance needed	cares for self; unable to carry on normal activity or to do work
60		requires occasional assistance from others
50		requires considerable assistance from others & frequent medical care
40	unable to care for self; requires institutional or hospital care or equivalent; disease may be rapidly progressing	disabled; requires special care
30		severely disabled; hospitalization indicates death not imminent
20		very sick; hospitalization necessary; active supportive treatment necessary
10		moribund
0		dead

Economic Outcomes. Economic outcomes estimate the cost impact of an intervention on the medical system or society, including cost determination, cost effectiveness, and cost benefit. They are of interest to individual hospitals and clinics, to payers, and to the society as a whole. These are the "evil necessities" of modern, fiscally aware, health care delivery.

In our neurooncology clinic, we have accumulated a great deal of data: demographic information, surgical information as to type and extent of procedure and location of disease, information regarding adjuvant treatment such as radio- and chemotherapy, as well as morbidity data, such as presence or absence of infection. We can calculate survival and, with more difficulty and less precision, determine the disease-free interval or time to progression. Review of our documentation for data extraction is challenging and imprecise, and the problem is confounded by an inability to draw clear distinctions from the measurements that are collected. Symptom documentation frequently is scant, and too many possible interpretations make it difficult to document patient function over time. The neurological examination is imprecise and lacks internal validity. The documentation of a hemiparesis or ataxia in the record does not allow for precise quantitative and qualitative distinctions to be made from one visit to another, unless one is using a recognized scale such as the National Institutes of Health Stroke Scale. Data concerning the results of timed interventions are frequently difficult to identify in the narrative record and thus raise real concerns about accuracy of all the information. The entire process of data extraction requires retrospective chart review, which is very costly, of questionable validity, and thus of questionable use.

This sad state of affairs therefore forces us as clinicians to look for more reliable measures to help in patient assessment. To be useful, these measures must define or screen for a functional change, are usually norm-referenced to a general population, and provide quantitative results. The measures must be reliable, consistent, and valid.[9] We need to redesign how we practice and the means by which we document what we do. A simple encounter form that documents the appropriate demographic, pathological, and diagnostic information and incorporates a standardized simple symptom assessment and neurological scale could be implemented to accurately measure patient change over time; this could easily be available on computers within the clinic. The measurements thus obtained would provide quantification of our assessment of neurological status of the patient but would not provide us any true reproducible functional information. The KPS was developed as an easily administered assessment tool to provide quantitative information about function in patients with brain tumors. This scale has been validated in the tumor population and is certainly simple and user friendly. However, although it is an integral part of most tumor therapy protocols at intake and at final assessment, it is rarely used by clinicians in ordinary practice not involving clinical trials. Through the implementation of a scale such as this, we can begin to relate the impact of the neurological examination on the patient's level of function. The symptom and neurological scale as well as the KPS are examples of clinical outcome scales meant to reflect the impact of the disease upon function, but they do not demonstrate the direct effect of the disease on overall quality of life.

The Short Form 36 is one of several scales used to measure the total impact of the disease on the patient's perception of his or her life. This instrument has been validated as an effective tool for evaluating the direct impact of the disease process and the effect of many potential interventions on patients.[1] This patient-report questionnaire takes only 10 minutes to fill out and is available in computerized format. Although well studied in stroke patients,[3] the Short Form 36 has not been used in studies of brain tumor therapy.

Dissemination and implementation of a simple encounter form, based on provider consensus, requires a major shift in our mindset. In this age of autonomy, we have a responsibility of providing patients with information on the potential harms and benefits of our interventional strategies. This must include clinical ("How long will I live?"), functional (What will I be able to do?), and well-being ("How well will I feel?") measures. Unless we include such measurements as these, it is impossible for our patients to make appropriate and informed clinical treatment decisions, as well as for us as clinicians to know what

treatments to offer. Only with such complete measures will we be able to know how well we are caring for the patient with a primary malignant brain tumor.

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