Quality of life in patients with stable disease after surgery, radiotherapy, and chemotherapy for malignant brain tumour

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Abstract

Objectives—to evaluate quality of life in patients with malignant brain tumour with stable disease after combined treatments in comparison to patients with other chronic neurological conditions, and to explore the relation of quality of life to clinical, pathological, affective and cognitive factors.

Methods—fifty seven patients who were stable after surgery, radiotherapy and chemotherapy and 24 controls with spastic paraparesis, peripheral neuropathies, myasthenia, ataxia, Parkinson’s disease, or multiple sclerosis, were studied. Patients were evaluated by functional living index-cancer, Karnofsky performance status, activity of daily living, self-rating depression scale, state-trait anxiety inventory, and tests for cognitive abilities.

Results—separate Mann-Whitney test comparisons did not show any difference in measures of health related quality of life (functional living index-cancer), autonomy in daily life (activity of daily living), or mood between tumour and control patients, although the first had slower mental speed and worse attention. Seventy three per cent of patients with brain tumour and 58% of the control patients continued or resumed previous work activity. Quality of life was significantly associated with depression, state anxiety, and performance status in the patients with brain tumour, whereas in control patients, state anxiety was the only factor related to quality of life.

Conclusions—after intensive multimodality treatments, selected patients with brain tumour with stable disease may have satisfactory quality of life that may be not worse than in patients with other chronic neurological illnesses. During the period of stable disease, depressed mood, possibly a reaction to impaired physical and cognitive performance, seems to play a major role in determining quality of life.

Keywords: malignant brain tumour; quality of life

Without further treatment after surgery, patients with high grade glioma survive about three months; whereas with intensive treatment patients with anaplastic astrocytoma can survive 36 to 60 months, and patients with glioblastoma survive 10 to 24 months. How-ever, combined postoperative therapies require repeated admissions to hospital that interfere with patients’ home and occupational lives and may also affect the lives of relatives. Furthermore these treatments cause early and late side effects that require clinical, haematological, neuroradiological, and neuropsychological assessment. Thus the efficacy of postoperative therapies in prolonging survival must be weighed against the possibly deleterious changes in patient lifestyle imposed by these therapies, and this can only be done by assessing the quality of life (QOL) during medium to long term follow up. Self reporting of acceptable or satisfactory QOL after aggressive multimodality treatments can reasonably justify such treatments even in the absence of greatly improved survival.

Unlike patients with other types of tumour (particularly lung, breast, and bowel cancer), patients with brain tumour are rarely assessed for QOL. Studies have assessed QOL in longterm brain cancer survivors and those with variable disease duration, but only a few studies have compared patients at different disease stages. The psychometric properties (face, constructional, and concurrent validity and reliability) of QOL instruments in patients with brain tumour have recently received more attention. For example, the functional living index-cancer (FLIC), a self administered visual analogue that explores different dimensions of QOL (physical, emotional, social and occupational aspects, and drug side effects), was investigated in a population of 837 patients with cancer and was shown to have appropriate content and structure validity, as well as concurrent validity with respect to Karnofsky performance status (KPS) and the state-trait anxiety inventory (STAI). In 101 patients with brain tumour, FLIC showed concurrent validity with respect to STAI, the self rating depression scale (SRDS), KPS, and attention tests, as well as discriminant validity with respect to disease status and tumour location. Another validated QOL instrument is the brain cancer module (BCM20); this is a structured questionnaire that explores emotional distress, future uncertainty, visual disorders, motor dysfunction, and communication deficit, using two parallel versions of 20 questions (one for the patient and the other for relatives). In 105 patients with brain tumour, BCM20 showed appropriate internal consistency, test-retest correlation, and discriminant validity for tumour recurrence and KPS score. There is also the brain module of the functional assess-
Quality of life in patients with brain tumour

The FLIC was used to measure QOL, and chosen because of its concurrent and discriminant validity in patients with brain tumour and its applicability to non-cancer patients. The FLIC contains 22 questions which cover six QOL dimensions: physical wellbeing (five questions), ability to work (three questions), emotional status (seven questions), sociability (two questions), family situation (three questions), and nausea (two questions). Patients answer the questions by placing a mark on a visual analogue scale divided into seven intervals; each interval corresponds to the response score and the total score is the sum of all responses (maximum score 154); higher scores reflect greater perceived wellbeing.

RATING SCALES FOR QOL

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The KPS, a physician assessed measure, was used only for the patients with brain tumour to evaluate daily and work performance. Part time work was included and daily activities (eating, dressing, bathing, mobility, and sphincter control) were assessed. Scoring was according to the original criteria (range 0–100), with a score of 90 or 100 indicating satisfactory functional status.40

The index of independence in activity of daily living (ADL)41 was administered to patients and relatives to assess patient autonomy in carrying out basic activities (eating, dressing, bathing, mobility, and sphincter control); high scores (range: 0–18) indicate good autonomy.

The psychological assessment of mood, STAI1 and STAI242 and SRDS42 were used. The scores (20–80) are proportional to the level of anxiety or depression; a score equal to or greater than 48 on STAI indicates anxiety; and a score equal to or greater than 50 on SRDS indicates mild to moderate depression. All scales were administered by the same neuropsychologist to all patients.

### NEUROPSYCHOLOGICAL TESTS

A preliminary clinical assessment was performed to verify that patients could understand the test procedures, thus excluding those with severely impaired auditory comprehension. Because cognitive abilities are often affected in patients with brain tumour,16 a short neuropsychological test battery was included to assess abstract reasoning (Raven’s coloured progressive matrices),43 attention (attentional matrices),43 visual-motor and conceptual tracking (trail making test),43 and episodic memory (story recall).43

### DATA ANALYSIS

To compare the mean scores provided by the self evaluation questionnaires and the neuropsychological tests in the two patient groups, separate Mann-Whitney tests were used, and the effects of age, education, and disease duration on the dependent variables were controlled for by separate regression analyses. Significance was assessed as a p level <0.005 (after Bonferroni’s correction for 10 measures at an overall error rate of α<0.05 for each factor).

In patients with brain tumour, Mann-Whitney tests were used to compare FLIC scores with demographic factors (sex, marital status) and surgical procedure (biopsy vs resection). Kruskall-Wallis one way analysis of variance (ANOVA) was used to compare patients on the basis of pathological factors (histological type, tumour location).

Pearson’s coefficients and multiple stepwise regression analysis were performed to explore the association of FLIC scores with KPS, STAI, SRDS, ADL, neuropsychological test scores, age, education, and duration of disease.

### RESULTS

Table 2 shows the mean scores, SD, and ranges for the scales and neuropsychological tests in the brain tumour and control groups.

#### COMPARISONS BETWEEN PATIENTS WITH BRAIN TUMOUR AND CONTROLS

Patients in the brain tumour group had a KPS score in the range 60 to 100, and 73% of them had resumed the job (including homemaker and part time work) they had ceased at the time of diagnosis. Fourteen control patients had impaired physical autonomy and sometimes needed a wheelchair or walking stick. Fourteen control patients (58%) resumed previous work (including part time work).

As required by the selection criteria, no patients had aphasic disorders of severity such as to impede test administration or form compilation. To control for deficits in abstract reasoning, individual scores on Raven’s coloured progressive matrices were adjusted for age and education. Four patients with brain tumour had an adjusted score of 18 that is the cut off for normal and pathological performance, and one patient obtained an adjusted score of 12

### Table 1. Demographic and clinical characteristics of patients with brain tumour and controls

<table>
<thead>
<tr>
<th>Tumour type:</th>
<th>Neoplastic tumour</th>
<th>10</th>
<th>Anaplastic oligodendroglioma</th>
<th>2</th>
<th>Anaplastic astrocytoma</th>
<th>37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumour location:</td>
<td>Posterior right hemisphere</td>
<td>9</td>
<td>Posterior left hemisphere</td>
<td>8</td>
<td>Midline</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Anterior right hemisphere</td>
<td>15</td>
<td>Anterior left hemisphere</td>
<td>11</td>
<td>Subtentorial</td>
<td>2</td>
</tr>
</tbody>
</table>

**Values in parentheses are SD.**

### Table 2. Mean scores (SD) and ranges for the self administered scales and neuropsychological tests in brain tumour and control patient groups

<table>
<thead>
<tr>
<th></th>
<th>Brain tumour</th>
<th>Control patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLIC</td>
<td>116.63 (21.37)</td>
<td>105.46 (19.5)</td>
</tr>
<tr>
<td>ADL</td>
<td>17.07 (1.82)</td>
<td>17.21 (1.56)</td>
</tr>
<tr>
<td>KPS</td>
<td>85.96 (12.66)</td>
<td>60–100</td>
</tr>
<tr>
<td>STAI-1</td>
<td>41.35 (12.66)</td>
<td>47.08 (12.09)</td>
</tr>
<tr>
<td>STAI-2</td>
<td>42.16 (11.47)</td>
<td>42.71 (10.67)</td>
</tr>
<tr>
<td>SDRS</td>
<td>39.28 (10.06)</td>
<td>37.42 (7.66)</td>
</tr>
<tr>
<td>Progressive matrices</td>
<td>27.86 (6.37)</td>
<td>26.0 (5.22)</td>
</tr>
<tr>
<td>Attentional matrices</td>
<td>20–73</td>
<td>17–61</td>
</tr>
<tr>
<td>Trail making test part A</td>
<td>7–36</td>
<td>7–35</td>
</tr>
<tr>
<td>Trail making test part B</td>
<td>15–60</td>
<td>15–60</td>
</tr>
<tr>
<td>Story recall</td>
<td>46.81 (12.74)</td>
<td>50.79 (6.21)</td>
</tr>
<tr>
<td></td>
<td>40–59</td>
<td>40–59</td>
</tr>
<tr>
<td></td>
<td>25–420</td>
<td>25–360</td>
</tr>
<tr>
<td></td>
<td>60–100</td>
<td>60–100</td>
</tr>
<tr>
<td></td>
<td>10–18</td>
<td>12–18</td>
</tr>
<tr>
<td></td>
<td>0–100</td>
<td>0–100</td>
</tr>
<tr>
<td></td>
<td>60–995</td>
<td>60–995</td>
</tr>
<tr>
<td></td>
<td>1.5–23.5</td>
<td>1.5–23.5</td>
</tr>
</tbody>
</table>
Quality of life in patients with brain tumour

The patients with tumour had better FLIC scores and worse trail making test (part B) scores than controls. However, separate Mann-Whitney tests did not show any differences between the tumour and control groups in terms of score for FLIC ($U=476.5$, $p=0.031$), ADL ($U=674$, $p=0.89$), STA1 ($U=502$, $p=0.059$), STA2 ($U=641$, $p=0.65$), SRDS ($U=618$, $p=0.49$), Raven’s coloured progressive matrices ($U=533$, $p=0.11$), attentional matrices ($U=624$, $p=0.53$), trail making test part A ($U=673.5$, $p=0.91$) and B ($U=624$, $p=0.53$), or story recall scores ($U=637$, $p=0.62$). As assessed by separate multiple stepwise regression analyses, the level of education had effects on the scores of STA2 ($p=0.03$), Raven’s coloured progressive matrices ($p=0.0001$), trail making test part A ($p=0.02$) and B ($p=0.001$), and story recall ($p=0.01$). Age had a significant effect on Raven’s coloured progressive matrices ($p=0.008$), whereas disease duration had no effect on any score.

RELATION OF FLIC SCORE TO PATHOLOGICAL, CLINICAL AND NEUROPSYCHOLOGICAL FACTORS

Separate Kruskall-Wallis one way ANOVAs comparing patients with brain tumour on the basis of tumour location (anterior right $112.66$ (SD 21.42)) surgical procedure (biopsy $119.50$ (SD 21.97), craniotomy $113.58$ (SD 20.79), resection $116.02$ (SD 21.88)) sex (males $114.73$ (SD 21.08), females $118.74$ (SD 21.13)), age, education, disease duration, or scores from the self evaluation and neuropsychological tests. Multiple stepwise regression analysis with the same independent factors used in patients with brain tumour showed that FLIC score was associated with STA1 score ($F=5.04$, $p=0.035$).

Discussion

This study explored QOL in a highly selected sample of patients with brain tumour who were well enough to receive combined postoperative radiotherapy and chemotherapy and were stable thereafter. The control group was a heterogeneous group of patients with chronic disabling disorders of the central or peripheral nervous system.

Mean FLIC score, a health related QOL measure, was 116 in our patients with brain tumour. This is higher than the 107 reported by Schipper et al in a general cancer population, and the 107 reported in patients with lung cancer. This suggests that aggressive combination treatment of patients with brain tumours does not necessarily affect QOL more than therapies used for cancer not involving the nervous system, although brain radiotherapy and chemotherapy may have late effects on cognitive abilities and daily performance. The results of this study further indicate that QOL, as expressed by FLIC and instruments assessing specific dimensions of QOL (mood, daily performance, autonomy), is not worse in patients with brain tumour than in patients with other chronic neurological diseases. This may be in part because the patients with brain tumour were chosen for chemotherapy on the basis of good performance status ($KPS \geq 60$) which could be a prognostic factor for good QOL after treatment. Furthermore, as required by the selection criterion of stable disease, these patients did not have seriously disabling motor or cognitive impairment, and only 14% had glioblastoma. Nevertheless, it is likely that these results can be generalised to patients with stable disease, including patients with glioblastoma, as status of disease, and not histological type, is the main influence on QOL after combined treatments. However, the present patient sample is not representative of patients with brain tumour in general, because it specifically excluded untreated patients and those with recurrence of disease.

It is noteworthy that 73% of patients of this tumour series resumed their previous occupations, compared with 38% of control patients, even though the level of autonomy in everyday activities (as expressed by ADL) was similar in the two patient groups. This suggests that the ability to work (closely related to the perception of satisfactory QOL) is not compromised by combination treatments in all patients with brain tumour and is in accord with the findings of Kleinberg et al who reported that 68% of patients with stable disease returned to work after surgery and radiotherapy, 62% of whom were at work 1 year later, and 58% of whom were still working after 2 to 4 years.

None of the patients with brain tumour in this study were demented or had disabling comprehension difficulties, thus the answers...
they gave in the self evaluation questionnaires are probably reliable and provide a real measure of QOL. Mental slowing was evident and related to the level of QOL, indicating that compromise of attention may play a part in determining wellbeing in these patients.

Patients with brain tumour and controls did not differ in self reporting of depression or anxiety. However, in the brain tumour group depression and state anxiety were closely associated with QOL, whereas in the control group QOL was associated only with state anxiety, suggesting that different factors are modulating mood in the two groups. Although the patients with brain tumour knew their diagnosis, a detailed assessment of what each knew about the prognosis was not carried out. In no case was survival or dying openly mentioned by these patients. Families tried to protect patients against the truth, and it is the policy of medical staff never to remove hope. The overall impression was that the QOL found in these patients represented that of patients who knew they had a serious disease, but that the prognosis was not hopeless. We therefore conclude that depressed mood in these patients with brain tumour, the main predictor of QOL, is a consequence of the disruption of everyday life and future plans brought about by the extended therapies; perhaps it is also a reaction to the physical and cognitive impairment caused by the tumour and its treatment, but is not due to awareness of a hopeless prognosis.

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