

A Follow up Study about Quality of Survival after Radiotherapy for Malignant Cerebral Glioma as well as the Views of Relatives

Wanfu Xie

Department of neurosurgery, First Hospital of Xi'an Jiaotong University, Xi'an 710061, China

Abstract Objective To explore the views of bereaved relatives about quality of survival after radiotherapy for malignant cerebral glioma. **Methods** 56 patients with cerebral glioma were treated at the First affiliated Hospital of Xi'an Jiaotong University from 2003 to 2006. All patients were followed up and their survival data and the views to life quality of bereaved relatives were analyzed retrospectively. **Results** Relatives described quality of life as "good or acceptable" when patients carried on some normal activities or enjoyed social relationships. They described restricted and dependent states, constant deterioration, or loss of social interaction as giving "poor or unacceptable" quality of life. Length of time lived in such states also appeared important. Relatives' views of good or acceptable quality of life were independently related to low initial cognitive or personality change or low distress in the patients after diagnosis, and to their subsequent survival free from physical disability for at least one month. Satisfaction with radiotherapy was related to low initial distress, some degree of surgical resection, and overall length of survival longer than six months. **Conclusion** Carefully exploring the views of bereaved relatives can bring a useful perspective to difficult treatment decisions. Their values support including disability and distress in quality of life measures, but cast doubt on the Quality Adjusted approach of using full years of survival or time free from disability to judge whether treatments are worthwhile.

Key words Cerebral glioma; Quality of survival; Radiotherapy

Radiotherapy for malignant cerebral glioma provides one example of a potential trade off between the quality and length of life. Two randomised controlled trials showed that radiotherapy prolongs the median survival after surgery from three months to about five years. However, radiotherapy takes six weeks and may cause many adverse effects including hair loss, tiredness and somnolence, deterioration, and irreversible cognitive problems. Because many patients present with some disability and most die within one year, Some report which has published estimates of the cost for each Quality Adjusted Life Year (QALY) have generally been

high. However, some clinicians find suggestions of withholding treatment to be nihilistic, whereas others question the value of life assumed in cost effectiveness evaluations.

We previously described a study of 92 patients and their close relatives or careers where we attempted to explore their views about this trade off. We had been surprised to find that only one quarter of the 75 patients whom we interviewed as they began radiotherapy appeared to be fully aware of their poor prognosis, compared with three times the number of relatives. However, most aware patients seemed willing to undergo treatment for the chance of longer survival. We did not find evidence that most of them regretted treatment, despite experiencing only brief remissions or adverse effects. We suggested that patients gained hope from treatment, from the protection relatives and doctors provided, and from their own psychological defences. We argued that this powerful response to life threatening illness makes any question of a rational trade off less

Correspondence to: Wangfu Xie

Department of neurosurgery, First Hospital of Xi'an Jiaotong University, Xi'an 710061, China

Email: goodwang2004@163.com

relevant than well individuals might predict. In our current study, we explore the views of bereaved relatives about the quality of patients' survival and compare these with some assumptions made by the QALY-type approach to judging brief periods of survival as worthwhile.

MATERIALS AND METHODS

Recruitment and follow up of relatives for the study

Our previous study comprised 92 patients received radiotherapy between 2001 to 2003 at the First affiliated Hospital of Xi'an Jiaotong University and 85 relatives. Eighty relatives saw us again after the initial interviews, and 73 became bereaved between 2003 to 2006. We obtained local ethical approval to interview bereaved relatives. We first sent a letter of condolence, and four to six months after the death we wrote again to ask to interview them concerning further thoughts about the illness or treatment. We emphasised that this was entirely voluntary and telephoned two weeks later to hear their decision. By late 2005, when the project ended, 69 relatives had been bereaved for at least four months and could be contacted. Fifty eight agreed, although four delayed the visit for up to 12 months and four preferred to talk on the telephone. To see whether their views changed we approached relatives again 13 months after bereavement. By late 2006, 32 relatives had reached this point, but we found that a higher proportion (12 of 32) declined interview here, mostly saying that they felt they had no more to tell us or did not wish to go over painful memories again. However, 20 did agree to a second interview, one by telephone. In all but one instance the same interviewer visited as before.

Data collection

Semi structured interviews with the bereaved relatives of 56 previously studied patients with glioma: Patients treated surviving between one and 46 months (median, eight). Subjects: Fifty six relatives (44 spouses, 12 others) were seen four to six months after bereavement and 20 again in 13 months. Main outcome measures: Views about quality of life and satisfaction with

radiotherapy.

We had previously collected data on the clinical state of each patient after the diagnosis, such as their initial disability, score on the Medical Research Council (MRC) Prognostic Index, the treatment times.

Information Analysis

Our method followed the tradition established by research into life events and illness. This has provided a model for attempting to move from initial qualitative descriptions of events to simple categorisations that can then be compared with independent clinical factors. This approach relies on: (1) a careful reading of the comments to identify common themes within examples, (2) devising explicit rules by which examples may be categorised depending on the themes within them. (3) checking the inter-rater reliability when two or more interviewers use the rules to make independent ratings on the same examples. For this exploratory analysis, we extracted all qualitative comments about quality of life and radiotherapy from the first 21 transcribed interviews. These had mostly been conducted by one of us (ED), who identified by content analysis some themes for descriptions of quality of life from them. It initially seemed that the examples might fall into a simple dichotomy—overall, whether relatives felt the patient's quality of life had been "good or acceptable" or whether they thought it had been "poor or unacceptable".

Some examples of the themes and comments made by the relatives about the patients' quality of life after radiotherapy. A similar dichotomy did not seem possible for views about radiotherapy because these appeared to fall into three responses: "satisfied", "uncertain", or "dissatisfied". The 21 examples were organised into these simple categories for quality of life and satisfaction with radiotherapy and discussed within the research team. Another interviewer then independently used them as a guide to extract comments and rate examples from the next 40 interview transcripts, most of which she had conducted herself. When ED independently rated this second set of examples, inter-rater reliability between the two interviewers was good (values: 0.73 for quality of life and 0.87 for radiotherapy). Given this high level

of reliability it did not seem necessary to undertake a more detailed qualitative analysis to identify further themes to guide the ratings. We settled differences by discussion and ED rated comments from the remaining 18 interviews that had mostly been conducted by a third interviewer. These ratings could not be made blind to any knowledge about the trajectory of each patient's illness because each case had been discussed within the team previously as the project progressed. However, the ratings were made several years before this and analyses already published. 10 Social class was rated directly into the then current Registrar General's classification using information on the relative's occupation. It is not possible to update this to a more recent classification because the supporting details were not retained.

Some examples of comments made by relatives about their satisfaction with radiotherapy. For the current analysis, we compared relatives' views to previous ratings and observations on the course of the illness using the two tailed Person's χ^2 test or χ^2 test for trend. We then explored, using a backwards conditional logistic regression analysis, which aspects of the initial illness and its course were most independently associated with the relatives' later views.

RESULTS

Characteristics of relatives and deceased patients

In two cases we did not collect enough information to rate individual views and we therefore report the results of 56 relatives four to six months after bereavement and 20 relatives at 13 months. At the first interview there were 35 widows, nine widowers, four parents, and eight other relatives (median age, 52; range 24~75 years). The 56 relatives seen for the first bereavement interview did not differ from those seen during the illness. However, of the 32 approached again 13 months after bereavement, those who had already described the quality of the patient's life as poor or unacceptable more often refused the second interview than those describing a good or acceptable quality of life (10 of 17 v 2 of 15; $\chi^2=5.23$; degrees of freedom (df), 1; $P<0.05$). The 56 patients described by relatives at their first interview had survived between one and 46 months (medi-

an, eight) and were broadly similar to the original cohort. We had data on the course of the illness for all 56 patients, and their own views about improved problems and radiotherapy for 34 who had been well enough for two interviews during the illness.

The point of view of bereaved relatives about quality of life

The first 21 comments from relatives suggested three themes contributing to the perception of good or acceptable quality of life. These were being "fit" and having "a normal life"—for example, working, carrying on interests, or looking after their family, improving some way towards "normal life", and being able to do some things and enjoying close relationships or friendships despite some disability. Using the simple scale based on these we rated two fifths (22 of 56) of relatives as feeling that the quality of life had been good or acceptable. In contrast, themes for poor or unacceptable quality of life for the remainder (34 of 56) were severe disability restricting activities leading to dependence or distress, loss of normal personality and interactions, constant deterioration, and existing in a state worse than death. Examples of comments around these themes. These may appear stark but their context was often a long, detailed description of both the illness and their grief. In this sample, relatives' views were unrelated to their own age, education, social class, or relationship to the patient. However, men were more likely than women to describe the quality of life of the patient as good or acceptable (eight of 12 v 14 of 44; $\chi^2=4.80$; (df), 1; $P<0.03$).

The point of view of bereaved relatives about radiotherapy

Just below one half of the relatives (26 of 56) were rated as satisfied with radiotherapy, judging that the patients had improved, remained able to do things they enjoyed, or that their deterioration had been slowed. Others placed value on the time the patients gained with their family and the hope that radiotherapy had brought. Nearly one fifth (10 of 52) were less certain, feeling that the patients had not improved or survived as long as they had expected. They observed that the pa-

tients had been willing to try treatment and that this may have been the correct decision for them, but looking back they would be sceptical of accepting such treatment themselves. The remainder—just over a third (20 of 56)—were dissatisfied, feeling that radiotherapy had made no difference, kept the patients alive in a damaged state, detracted from the quality of life, or simply wasted precious time. Satisfaction with radiotherapy and views about quality of life were closely related. Only one relative who thought quality of life had been good or acceptable (one of 22) felt dissatisfied with radiotherapy compared with just over one half (19 of 34) of those who perceived quality of life to have been poor or unacceptable ($\chi^2=23.86$; $df, 2$; $P<0.001$). Of the remaining 15, eight were uncertain about the value of radiotherapy. Too few patients (seven of 34) had been dissatisfied to relate this to relatives' views. However, relatives' views were not related to demographic characteristics, and only two of the 20 seen again expressed different views at the second bereavement interview.

The point of view of bereaved relatives relate to the course of the patients' illness

The relatives' views about quality of life were related to the patient's age and score, a range of initial aspects of the illness (extent of surgery, initial distress, and disability), its course (time lived free from disability and overall survival), and to patients' and relatives' reports of improvement after treatment (in the 34 cases where we had these data). There were similar associations with satisfaction with radiotherapy. At least one half of the relatives expressed satisfaction with radiotherapy even when patients had lived for only one to five months free from disability (10 of 18) and survived six to 12 months overall (12 of 21).

A backwards conditional logistic regression analysis

To determine which factors were independently associated with bereavement views, we entered those factors that seem to be related, and for which we had near complete data, into a backwards conditional logistic regression analysis (This analysis concerned 53 cases because data on distress were missing for three patients who had been too confused for us to make this initial

rating confidently). The factors that emerged as associated with good or acceptable quality of life were initial cognitive or personality change in the patient (partial odds ratio (OR), 4.39; confidence interval (CI), 1.40 to 13.79), the time they lived free from physical disability (partial OR, 2.5; CI, 1.00 to 6.29), and the degree of the patient's initial distress (partial OR, 2.56; CI, 0.98 to 6.73). (We include the last factor because it is very close to a two tailed level of significance: $P<0.055$). When these initial aspects of the illness and its course are considered together a fairly straightforward picture emerges. Where there was initially either high psychological change or distress, very few relatives considered that the quality of life had been good or acceptable, irrespective of the time the patient lived free from severe physical disability. However, without these initial profound problems, there is a clear gradient in terms of the acceptability of the patient's life according to the length of time they lived free from physical disability: over four fifths felt that quality of life had been acceptable when the patient achieved six or more months free from physical disability ($\chi^2=4.88$; $df, 2$; $P<0.03$).

Following the same procedure, extent of surgery (partial OR, 6.40; CI, 1.61 to 25.40), overall length of survival (partial OR, 3.15; CI, 1.22 to 8.16), and initial distress (partial OR, 2.59; CI, 0.99 to 6.82) emerged as associated with later satisfaction with radiotherapy (again, we include the last factor with a p value of 0.053). There was a high rate of satisfaction among relatives of patients who had either partial or complete resection, irrespective of the length of time the patient survived. The slight drop for those with less than six months of survival is well short of significance. However, for relatives of patients who had only a biopsy, there is a marked correlation between satisfaction with radiotherapy and the length of time the patient survived ($\chi^2=5.38$; $df, 1$; $P<0.02$). If initial distress is taken into account the same picture emerges (data available on request).

DISCUSSION

In our study, we interviewed bereaved relatives of adults with malignant cerebral glioma to explore their views on the quality of survival of 56 patients we had

previously studied. We found that relatives expressed a wide range of views about quality of life^[1], describing this as good or acceptable when they saw that patients carried on some normal activities or enjoyed social relationships, and as poor or unacceptable when the patients were restricted and dependent states, constant deterioration, or loss of social interaction. Their descriptions of good or acceptable quality of life could be related to previously recorded aspects of the course of the illness and to the patients' and relatives' own reports of improvement after treatment. Three aspects—the patient's initial distress, cognitive or personality change shortly after the diagnosis, and the time they lived free from disability—emerged as independently associated with relatives' later views. Where the patients did not suffer initial profound psychological change or distress, relatives saw increased time lived free from physical disability as providing good or acceptable quality of life^[2]. For satisfaction with radiotherapy the extent of surgery, initial distress, and overall length of survival were most important. Relatives of patients undergoing some form of resection were satisfied with radiotherapy, irrespective of overall length of survival, but the relatives of patients undergoing only biopsy were less likely to be satisfied with radiotherapy unless the patient survived longer than 12 months.

This is an exploratory study comprising a small number of relatives, most of whom were come from higher social classes describing similar men. We used standard measures to assess disability and attempted to develop other ratings for quality of life and satisfaction with radiotherapy based on the views and emotions expressed independently by patients and relatives at separate interviews. We achieved high reliability for our ratings but we did not include a detailed formal assessment of the patients' cognitive ability or of the relatives' grief. The relation between the relatives' views after bereavement and those obtained during the illness could possibly represent some measurement bias in interviews. Although our study elicited relatives' views about quality of life that described mostly its health related aspects, these were not entirely explained by objective aspects of the illness that we were able to measure. Undoubtedly, there are other relevant meanings for quality of life in-

cluding cultural, spiritual, and personal aspects that we could have explored further^[3]. However, the strength of relatives' views surprised us, and as far as we could determine these did not change radically in the first year after bereavement.

One other study of adults with malignant cerebral glioma has combined data from 28 patients and their bereaved relatives to define the "time of everyday life" where life resembled that before the illness in at least a couple of areas such as work, family, and social life. Sallander and colleagues^[4] found a median of six months and distinguished this from "time of disease"—where life was disrupted and centred around the illness and its treatment (median, 5.4 months). They argued that patients could experience "time of everyday life" despite objective disability or disease progression, and suggested that hope is not simply about cure, but may be created by the patient's ability to adapt and re-experience everyday life. No study has asked bereaved relatives about radiotherapy. Our earlier study showed the difficulty in asking patients directly about any trade off from treatment, but suggested that they were willing to undergo this for the chance of improvement or longer survival. The emphasis that bereaved relatives place on relatively brief periods of improvement and survival is consistent with this impression.

Although our sample seems similar to patients in treatment trials, critics disputed that it was typical of those receiving modern focused radiotherapy within specialised centres. If, as we suggested, some patients experienced adverse effects from treatment, there might be higher satisfaction after more effective palliation. Our finding that relatives' satisfaction with radiotherapy was higher in patients who had undergone some surgical resection might be explained by the fact that removing part of the tumour made patients better able to tolerate any subsequent oedema or tissue damage as a result of radiotherapy^[5]. We believe our results support the clinical view that radiotherapy can provide short periods of survival that are highly valued, but should be offered hesitantly to patients already disabled after diagnosis. The views of bereaved relatives are not a proxy for patient choice, because with time relatives may reinterpret events and overestimate specific symptoms. Therefore,

our results provide useful information for clinicians counselling patients, but not an easy answer for treatment decisions.

In recent years, health economists have been interested in developing models to compare the cost of different treatments in terms of each QALY gained. This has generally involved asking well individuals to predict the value or "utility" they place on varied future states of disability and distress, combining and weighting their scores, and applying them to different clinical trajectories. Where outcome or survival is poor, data from several patients may need to be combined to achieve one QALY. Early calculations based on estimated trajectories suggested a cost of over 50000¥ for treating malignant cerebral glioma, although retrospective and prospective studies of real patients now find lower costs. Our finding that relatives' views about quality of life are related to initial distress and time spent without disability supports including these factors within such indices as they were originally developed. However, the value relatives place on brief periods of survival questions the later notion of assessing treatments as worthwhile by full years free from disability and distress, and of summing individual trajectories across one diagnosis of varying prognoses.

Malignant cerebral glioma is an extreme disease that gradually steals physical, cognitive, and social ability, and therefore tests our conception of quality of life ^[6]. Our study and others suggest that, despite the severity of the situation, patients can cope with and find hope within their situation. With first hand knowledge of an individual trajectory, their relatives did not always reinterpret

this earlier hope as "false", or necessarily regret radiotherapy. These outcomes may seem modest but the issue seems one of perspective. If doctors see things differently from the patients they treat, and relatives in turn have different views from the patients they care for, there seems little chance of well individuals accurately predicting their own response. We suggest that to be meaningful, QALY-type approaches need to be more grounded in the situations they purport to represent, rather than in the statistical manipulation of values expressed in the abstract.

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