

Quality of survival in treated patients with supratentorial gliomata

M. J. BETTY

From the Department of Neurological Surgery, Royal Infirmary, Sheffield

Many papers on the results of surgical removal of gliomata have been published, but few have given adequate details of the quality of survival. In the last decade, reviews of large series, consisting mainly of cases of glioblastoma multiforme, have been given by Davis, Martin, Goldstein, and Askenazy (1949), Penman and Smith (1954), Frankel and German (1958), Tönnis and Walter (1959), Bettag (1959), Roth and Elvidge (1960), and Ley, Ley, Guitart, and Oliveras (1962). These have been concerned with detailed analyses of symptoms and signs and the duration of post-operative survival, but the quality of survival has been only briefly mentioned. This may be due to difficulty in obtaining adequate follow-up information, and some of the papers deal with the combined results of several surgeons. The present paper is concerned mainly with the quality of survival in a group of patients treated by one surgeon, and the pathology has been studied by one neuropathologist, so that there has been uniformity in treatment and histological grading.

MATERIAL FOR ANALYSIS

There were 430 adult patients with supratentorial gliomata, diagnosed, treated, and followed up by Mr. James Hardman over a nine-year period from 1950 to 1958. The tissue obtained at operation and necropsy was studied by Dr. Lionel Wolman. In-

formation about the patients has been obtained mainly by regular follow up in the Out-patient Department, supplemented by information from the family doctor, and in a few by letters from relatives.

Analysis of the quality of survival has been carried out on 260 treated patients for whom full histological details are available. Table I gives the incidence of tumours in the different sites and the type of treatment given.

All the tumours have been graded according to the degree of malignancy, using Kernohan's simplified classification of gliomata (Kernohan, Mabon, Svienc and Adson, 1949). Astrocytomata grades III and IV would correspond to the glioblastoma multiforme of other surveys. The incidence of the various types and grades is given in Table II.

The operation specimens have been studied microscopically in multiple sections taken at right angles to determine the completeness of removal of tumour. One must emphasize here that all except three of the resections were reported as incomplete removals. Complete removal of a grade IV astrocytoma in the occipital lobe was confirmed at necropsy the patient dying from a post-operative haemorrhage. One patient who was believed to have had complete removal subsequently died from a recurrence of the tumour. The third patient is still alive eight years after an occipital lobectomy for an oligodendroglioma.

TABLE I

TREATMENT GIVEN FOR EACH SITE¹

Site	Total	Not Treated	Lobectomy	Local Excision	Decompression	Torkildsen	Deep X-ray Therapy
Frontal	111	30	64	16	—	—	—
Temporal	122	25	95	1	1	—	—
Occipital	36	11	24	1	—	—	—
Parietal	31	11	—	18	—	—	2
Central	40	23	—	11	3	—	3
Multiple lobe	43	24	10	5	1	—	3
Deep (basal ganglia + thalamus)	23	16	—	—	1	4	1
Corpus callosum	22	18	—	—	—	3	1
Lateral ventricle	2	—	—	2	—	—	—
Total	430	160	193	54	6	7	10

¹In the patients included in the lobectomy and local excision columns approximately two-thirds of those with malignant tumours were given deep x-ray therapy as well. In the last column this was the only form of treatment given.

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TABLE II
HISTOLOGICAL GRADES

Grade	No. of Cases
Astrocytoma grade IV	173
Astrocytoma grade III	95
Astrocytoma grade II	36
Astrocytoma grade I	38
Oligodendroglioma	7
Oligo-astrocytoma grade IV	6
Oligo-astrocytoma grade III	12
Oligo-astrocytoma grade I	2
Ependymoma grade IV	5
Ependymoma grade III	2
No histology available	54
Total	430

TREATMENT

Just over one third of the 430 patients did not receive any treatment, either because they died soon after admission or because severe neurological defects made treatment unjustifiable. The aim in the management of the supratentorial tumours in this series has been to provide a large internal decompression wherever possible. To this end 193 extensive resections of the frontal, temporal, and occipital lobes were carried out. Removal of this amount of brain tissue will relieve the pressure and at the same time provide room for later growth of the tumour.

Tumours in the parietal, central, and posterior frontal areas cannot be treated by extensive resections without producing unjustifiable neurological deficits, and in these sites 54 small removals, referred to in this paper as 'local excisions', were performed.

Simple decompression of the tumour is regarded as a bad practice because of the hideous deformity which results when the flap bulges following continued growth of the tumour. A decompression was carried out on only six patients in this series, and in these only because of uncertainty about either the location or pathology of the tumour at the time of the operation.

Deep x-ray therapy was given post-operatively to about two-thirds of the malignant tumours (astrocytomata grades III and IV). The exploration rate has been kept high in this series even in the older age groups. Tumours in the dominant hemisphere have been treated in exactly the same way as those on the non-dominant side, and extensive resections (lobectomies) performed.

METHOD OF ANALYSIS

For each site the patients have been allocated to one of four groups: 1 post-operative death; 2, chronic sick bed; 3, work; and 4, home. Post-operative death was regarded as such if it occurred within the first month.

The 'chronic sick bed' group included all those who died without leaving hospital. They either remained in the neurosurgical unit, were sent back to the referring hospital, or were transferred to a chronic sick hospital.

It was necessary to consider men and women separately in the 'work' and 'home' group. Most of the women were married and would be expected to return home, so it was decided to ascertain the number capable of full domestic duties (which would correspond with the 'work' group for men) and those only capable of partial domestic duties (corresponding with the 'home' group for men). In expressing figures and percentages for all treated adults, the 'full domestic duties' group for women has been combined with the 'work' group for men, and the 'partial domestic duties' group for women combined with the 'home' group for men.

Information for allocation of patients to these groups has been obtained from the patients themselves, their relatives, and from the family doctor. The decision to place a woman in the 'full domestic duty' group usually depended on her being capable of doing all the shopping, but the two subdivisions for women probably do not have the same accuracy as the 'work/home' groups for men. Even for the latter, the fact that a man returned to work does not necessarily mean that he was capable of his pre-illness efficiency, as he might be 'carried' by considerate employers or sympathetic colleagues.

The patients who returned home have been studied further to determine the incidence of major neurological defects. These will greatly influence the quality of survival, and will indicate if the patient has been kept alive with an unjustifiable handicap.

DURATION OF SURVIVAL

The results in the present series of patients are very similar to those previously published. All the patients who have died did so as a result of the cerebral tumour, except one, who died from a coronary thrombosis three years after a lobectomy.

The malignant tumours (astrocytoma grades III and IV) will be considered first. Taking all lobectomies performed for frontal, temporal and occipital tumours, the average post-operative survival time for the combined grades III and IV was 8.3 months (110 patients). For the astrocytomata grade III alone it was 10.7 months (39 patients), and for astrocytomata grade IV alone it was 6.9 months (71 patients). Local excisions were performed in 27 patients with malignant tumours (9 frontal, 13 parietal, 4 central, 1 temporal), and the average survival for grade III plus grade IV was 11.7 months. The longest survival time following treatment for a

malignant astrocytoma was three years six months. There were two patients who survived for this time. One had a frontal lobectomy and deep x-ray therapy for a grade III astrocytoma, and the other had a local excision followed by deep x-ray therapy for a grade IV astrocytoma in the central area.

The relatively benign astrocytomata, grades I and II, give much better results for length of survival following operation. For all sites, except the corpus callosum and basal ganglia region, and for combined lobectomy and local excisions, the average survival time for grade I plus grade II was 3.9 years (35 patients). Table III gives a better picture of the survival time of the patients with benign gliomata, by stating the number alive after given periods. It includes all forms of treatment, and besides the astrocytomata grades I and II, includes the oligodendrogliomata and oligo-astrocytomata grade I (total 61 patients).

TABLE III

POST-OPERATIVE SURVIVAL TIME IN ADULTS WITH ASTROCYTOMATA GRADES I AND II AND OLIGODENDROGLIOMATA

Survival Time	No. of Cases
Post-operative deaths (first month)	7
1 to 6 months	9
6 months to 1 year	6
1 to 2 years	9
2 to 4 years	11
4 to 6 years	9
6 to 10 years	10
Total	61

PATIENTS STILL ALIVE

There are 23 patients still alive and being followed up. The shortest follow-up period was 1 year 8 months. Nine patients are working and 14 are at home (eight men and six women, doing partial domestic duties). Ten of the 14 at home have major neurological defects. Twelve patients have survived four years or more and these all have relatively benign tumours, except for one with an oligo-astrocytoma grade III.

RESULTS

The operative mortality for the 250 patients treated by surgery was 15.3% (Table IV). The causes of these deaths in the first month included tentorial coning unrelieved by operation, post-operative oedema or haemorrhage, cerebral infarction, meningitis, pulmonary embolism, bronchopneumonia or lung abscess, and massive pulmonary collapse.

Of the patients, 18.4% were too ill or too disabled to be sent home and spent the rest of their days in chronic sick beds. Only 12.6% were able to return to work or full domestic duties. The men did better

TABLE IV
QUALITY OF SURVIVAL IN 260 TREATED ADULTS

Site	Treated	Work	Home	Chronic Bed	Operative Mortality
Frontal	76	14 (18.4%)	40 (31.3%)	12 (15%)	10 (13.1%)
Temporal	97	10 (13.7%)	56 (56.7%)	18 (18.5%)	13 (13.4%)
Occipital	25	2	18	2	3
Parietal	20 (2)	1	13	5	1
Central	17 (3)	2	9	3	3
Multiple lobe	19 (3)	3	2	7	7
Deep	2 (1)	—	—	1	1
Corpus callosum	2	—	—	—	2
Lateral ventricle	2	1	1	—	—
Total	260 (9)	33 (12.6%)	139 (53.4%)	48 (18.4%)	40 (15.3%)

Figures in brackets in treated column refer to those given only radiation treatment.

than the women, as 15% returned to work, compared with 8.8% of the women returning to full home duties.

Comparing the patients with tumours in the right and left hemispheres, the number returning to work was almost equal, 17 on the right and 16 on the left. The number of right and left tumours in the whole series was approximately equal (right 214, left 208) but more patients with left-sided tumours were rejected for treatment (80 compared with 62 on the right). As equal numbers returned to work for each side, it seems that those with left hemisphere tumours actually treated have at least an equal chance of returning to work as those with right hemisphere tumours.

As might be expected the frontal tumour group produced the highest percentage at work (18.4%), followed by temporal tumours (13.7%).

The post-operative survival period for those returning to work ranged from less than one year (two patients) to nine years. Eighty per cent or more of the post-operative survival time was spent at work by the patients except one, in whom it was only 50%.

Table V gives the details of those patients returning to work for each affected hemisphere. Although this small group managed to return to work they were not all free from neurological deficits but in many these were slight. The majority of the treated patients continued to live at home, handicapped in various ways as a result of the tumour damage, or that unavoidably inflicted by the surgery which aimed at producing a large internal decompression. Out of 180 men treated, 51.6% remained at home and 56.6% of 90 women treated were at home and capable of performing only some of their domestic duties.

Those patients at home have been analysed to find the incidence of major neurological defects (Table VI). Inclusion in this category has been determined by taking all those patients with one or more of the following defects: 1 A hemiplegia or paralysis

TABLE V
PATIENTS RETURNING TO WORK

Site	Sex	Age (yr.)	Histology	Treatment	Survival Time	Occupation	
<i>Left hemisphere tumours</i>							
Frontal (8)	M	43	Astrocytoma grade IV	Lobectomy + deep x-ray	11 mth.	Joiner	
	F	52	Astrocytoma grade IV	Lobectomy + deep x-ray	1 yr.	Housewife	
	M	54	Astrocytoma grade IV	Lobectomy	1 yr. 9 mth.	—	
	M	38	Astrocytoma grade III	Lobectomy + deep x-ray	1 yr. 11 mth.	Fitter	
	M	57	Astrocytoma grade III	Lobectomy + deep x-ray	1 yr. 6 mth.	Clerk	
	M	30	Astrocytoma grade III	Lobectomy + deep x-ray	1 yr. 9 mth.	—	
	F	30	Astrocytoma grade I	Local excision	8 yr.	Housewife	
	M	33	Ependymoma grade IV	Lobectomy + deep x-ray	1 yr. 2 mth.	—	
	Temporal (5)	M	40	Astrocytoma grade III	Lobectomy + deep x-ray	3 yr.	Labourer
		F	36	Astrocytoma grade II	Lobectomy	8 yr. 2 mth.	Shop manager
M		37	Astrocytoma grade I	Lobectomy	9 yr. 5 mth.	—	
M		31	Astrocytoma grade I	Lobectomy	6 yr. 3 mth.	—	
M		46	Oligodendroglioma	Lobectomy	8 yr. 4 mth.	Foundry manager	
Occipital (2)	M	36	Astrocytoma grade IV	Lobectomy + deep x-ray	1 yr.	Engineer	
	M	45	Oligodendroglioma	Lobectomy	8 yr. 3 mth.	Publican	
Multiple lobe	F	45	Astrocytoma grade I	Local excision	4 yr. 6 mth.	Shopworker	
<i>Right hemisphere tumours</i>							
Frontal (6)	M	36	Astrocytoma grade III	Lobectomy + deep x-ray	3 yr. 6 mth.	?	
	M	49	Astrocytoma grade IV	Lobectomy	10 mth.	?	
	M	54	Astrocytoma grade IV	Local excision + deep x-ray	3 yr. 8 mth.	—	
	M	35	Oligoastrocytoma grade III	Lobectomy	8 mth.	Clerk	
	M	47	Ependymoma grade III	Lobectomy + deep x-ray	2 yr. 4 mth.	Fettler	
	M	57	Astrocytoma grade II	Lobectomy	1 yr. 9 mth.	Electrical engineer	
Temporal (5)	M	35	Astrocytoma grade III	Lobectomy + deep x-ray	1 yr. 7 mth.	Commercial artist	
	M	38	Astrocytoma grade II	Lobectomy	4 yr.	Storeman	
	M	59	Astrocytoma grade I	Lobectomy	3 yr. 7 mth.	?	
	F	35	Astrocytoma grade I	Lobectomy + deep x-ray	2 yr.	Housewife	
	F	61	Astrocytoma grade I	Lobectomy	3 yr.	Housewife	
Central (2)	M	53	Astrocytoma grade IV	Local excision + deep x-ray	3 yr. 6 mth.	Electrical fitter	
	M	36	Astrocytoma grade II	Local excision	5 yr. 8 mth.	Storekeeper	
Multiple lobe	M	60	Astrocytoma grade IV	Lobectomy	8 mth.	Shopkeeper	
	M	59	Astrocytoma grade III	Biopsy + deep x-ray	1 yr. 3 mth.	?	
Lateral ventricle	F	23	Astrocytoma grade II	Local excision	8 yr.	Housewife	
Parietal	M	47	Astrocytoma grade I	Local excision	4 yr.	Remploy	

TABLE VI

MAJOR NEUROLOGICAL DEFECTS IN MEN AT HOME AND IN WOMEN IN PARTIAL DOMESTIC DUTY GROUP

Site	Treated	Home	Major Defects	Hemisphere	
				Right	Left
Frontal	76	40	17 (42.2%)	9 (22)	8 (18)
Temporal	97	56	30 (53.3%)	10 (32)	20 (24)
Occipital	25	20	11 (55%)	5 (9)	6 (11)
Parietal	20	13	7 (53.8%)	2 (4)	5 (9)
Central	17	6	6 (100%)	4 (4)	2 (2)
Multiple lobe	19	2	2	—	2 (2)
Deep	2	—	—	—	—
Corpus callosum	2	—	—	—	—
Lateral ventricle	2	1	—	—	—
Total	260	139 (53.4%)	73 (52.5%)	30	43

Figures in brackets refer to the number treated.

hand; 2 moderate to severe dysphasia; 3 mental disturbances; 4 poor visual acuity resulting from secondary optic atrophy. The presence of a visual field defect has not been used as one of the criteria, although this was invariably present following a temporal or occipital lobectomy. A few patients are known to have driven cars following a temporal lobectomy.

Major neurological defects were present in 52.5% of those at home. Comparing the two cerebral hemispheres, there were 30 right-sided tumours, and 43 on the left, resulting in major defects. One would have expected a higher number of left-sided tumours causing severe defects, but fewer left-sided tumours were treated, as those patients with severe speech disturbances would not be considered for operation.

There were 70 patients at home in good condition, without severe neurological defects. However, the incidence of the latter has probably been underestimated, as some of the milder mental changes, which would prevent a man working, may not have been recorded.

Table VI shows the frequency of patients with major defects for each site. Frontal tumours are the least damaging, 42.2% having major defects, and temporal lobe tumours come next with 53.3% showing major defects. Tumours in the central and parietal areas must inevitably produce a high incidence of neurological defects.

At this point it would have been appropriate to discuss the incidence of epilepsy in the treated patients, as these episodes greatly influence the chances of a patient returning to work. Unfortunately

there was insufficient information for an accurate analysis to be carried out.

DISCUSSION

Comparison of the operative mortality in different surveys of gliomata is difficult because of the different criteria adopted. Deaths occurring either in the first week or in the first month or at any time before the patients leave the neurosurgical unit have been adopted as the operative mortality by different writers. Frankel and German (1958), in a series of glioblastoma multiforme, recorded a mortality of 18.5% in the first week and 27.3% in the first fortnight. Roth and Elvidge (1960), for the same type of tumour, found that 22% died in hospital. The operation mortality for the present series (15.3%) was not unduly high considering that all those dying in the first month were included, and the large proportion of patients accepted for operation, even in the older age groups.

The quality of survival has been inadequately dealt with in previous reviews, so close comparison with the present results cannot be made. Ley *et al.* (1962) in a paper from Barcelona emphasize the difficulty which surgeons in some countries have in following up their patients.

Bettag (1959) reviewed 251 glioblastoma multiforme tumours and found that for those patients surviving more than two months after operation 17.2% returned to full work, 26.5% to partial work, 28.5% were unemployed, and 27.8% were in need of nursing care. Bettag divided all the operated tumours into those that were circumscribed and those that were diffuse on naked-eye examination, and found that the quality grades correlated with the gross appearance of the tumour. The circumscribed group produced 28.6% patients in full work, and the diffuse group produced only 10.5%. For the partial work group the circumscribed group produced 32% and the diffuse only 23.2%. Similarly, the unemployed group was made up of more diffuse than circumscribed tumours. In 251 patients studied, 71 (31.4%) had circumscribed tumours and 172 (68.8%) had diffuse tumours. In the present review the correlation between quality grades and the gross appearance of the tumour has not been studied.

Frankel and German (1958) found that in 172 patients treated for glioblastoma multiforme, 33.1% were left with severe defects, 27.3% with slight defects but not needing nursing care, and 12.2% were in useful occupations. They did not give any figures for individual sites, and did not study the sexes separately, but their figure for those at work is close to that for the present review, which was 12.6%.

Roth and Elvidge (1960) operated on 399 patients with glioblastoma multiforme, and detailed the quality of survival for 306 as follows:—In 9.8% no neurological change; 30% ('good condition') minimal changes, *e.g.*, facial paresis; 26% ('fair condition') pareses and other severe defects but walking and looking after themselves; 19% ('poor condition') severe defects (hemiplegia and dysphasia); and 14.1% very severe, in need of terminal nursing care.

Gol (1961), discussing 194 relatively benign astrocytomata of the cerebrum, found that 19% of patients returned to work. Of those treated (87), 17 had little or no neurological defect, 24 had marked neurological changes but were able to lead an independent existence (at work or school), and 46 were able to work. In the present review out of 64 relatively benign tumours operated (astrocytomata grades I and II, oligodendrogliomata, and oligo-astrocytomata grade I) 15 patients (23.4%) returned to work compared with 18 (8.5%) of 211 malignant tumours treated.

Penman and Smith (1954) considered only those patients who lived more than one year after treatment (84) and found that 52 lived usefully. This figure covers both infra- and supra-tentorial gliomata, and includes cerebellar astrocytomata which have a prognosis completely different from those at other sites.

The factors which will influence the chances of a patient with a glioma returning to work include the presence of severe neurological defects, age, histological grade (degree of malignancy), amount of cerebrovascular disease, and the attitude of the patient and his employer. These factors are closely interrelated.

Mention has been made above of the different percentages of patients returning to work for benign (23.4%) and malignant (8.5%) treated tumours. The survival period for the malignant tumours is much less than for the benign astrocytomata, and no patient with a malignant astrocytoma lived more than four years. The number of malignant tumours increases with age. The ratios of malignant to benign tumours for the third, fourth, fifth, and sixth decades were 1.4, 1.2, 3.5, and 4.1. The incidence of astrocytomata grades I and II remained fairly constant in the fourth, fifth, and sixth decades, there being 21, 23, and 21 patients in each (these figures refer to all patients diagnosed). Age has the most important influence in determining the prognosis of a glioma patient and this was the conclusion reached by Penman and Smith (1954). In the present series there were 60 patients treated between the ages 20 and 40 years and 16 (26.6%) returned to work, whilst out of 182 patients between 40 and 60 years only 17 (9.3%) returned to work.

With advancing age people became less adaptable and it is likely that there were several patients who might have returned to work but were unable to cope with minor neurological defects. On the other hand if a man is liable to epileptic attacks, employers are reluctant to take him back because of the risks of accident and compensation claims. A miner, for instance, is unable to return to work underground and surface work is difficult to find. There were probably several patients unable to work because of epilepsy, and one labourer had to stop work after three years because of fits.

With increasing age a variable amount of cerebral atrophy occurs, and although there may have been no detectable changes before the onset of the illness, the destructive effects of the tumour and a lobectomy in association with the senile changes may result in lack of initiative and poor memory, which would not occur in a younger man.

Other reviews do not compare the quality of survival for right and left hemisphere tumours. As mentioned in the 'work' group, despite the greater rejection of left-sided tumours, those accepted for treatment have at least an equal chance of returning to work as those with a glioma in the right hemisphere. In fact, as only 128 left-sided tumours were treated compared with 152 on the right side, the chances are rather better for those in the left hemisphere. Frontal and temporal sites both produced equal numbers of patients with right and left tumours at work (Table V). Exploration and resection of left-sided tumours has been kept high in the period under discussion. Many neurosurgeons feel that it is unjustifiable to perform extensive resections in the dominant hemisphere and are content to biopsy the tumour and return the patient to the referring hospital. If this policy is adopted a few patients are bound to be lost who might have returned to work. The number is small but the individual is more important than averages and percentages. Table V shows in detail some of the patients who might have been discarded.

I have tried in this paper to focus attention on the quality of the survival in patients with gliomata and on the work potential of patients with tumours in the dominant hemisphere. In the present state of knowledge a resection of the tumour, with or without radiotherapy, is the only form of treatment likely to benefit the patient. Unfortunately, it is impossible to pick out which patient is likely to do well, so a large number must be operated on to avoid losing the ones who will give a worthwhile result. Operating on these tumours gives the relatives some hope, and the terminal stage is frequently brief, as the patient lapses into coma when the basal ganglia and brain-stem are invaded.

SUMMARY

The quality of survival has been studied in 260 treated adults with gliomata in the cerebral hemispheres.

The results have been studied in men and women separately, and the results for tumours in different sites compared.

Attention has been drawn to the various inter-related factors which determine whether a patient will return to work. These include age, degree of malignancy, amount of cerebral arteriosclerotic disease, liability to epilepsy, and the attitude of employers.

The commonest operation performed was a lobectomy, with a smaller number of local resections, and simple decompression has been avoided. The operative mortality rate was 15.3%.

Analysis showed that, for men and women combined, 12.6% returned to work or full domestic duty, 53.4% remained at home, or were capable of performing only partial domestic duties, and 18.4% remained in chronic sick beds till the time of death. Equal numbers of patients with tumours in the left and right hemispheres returned to work demonstrating that the work potential in patients with treated dominant hemisphere tumours is equal to that for right hemisphere tumours. In the present state of knowledge it is impossible to decide which patients will do well following operation, and it is felt that wherever possible the affected lobe should be extensively resected, regardless of the side of the lesion.

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