



Trends in peri-operative performance status following resection of high grade glioma and brain metastases: The impact on survival

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ABSTRACT

Objectives: Maximal surgical resection of high grade brain tumours is associated with improved overall survival (OS). It carries the risk of neurological deterioration leading to worsening performance status (PS), which may affect overall survival and preclude patients from adjuvant therapy. We aim to review the changes in performance status of patients undergoing resection of high grade tumours and metastases and the impact of changes on overall survival.

Patients and methods: A prospective study of the perioperative performance status of 75 patients who underwent primary resection of malignant primary brain tumour or solitary metastasis in a single centre. Data on patients' demographics, tumour histology and overall survival were also collected. WHO performance status was recorded pre-operatively and at intervals following surgery.

Results: Of the 75 patients (35 males, 40 females, median age 61 years at diagnosis), 50 had primary malignant brain tumours, 25 had metastasis. Although PS dropped at postoperative day 1 in 14 patients (18.7%), 28% improved by day 5 and there was significant improvement by day 14 (41%, $p = 0.02$). The number of patients with PS 3 or worse changed from 4% pre-operatively ($n = 3$) to 8% ($n = 6$). Overall survival is better in those whose PS remained improved or unchanged at 2 weeks after surgery compared to those whose PS deteriorated; high grade glioma median survival 15.67 vs. 2.4 months ($p = 0.005$) and metastasis median survival 8.53 vs. 2.33 months ($p = 0.001$).

Conclusion: Our data demonstrates that although PS may deteriorate immediately after surgery, the majority of patients regain their baseline PS or improve by 2 weeks postoperatively; decisions on fitness for adjuvant treatment should therefore be delayed until then. In those patients whose PS declines following surgery overall survival is poor.

1. Introduction

Despite radical treatment of malignant glioma and brain metastases the overall prognosis remains poor. The impact of treatment on functional status and quality of life is a key factor in decision making. In glioblastoma there is growing evidence that resection of tumours even in elderly patients leads to improved overall survival (OS), including level 2B evidence (Oxford Centre for Evidence based Medicine) that gross total resection prolongs survival [1–3]. The goal of gross total resection is not achievable in all cases of intrinsic tumours with established resection thresholds of 70–80% associated with improved survival [4–6]. Therefore maximal safe resection is the surgical goal in intrinsic glioma to reduce the risk of acquired neurological deficit. Resection of brain metastases is well established as superior to whole

brain radiotherapy alone in terms of survival [7].

However, in any setting such resections carry the inherent risk of neurological deterioration affecting the post-operative performance status (PS) of these patients, which has the potential to impact on overall survival and may preclude adjuvant therapy [8].

There is also the tendency to offer radical surgery only to those patients with good PS between 0–2. There is currently limited data on PS changes in the post-operative period after high grade tumour surgery and its impact on overall survival [9]. It is also not well documented if PS can improve significantly after tumour resection in those with a poor pre-operative status [10–12].

We prospectively analysed all patients who underwent craniotomy for malignant brain tumours and metastases in our institution over a period of 8 months. The study aimed to identify the effect of tumour

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resection on perioperative performance status and whether any neurological deterioration was temporary or permanent, if any gains in performance status were made after surgery and the impact on overall survival (OS), in order to determine the overall safety of a radical approach to tumour management.

2. Patients and methods

We prospectively collected data of all patients who underwent surgery for malignant primary brain tumour or solitary metastasis in our department between November 2013 and June 2014. A total of 94 patients were accepted for surgery after discussion in the regional neurooncology multidisciplinary meeting during the study time period. 75 (79.8%) patients underwent craniotomy with an intention of maximal safe resection and 19 (20.2%) underwent stealth guided burr hole brain biopsy and were excluded from the study. Only patients with a histological diagnosis of malignant glioma (grade 3 or 4) or metastasis were included.

For all the eligible 75 patients, the WHO performance status was recorded pre-operatively, on day 1 post-operatively, day of discharge (or day 5 if not yet discharged) and at 2 weeks (either following discharge when patients returned to the ward for review prior to starting adjuvant therapy or during inpatient stay). Performance status was assigned by the neurosurgeon or CNS oncology specialist nurse in all cases. Data including age at presentation, symptoms at presentation, primary tumour site if appropriate and cause of post-operative deterioration were also recorded.

All patients underwent craniotomy and with the intention of maximal safe resection of intrinsic tumour or complete resection of metastasis. Awake craniotomies were used when deemed necessary by the senior surgeon for motor or language mapping. Neuro-navigation was used in all cases. All operations were performed by dedicated neurooncology surgeons. 5-ALA fluorescent surgery was not used in this cohort and post-operative imaging was not routinely undertaken to confirm extent of resection. Survival data was extracted from the All Wales Cancer Clinical Database (CANISC), which tracks outcome data for all cancer patients in Wales.

PS data for 75 patients and survival data for 68 patients that was available from the CANISC up to 1st September 2016, was analysed using the software SAS 9.4 (SAS Institute Inc. Cary, NC, USA) and GraphPad Prism (version 7, La Jolla, CA, USA). Pearson's Chi-squared test or Fisher's exact test was used for categorical data and survival analysed by the Kaplan Meier method and compared with log rank test. A value of ≤ 0.05 was considered statistically significant.

The study was approved by the University Health Board ethics review panel.

3. Results

Of the 75 patients, 35 were males and 40 females. The median age was 61 (range 23–78). 28 patients (37%) were aged over 65. 50 patients had primary malignant brain tumours and 25 had brain metastases (22 with solitary metastasis and 3 patients with 2 metastases resected but no additional intracranial disease). The primary sites of cancer in the metastatic group are depicted in Table 1. The tumour location was frontal in 45%, temporal in 23% and parietal in 16% (Table 2). The median length of stay was 5 days (range 2–33 days). There was one peri-operative death in the cohort at 11 days following surgery.

3.1. Peri-operative performance status

At the time of admission prior to surgery 77.3% of patients has a PS of 0 or 1 (PS 0 in 22 patients, 1 in 36 patients). 14 (19%) patients had a PS of 2, 2 (2.7%) of patients had a score of 3 and one patient was PS 4 (Table 3). Performance status changes in PS following surgery at each recorded time point are depicted in Table 4.

Table 1
Primary tumour site in metastatic group (n = 25).

No. of patients	Primary site of cancer	Percentage (%)
8	Lung	30.7
5	Breast	20
5	Melanoma	19.2
3	Ovary	11.5
1	Renal	3.84
1	Bowel	3.84
1	Oesophagus	3.84
1	Unknown primary	3.84

Table 2
Tumour Location.

No. of patients	Tumour location
34	Frontal
12	Parietal
17	Temporal
8	Occipital
4	Cerebellar

Table 3
Pre-operative performance status in metastatic and glioma groups.

Performance Status pre-op	Metastasis (n)	Glioma (n)
0	6	16
1	14	22
2	6	8
3	1	1
4	1	0

Table 4
Post-operative changes in PS.

WHO PS	Immediate post op	Discharge (Day 5)	2 weeks
Improved	3 (4%)	21 (28%)	31 (41%)
Unchanged	58 (77%)	44 (58.6%)	40 (53%)
Deteriorated	14 (18.6%)	10 (13%)	4 (5%)

On day 1 following surgery PS declined in 14 (18.7%) of patients. In 12 patients PS declined by only 1 grade but 2 (2.7%) of the patients declined significantly to PS 4. Of those that declined new neurological deficit occurred in 6 (43%) and seizures in 3 (21%). The remaining patients declined by only 1 point on the WHO scale due to transient cognitive decline, confusion or fatigue. New neurological deficit occurred in 8% of the entire cohort and were attributed to the extent of the resection as no patients suffered additional complications such as haematoma or infarction and most deficits improved. New onset seizures occurred in 4% of the whole cohort.

By day 5 or discharge 28% of patients improved in PS and by 2 weeks 41% had improved. There is a significant improvement in performance status by 2 weeks ($p = 0.02$) but not at day 5 ($p = 0.44$). Of the 14 that initially declined 12 (85%) had improved by 2 weeks. In the whole cohort 4 patients deteriorated by 2 weeks and 94.6% were either the same or better. The number of patients with PS 0 increased from 22 (29%) to 32 (42.7%) by 2 weeks. However, the number of patients PS 3 or worse increased from 3 (4%) prior to surgery to 6(8%). The one patient who presented with PS 4 remained unchanged having presented as an emergency with a haemorrhagic tumour. One patient who presented PS 3 improved to PS 2 following resection of the tumour. Overall trends in PS following surgery are depicted in Fig. 1. There is no significant difference in changes in PS between the primary and metastatic tumour groups ($p = 0.73$).

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