

Original Article:

Mapping the patterns of care, the receipt of palliative care and the site of death for patients with malignant glioma.

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Abstract

High-grade malignant glioma patients face a poor prognosis, preceded by rapid functional and neuro-behavioural changes, making multidisciplinary care incorporating supportive and palliative care important. This study aimed to quantify the association between symptoms, receipt of supportive and palliative care and site of death. We undertook a retrospective cohort study between 2003-2009 of incident malignant glioma cases who survived for at least 120 days between their first hospitalisation and their death (n=678) in Victoria, Australia, using linked hospital, emergency department and death data. The median age of patients was 62 years, 40% were female, and the median survival was 11 months. Twenty-six percent of patients died outside of hospital, 49% in a palliative care bed/hospice setting and 25% in an acute hospital bed. Patients having 1 or more symptoms were more than 5 times as likely to receive palliative care. Patients who receive palliative care are 1.7 times more likely to die outside of hospital. In conclusion malignant glioma patients with a high burden of symptoms are more likely to receive palliative care and, in turn, patients who receive palliative care are more likely to die at home.

Key Words: Malignant Glioma; Palliative care; Symptom burden;
Population cohort study; Coded hospital data;
Adjusted odds ratio.

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Primary malignant gliomas are the most common primary brain tumours in adults.^[1] Despite advances in treatment, glioblastoma patients face an overall median survival of 14·6 months,^[2] preceded by a rapid decline of physical function and behavioural and neuro-cognitive changes.^[3] Multidisciplinary care, incorporating supportive and palliative care, is therefore an important aspect of management.

Unfortunately, there is limited evidence regarding the current provision of supportive care and palliative care to this patient group.^[4] Care needs following diagnosis, including subsequent emergency department (ED) visits, admissions to hospital, palliative care and the circumstances around death, have mainly been described in small, single-site retrospective case studies. This limits their generalizability and the extent to which evaluation of relationships between symptom burden, health care utilisation and end of life care can be made.^[5-7]

The aim of this study was to quantify the association between symptoms (defined broadly to include patient reported complaints as well as clinical complications) and receipt of supportive/palliative care in the 120 days prior to death and site of death for patients with high-grade malignant glioma. We chose the time period of 120 days prior to death as our window of analysis after consideration of the length of time it may take to establish care relationships and institute effective ongoing support, including community support, for both patients and their carers after an initial referral to hospital supportive and palliative care.

Methods

Setting

Victoria, Australia has a population of 5.6 million.^[8] All residents of Australia have universal access to publicly funded medical care provided in both community settings and in public hospitals. For approximately 51% of Australians this public coverage is complemented by private health insurance which allows access to private hospitals.⁹

Palliative care services in Victoria are organised into three main areas of service provision: 1) acute hospital consultancy services; 2) community palliative care services providing care in the patient's residence; and 3) specialist inpatient palliative care facilities/hospice units. A patient may receive care from one or each of these areas of service according to their needs and illness course. Patients receiving palliative care at any site may continue to receive tumour directed therapy and indeed for patients at home, this is common.

Patients in the community may be directly admitted to an inpatient palliative care unit in the event they can no longer be cared for at home. This is less likely for those patients not known to palliative care services, who will generally present to emergency and be admitted to an acute bed, with later transfer to palliative care bed as appropriate.

Data Sources

Hospital and ED data are compiled by individual hospitals and maintained by the Victorian State Department of Health.^[10-12] The two datasets contain demographic and clinical information on each episode of patient care. The quality of Victoria's hospital data is maintained using an independent audit program.^[13]

Death certificate data are maintained by the Registry of Births, Deaths and Marriages.^[12]

Emergency, hospital and death data undergo a stepwise deterministic linkage at the Victorian Department of Health.^[14] Linkage staff assess data quality by a series of internal logic checks and manual review of randomly selected case groups.

Notably, these data report patient contacts with hospital sector but do not include community based care contacts.

Malignant glioma cases

Malignant glioma cases (January 1, 2003 and December 31, 2008) were defined based on ICD-O-3 morphology codes within the hospital data: Glioblastoma (9440); Astrocytoma (9401); Oligodendroglioma (9451); Ependymoma (9392) and Gliosarcoma (9442).^[15] A 5th digit of '3' was used to restrict the cases to "Malignant, primary site".

We included only incident malignant glioma cases who survived for at least 120 days between their first glioma hospitalisation and their death. Follow up was to 30-June-2009.

Covariates

We defined supportive care as consultation by (one or more) social work, physiotherapy, occupational therapy, psychology or speech pathology. Palliative care was defined as consultation or care with the hospital based palliative care service.

Relevant symptoms were selected based upon clinical opinions from neurosurgery, palliative and supportive care clinicians [MM, JP, MG, CL], a review of the literature,^[3,5,16] and diagnoses from malignant glioma cases. This approach was employed in order to maximise face validity (expert opinion and literature review) and completeness ('bottom up' enumeration based on data). The symptoms were defined using ICD-10AM codes (Appendix A).^[17]

Outcome

Site of death was based on a combination of hospital and death data in order to classify site into 3 mutually exclusive groups: outside hospital; in a palliative care-funded bed (hospice bed); and in an acute care hospital bed.

Statistical analysis

The sample was described at key time intervals: diagnosis admission, at the end-of-life (120 days before date of death) and the death admission.

Logistic/multinomial regression models were fitted for two questions: what are the factors related to the receipt of palliative care at the end-of-life -and, in turn, how does this receipt of palliative care relate to site of death?

Two multiple logistic regression models were fitted for receipt of palliative care (consultation and hospice bed) at the end-of-life as the outcome. The models differed in the variable(s) used for symptoms: the first used the number (0, 1 and 2+); and the second, individual symptoms. There was no a priori weighting given to either the number or to individual symptoms.

A multinomial logistic regression model for the 3 sites of death was then fitted, and provided two separate sets of results: one for site of death in a hospice bed vs. an acute care hospital bed; one for death outside hospital versus in an acute care hospital bed.

Stata 11.1, Stata Corporation, College Station, Texas, USA, 2006 was used for all statistical analyses.

Ethics approval

This study was approved by the Monash University Human Research Ethics Committee.

Results

From January 2003 to June 2009 (6.5 years) there were 2011 patients meeting the inclusion criteria for incident malignant glioma diagnosis. Of these, 512 (25%) did not survive at least 120 days and 821 (41%) did not die by the end of follow up (30-June-2009), leaving 678 (34%) patients who survived longer than 120 days from diagnosis and died within the follow-up period.

The median age of our cohort was 62 years (25th-75th percentile: 52-70 years) and 60% were male (Table 1).

Place of death

Twenty-five percent of patients died outside of hospital, 49% in a palliative care bed/hospice setting and 25% in an acute hospital bed (Table 2). Of those 331 patients who died in a palliative care unit, 157 (47%) had been transferred to a palliative care bed after being admitted to an acute care bed.

Survival

In this study, which considered only people who died within the follow-up period, the overall median survival for malignant glioma was 11 months, with 75% surviving at least 7 months and 25% 17 months or more. These figures did not differ by place of death ($p=0.11$). Median survival for glioblastoma patients was 10.4 months, and 14.3 months for all other patients with grade 3 tumours.

Symptoms, supportive and palliative care over the care trajectory from diagnosis to death

At diagnosis, the most common symptoms were paresis/weakness (15%), speech/communication or swallowing difficulties (14%), seizures (14%) and cognitive/behavioural difficulties (12%) (Table 2). Cognitive/behavioural difficulties (20%), incontinence (20%), and paresis/weakness (19%) were more prevalent in the hospitalisation in which they died.

In general, receipt of supportive care declined over the trajectory from 84% at diagnosis to 53% during the hospitalisation in which they died; in distinction, palliative care consultation increased from 5% to 63% and use of a hospice bed from 2% to 49%.

Of note there was not a difference in the median number of diagnostic codes over the care trajectory by palliative care status (without palliative care total number unique diagnoses was 9 codes, with was 7 codes), indicating no difference in the completeness of records by whether there was involvement of a palliative care team in the patient's care.

Patterns of ED and hospital use over the care trajectory from diagnosis to death

Nearly half of the malignant glioma patients (46%) were admitted through the ED for their diagnostic admission (48% via ambulance, data not shown). The proportion of patients receiving ED care in the 120 days prior to their death was 54% (80% via ambulance).

Approximately 40% of patients who died in hospital were admitted via the ED (majority via ambulance).

Malignant glioma patients spent a median of 9 days in hospital during their diagnosis admission, 11 days, during the 120 days prior to death, and 23 days for those who died in hospital/hospice (Table 3). Intensive care was limited throughout the patients' trajectory to

between 3-6%. Approximately 50% of patients used a private hospital during their diagnosis hospitalisation. Patients with 1 symptom coded had a median of 11 beddays whereas those with 2 or more were in hospital for 18 days ($p=0.001$). The majority of patients (75%) had an excision of their tumour (as distinct from biopsy, see Appendix A and Table 3) during their diagnostic admission; this reduced to 13% in the 120 days prior to death and 4% during their death admission.

Factors associated with the receipt of palliative care at the end-of-life

Patients having 1 or more symptoms were more than 5 times as likely to receive palliative care (Table 3). Demographic factors and survival were not of significance.

Factors associated with place of death

Patients who received any palliative care in the last 120 days before death and women were 2 times more likely to die out of hospital rather than dying in an acute hospital bed (Table 4).

Women and those 40 and over were more likely to die in a palliative care bed while those from rural areas were less likely.

Discussion

This is the first study worldwide to demonstrate at a population-level that malignant glioma patients who receive palliative care in the last 120 days before death are more likely to die out of hospital. These results have important implications both for the individual and for the healthcare system.

For the individual (and their carers) studies show a strong and consistent preference to die at home in the event of a terminal illness.^[18,19] Notably, these preferences are maintained across age groups and different cultures and are similar for those who have direct experience of illness as well as those who do not. In our study, the factors shown most likely to facilitate dying at home in patients with malignant glioma are the involvement of palliative care services in the last 120 days of life and female gender. Our results are consistent with those of McNamara and Rosenwax who demonstrated that those who received community based palliative care services were seven times more likely to die at home.^[20] The association between female gender and death at home has been previously demonstrated,^[21,22] although there is some inconsistency of findings.^[23] There is a need to further explore differences in gender and factors related to place of death.

Referral to palliative care in the last 120 days before death allows sufficient time for relationships and confidence in community health services to be established, as well as ensure that the needs of informal or family carers in preparation for the caregiving role can be met.^[24] These needs, which have been documented as critical to facilitating successful care, include education to provide the tasks of care, clear information, emotional support and access to equipment.^[25,26] Palliative care services explicitly attend to such carer needs as well as those of the patient. A focus of support that builds capacity to care through the provision of clear information, exploration of preferences, and informed decision-making requires trust and takes time. Hence in order to maximise possible benefits, referral to palliative care should occur in a timely manner, ideally before the final month of life.

The engagement with palliative care services earlier in the patient's illness also has implications for the broader health care system as it strives to maintain quality of care and

simultaneously contain costs. Pace et al^[27] demonstrated that the rate of hospitalisation in the final 2 months of life for a group of patients with brain tumours was lower (16.7%) for those who had received palliative home-care services than those who had not (38%), leading to substantial savings through reduced hospitalisation in those patients who had received palliative home-care services (517€) compared to those who had not (24,076€).^[27]

Importantly, in our study, although one quarter of malignant glioma patients died at home from what is likely to be an expected death, 44% died in an inpatient bed palliative care/hospice unit. The high use of palliative care beds by this patient group suggests that their care needs are very great and may overwhelm even the most dedicated family carers. In general it appears that for those requiring hospitalisation, palliative care inpatient beds are accessed frequently and preferentially as death nears.

Our study shows that the burden of symptoms steadily increases during the illness period, and those with greater symptoms have an increased odds of receiving palliative care. Supportive care modalities, such as speech and physiotherapy reach higher levels early around time of diagnosis, whereas palliative care rises more slowly, reaching more than 60% for those who die in hospital. It is possible that a number of the components of supportive care are taken on by palliative care, which may assist, for example, with organising mobility aids or providing information on financial supports available.

The pattern of symptoms deserve specific mention. In this study, the symptoms are substantially less frequent than those reported elsewhere. Other authors detailing symptoms in the final weeks of life have noted levels of epilepsy at 30-50%, headache 33-36%, dysphagia 71-85%, death rattle 12%, drowsiness 85-87%, agitation and delirium 15-29%.^[5,7] These studies relied upon reports of symptoms that were specifically enquired for, whereas our study relies upon the recording of symptoms in the medical record which are then coded.

Of note, a discrepancy between hospital recording of symptoms and those elicited from interviews with patients and relatives has been demonstrated by Davies and Clarke,^[28] although the statistical significance of this discrepancy is not clear. In particular they noted that epilepsy, sensory and cognitive loss, personality change and fatigue were more frequently noted by patient and family than reported in the medical records. Meanwhile weakness and dysphasia were more frequently recorded in the medical records than by the patient.^[2828] The methodological differences in recording symptoms may account for the differences in incidence between our study and these other reports. If symptoms are underreported in medical records overall then supportive and palliative care needs would be anticipated to be even greater than currently recognised.

Limitations

There are several limitations to this study. As noted above, we were working with routinely collected, hospital data and relied on coded information based on documentation within the patient medical record. Utilising a secondary data source raises the possibility of under-reporting of need and data inaccuracies, particularly with respect to symptom ascertainment. Our data do not include community-based information, such as community palliative care or general practice care. Further, as we only included patients who survived more than 120 days from diagnosis to death, we have excluded the most severe cases of malignant glioma whose care utilisation is likely to have been systematically different. We acknowledge these limitations in our approach, which we believe are offset by our population-level data and the ability to quantify the associations between symptom burden, palliative care, hospital use at the end of life and site of death.

Conclusion

Our population level study shows that the timely receipt of palliative care, by either referral to a palliative care program or hospital palliative care consultation, increases the odds of dying at home. Supportive care with a broad range of health services further facilitates the successful management of patients with malignant glioma at the end of life so that these patients and their carers can receive appropriate care and support at the end of life.

From these findings, we propose that a model of care for this population should incorporate an earlier routine palliative care referral, heralded by the onset of symptoms. The response of treating clinicians to a relapse may include further anti-cancer therapies, but should also routinely offer referral to palliative care. For patients whose survival may be measured in months, this should ensure receipt of palliative care involvement prior to their last days of life. It may also improve the chance of greater involvement with patients living in rural areas where access to this form of care is known to be limited. While some acute hospitalisations are unavoidable, a mechanism to involve palliative care earlier through the consultation service, may avoid later recurrent hospitalisations, including those towards the end of life.

Future work is needed to explore the recommended timing of referral for the cohort of patients with poorer prognostic status, who are dying within 120 days of diagnosis. Such patients are likely to present particular challenges to the both the hospital and community based health services as they rapidly progress through diagnosis to death.

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Table 1. Characteristics of primary malignant glioma cases

Total	678
	N (%)
Age group	
	<40 57 (8)
	40-60 246 (36)
	>60 375 (55)
Sex	
	Male 408 (60)
	Female 270 (40)
Country of birth	
	Australian born 447 (66)
	English-speaking country of birth 500 (74)
Married	471 (69)
Rurality	239 (35)
Histology at diagnosis	
	Glioblastoma 569 (84)
	Astrocytoma 94 (14)
	Oligodendroglioma/ Ependymoma 21 (3)
Location of tumour at diagnosis	
	Frontal 217 (32)
	Temporal 181 (27)
	Parietal 145 (21)
	Multifocal 137 (20)
	Occipital 48 (7)
	Brain stem/cerebellum 11 (2)
Place of Death	
	Out of Hospital 176(26)
	Hospice/palliative care bed 331 (49)
	Acute Bed 171 (25)

Table 2. Symptom burden, palliative care and supportive care over the care trajectory of patients with primary malignant glioma, N=678

Site of care	Factor	Diagnosis Admission	From 120 days to death	Death Admission*
Emergency Department	Any visits, Number of patients	310	365	216
	Number of visits per patient, (median)	1	1	1
	Overall duration of stay per patient in hours, (median)	8	10	4
Hospital	Admissions, number of patients	678	506	502
	Admissions per patient, (median)	1	2	1
	Total beddays per patient, (median)	9	11	23
	Emergency admission, %	60%	51%	44%
	ICU, %	6%	4%	3%
	Private hospital used, %	49%	36%	30%
	Surgery			
	Biopsy	16%	2%	1%
	Resection	75%	13%	4%
	Total symptoms			
0	54%	51%	47%	
1	28%	23%	21%	
2+	18%	26%	32%	
Total supportive care				
0	16%	44%	47%	
1	15%	10%	13%	
2+	70%	46%	40%	
Supportive and palliative care				
Palliative care consult	5%	26%	63%	
Palliative care bed	2%	16%	49%	
Social Work	48%	34%	35%	
Occupational therapy	63%	40%	27%	
Physiotherapy	79%	51%	41%	
Speech pathology	29%	17%	22%	
Psychology	4%	2%	2%	
Pharmacy	13%	8%	5%	
Rehabilitation bed	10%	5%	3%	

*Only for those who died in hospital or in an inpatient palliative care bed

Table 3. Factors associated with the receipt of palliative care in the 120 days before death for patients with primary malignant glioma

Factor	OR *	LCL	UCL	p-value	
Age category	<40	1.00			
	40-59	1.02	0.51	2.04	0.95
	60+	0.96	0.49	1.88	0.90
Gender	Male	1.00			
	Female	1.14	0.79	1.65	0.49
Residence	Urban	1.00			
	Rural	1.07	0.72	1.59	0.74
Country of birth	Non-English speaking	1.00			
	English speaking country of birth	1.28	0.81	2.01	0.29
Marital status	Not married	1.00			
	Married	0.78	0.51	1.18	0.232
Hospital type	Public hospital only	1.00			
	Any private hospital use	0.95	0.64	1.39	0.77
Number of symptoms	0	1			
	1	3.75	2.37	5.92	<0.001
	2+	5.39	3.48	8.35	<0.001

* OR: odds ratio; LCL: lower 95% confidence limit; UCL: upper 95% confidence limit.

Table 4. Factors associated with receipt of palliative care for patients with primary malignant glioma

nts with primary malignant glioma

Factor		Out of hospital in comparison to an acute care bed.			OR
		OR [*]	95% CI*	p-value	
Palliative care, at least 120 days prior to death.	None				1
	Any	1.72	(1.05,2.81)	0.03	1.29
Residence	Urban	1.00			1.00
	Rural	0.86	(0.55,1.35)	0.52	0.38
Gender	Male	1.00			1.00
	Female	1.91	(1.23,2.98)	0.00	1.60
Age category	<40	1.00			1.00
	40-59	1.07	(0.50,2.26)	0.87	3.09
	60+	1.09	(0.53,2.22)	0.82	2.40
Country of birth	Non-English speaking	1.00			1.00
	English Speaking	0.68	(0.41,1.14)	0.15	1.13
Marital status	Not married	1			1
	Married	0.75	(0.48,1.17)	0.21	0.89
Hospital type	Public hospital only	1.00			1.00
	Any private hospital use	0.95	(0.61,1.48)	0.81	0.94

*OR: odds ratio; CI confidence limit.