Clinical study:

Clinical presentation and patterns of care for short-term survivors of malignant glioma

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Abstract

Palliative care provision for patients with high-grade malignant glioma is often under-utilised. Difficulties in prognostication and inter-patient variability in survival may limit timely referral. This study sought to (1) describe the clinical presentation of short-term survivors of malignant glioma (survival time <120 days); (2) map their hospital utilisation, including palliative and supportive care service use, and place of death; (3) identify factors which may be important to serve as a prompt for palliative care referral. A retrospective cohort study of incident malignant glioma cases between 2003-2009 surviving less than 120 days in Victoria, Australia was undertaken (n = 482). Cases were stratified according to the patient's survival status (dead versus alive) at the end of the diagnosis admission, and at 120 days from diagnosis. Palliative care was received by 78% of patients who died during the diagnosis admission. Only 12% of patients who survived the admission and then deteriorated rapidly dying in the following 120 days were referred to palliative care in their hospital admission, suggesting an important clinical subgroup that may miss out on being linked into palliative care services. The strongest predictor of death during the diagnosis admission was the presence of cognitive or behavioural symptoms, which may be an important prompt for early palliative care referral.

Key Words:

Malignant Glioma; Palliative care; Symptom

burden;

Population cohort study; Coded hospital data;

Adjusted odds ratio.

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Palliative and supportive care services play an integral role in the management of high-grade primary malignant glioma (PMG). The timeliness of referral to palliative care, nevertheless continues to be of great interest among health professionals involved in the care of people with PMG[1]. Clinicians must navigate the complexities of balancing patients' hopes for prolonged survival with information around poor prognosis[2, 3].

PMG patients, with an expected poor prognosis, have particular needs for appropriate support, and timely referral to palliative care. Currently palliative care is under-utilised or initiated sporadically[2, 4, 5], most often late in the illness course[6, 7], meaning there are fewer opportunities to initiate community based services to maintain support at home[8]. In addition, the opportunity to have important discussions with the patient about advance care directives and end-of-life treatment may be lost[9].

Several factors have been associated with poorer survival, including older age (>60 years), poor functional status (Karnofsky <70), high histopathological tumour grade, and extent of surgical resection[10-14]. Nevertheless, there remains significant inter-patient variability in survival[15], and clinical experience suggests it can be difficult to distinguish the sub-set of patients with poor prognostic status who will deteriorate rapidly from those who may live longer[2]. Such patients are likely to present particular challenges to health services, as well as to the patients' families, as they rapidly progress through diagnosis to death.

Previous research in this patient group has been restricted to retrospective case reviews at single sites of care[4-6, 9, 16], and has not focused on people with poor survival outcomes. Using population data in the Australian state of Victoria (population >5.5 million), we sought to: (1) describe the clinical presentation of short-term surviving PMG patients (survival time <120 days); (2) map their hospital utilisation, including palliative and supportive care service use, and place of death; (3) identify factors which may be important to serve as a prompt for palliative care referral.

METHODS

A retrospective cohort study was undertaken to track patients with PMG from the time of in-hospital diagnosis until death. We examined a nested subset of data from within a larger study (N=1160) of all incident cases of PMG in Victoria over a 6.5-year period (January 2003-June 2009), based on longitudinally linked inpatient hospital, emergency department and death data[17]. The study was approved by the Institutional Human Research Ethics Committee.

All Australians have universal access to publicly funded health care, including all arms of palliative care provision: (1) acute hospital-based palliative care consultation services; (2) specialist inpatient/hospice palliative care beds; and (3) community based services providing care in the patient's residence. People receiving any arm of palliative care are not precluded from active treatment and may continue to receive tumour-directed therapy concurrently.

Referrals for the diagnosis and treatment of PMG in Victoria are directed toward four key tertiary neuro-surgical services. Statewide recommended care protocols for PMG patients exist[18], but limited detail regarding optimal palliative care pathways is provided. Particular gaps exist for patients with poor prognoses who have extensive tumour at diagnosis which is not deemed suitable for treatment and thus do not reach tumour recurrence, when palliative care is typically considered.

Detailed information describing the hospital episode data source, selected ICD-10 codes, data collection methods and data reliability has been previously published[17]. In brief, hospital and ED data was sourced from the Victorian State Department of Health who maintain the Victorian Linked datasets and undertake stepwise deterministic linkage with death data compiled from the Registry of Births, Deaths and Marriages. Demographic, administrative and clinical details for each patient episode of care within the hospital admission are contained in the datasets. Comorbid disease status was coded using the Charlson Comorbidity Index[19]. The data is subjected to random quality auditing and has been demonstrated to be of high quality[20].

For the purposes of this analysis, we were interested in patients with the poorest survival outcome who died within 120 days of ascertainment (n=482). The sample was stratified according to the patient's survival status (dead versus alive) at key time points, including at the end of the diagnosis admission, and at 120 days from diagnosis. We chose this split as a significant proportion (45%) of those short-term survivors who died within 120 days did so during this initial diagnosis hospitalisation.

This stratification resulted in three groups (Figure 1): patients who died during the diagnosis admission (group 1), patients who survived the diagnosis admission but died quickly within 120 days from diagnosis (group 2), and longer survivors dying thereafter, whom we have previously described (group 3)[17]. The longer-term survivors (group 3) are therefore not included in the main analyses of this study but their characteristics are referenced against the shorter term survivors for comparison.

Figure 1. Patients stratified by time of death

^a Group 3 is the longer survivors previously published, included here for comparison to short-term survivors[17]

Statistical analysis

Descriptive analysis and Pearson χ^2 tests, t-tests or Fishers Exact tests were used to compare differences in clinical characteristics between patient groups. All tests were done on a two-tailed basis and a p -value $<.05$ was considered significant.

Characteristics which significantly differed between patient groups in the univariate analysis or were considered to be potentially clinically significant were then examined in a multiple logistic regression analysis, to determine their predictive value associated with: (1) death during the diagnosis admission; and (2) death prior to 120 days from diagnosis; controlling for confounding factors and interaction.

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

RESULTS

From January 2003 to July 2009, there were 1,160 patients who died with an incident PMG diagnosis. Of these, 482 were shorter-term survivors: 218 (19%) died during the diagnosis admission (group 1) and 264 (23%) survived the diagnosis admission but died within 120 days from diagnosis (group 2); 678 (58%) died thereafter (group 3)[17].

Group 1

Patient characteristics (Table 1)

Patients not surviving the diagnosis admission were mostly male (54%); married (58%); aged ≥ 75 years (46%); and Australian-born (65%). Eighty-nine percent were diagnosed with Glioblastoma, and most had multi-focal tumour (45%). Two thirds (59%) of Group 1 had two or more symptoms recorded at the end of their diagnosis admission. Cognitive or behavioural difficulties (41%), paresis (35%), incontinence (33%), speech, communication and swallowing difficulties (32%) and seizures (21%) were most prevalent.

Hospital utilisation (Table 2)

The mean number of hospital beddays for patients in Group 1 was 40 (median 33). Eighty percent of patients were admitted through the emergency department, with 39% arriving by ambulance. Just 28% of patients had their tumour resected, while 31% underwent a biopsy only. Intensive care was utilised by 14% of patients.

Sixty-two percent of Group 1 was admitted to a palliative care bed during the diagnosis admission, including some who were transferred to the palliative care unit following a hospital-based palliative care consultation. These patients spent 49% of their total hospital bed days in the palliative care setting (median 15 days; 1-108). While 78% of patients not surviving the admission had a consultation with the hospital-based palliative care service, 22% of the cohort died without any palliative care contact. Other supportive care use was prevalent, with 85% of patients accessing two or more supportive care modalities, including physiotherapy (85%), social work (71%), and occupational therapy (64%).

Place of death

Of the patients not surviving the diagnosis admission, 62% died in a palliative care bed/hospice setting and 38% in an acute hospital bed.

Group 2

Patient characteristics (Table 1)

Patients surviving the diagnosis admission (but dying during the first 120 days) were mostly male (57%), older than 75 years (33%), married (79%) and Australian-born

(69%). Eighty-six percent were diagnosed with Glioblastoma; 31% and 30% with a multi-focal or frontal tumour, respectively. Approximately two thirds had one (28%) or at least two symptoms (27%) reported at their diagnosis admission. Paresis (20%), cognitive or behavioural difficulties (19%), speech, communication or swallowing difficulties (17%), seizures (13%) and incontinence (12%) were most prevalent.

Hospital utilisation (Table 2)

The mean number of hospital beddays for Group 2 was 17 (median 11). Sixty-six percent of patients were admitted through the emergency department, with 39% arriving by ambulance. Almost half of these patients (46%) had their tumour resected, while 28% had a biopsy only. Intensive care use was limited to 5%.

Only 12% of Group 2 had a palliative care consultation during their diagnosis admission. Just 3% of patients were transferred to a palliative care bed during this admission, and these patients spent approximately half (54%) of their total hospital bed days in the palliative care setting (median 9 days; 1-46) before being discharged to the community. Other supportive care use was prevalent, with 71% of patients accessing 2 or more supportive care modalities, including physiotherapy (82%), occupational therapy (61%) social work (50%), and speech pathology (35%).

Place of death

Of the patients who survived the diagnosis admission, but subsequently died in the 120 days following, 32% died outside of hospital (either at home or their usual residence), 38% in a palliative care bed/hospice setting and 30% in an acute hospital bed.

Differences between Groups 1 and 2

There were significant differences between the short surviving cohorts. Group 1 who died in the diagnostic hospital admission, comprised a greater proportion of patients aged ≥ 75 years ($p=0.015$); fewer patients who were married ($p=0.019$); more patients with multifocal tumour ($p=0.001$); and more patients with one or more comorbidities ($p=0.001$). Group 1 patients had a greater number of symptoms recorded ($p<0.001$), including: a greater incidence of paresis ($p<0.001$); speech and swallowing difficulties ($p<0.001$); seizures ($p=0.02$); cognitive and behavioural difficulties ($p<0.001$); cerebral oedema ($p=0.03$); incontinence ($p<0.001$); and vomiting ($p=0.004$).

Hospital utilisation differed between-groups, with group 1 having higher total bed days per patient ($p<0.001$), greater emergency department use ($p=0.001$), greater ICU use ($p=0.001$) and lower rates of resection ($p<0.001$). Palliative and supportive care utilisation differed, with group 1 having greater consultation ($p<0.001$) and use of a palliative care bed ($p<0.001$), and greater total supportive care utilisation ($p=0.001$), including social work ($p<0.001$), speech pathology ($p<0.001$) and pharmacy ($p=0.007$).

Differences between Groups 2 and 3

Groups 2 and 3, both of whom survived the discharge from hospital, differed by patient age, with group 3 comprising a greater proportion of patients aged <54 years ($p<0.001$); and fewer patients with multifocal tumour ($p=0.001$), one or more comorbidities ($p=0.048$), cognitive and behavioural difficulties ($p=0.004$), incontinence ($p<0.001$) and overall number of symptoms ($p<0.001$). Group 3 had

lower use of the palliative care consultation service ($p<0.001$); and lower rate of biopsy ($p<0.001$), but higher rate of resection ($p<0.001$).

Factors predicting likelihood of shorter survival

A multivariate logistic regression model including relevant demographic and clinical characteristics was conducted to examine factors predicting shorter survival (Table 3).

Patients with PMG were more likely to die in the diagnosis admission (compared to the 120 days following) if they had: cognitive or behavioural difficulties (3.1 times more likely); vomiting (2.9 times more likely); incontinence (2.2 times more likely); speech and swallowing difficulties (2.1 times more likely); one or more comorbidities (2.1 times more likely); multi-focal tumour (1.8 times more likely); paresis (1.7 times more likely); or if they did not have their tumour resected (0.4 times more likely).

In turn, patients surviving the diagnosis admission were more likely to die during the first 120 days (compared to longer term survivors) if they were aged 55 years and above (55-64: 1.6 times more likely; 65-74: 2.5 times more likely; ≥ 75 : 4.3 times more likely); if they had incontinence (2.2 times more likely); or if they did not have the tumour resected (0.3 times more likely).

DISCUSSION

Our study uses population data to describe the clinical presentation and patterns of supportive and palliative care utilisation for high-grade PMG patients with poor prognostic status in Victoria, Australia. To our knowledge, this is first study worldwide to report on supportive and palliative care management for this sub-set of

short-term surviving PMG patients who die within 120 days of diagnosis. Given the importance of palliative care for this patient cohort, the findings of the present study are important because they allow us to: (1) identify gaps in the provision of palliative care; (2) determine systematic, identifiable differences in the presentation of PMG patients who do poorly; and therefore (3) identify opportunities for timely referral to palliative and supportive care services and ensure that families are receiving the necessary supports.

Identifying short-term survivors of PMG

In this study, the symptom profile of short-term surviving patients during the diagnostic admission was distinguishable at the between group level, such that group 1 had significantly more symptoms (2+ symptoms: 59%), when compared with group 2 who initially survived the diagnosis admission (2+ symptoms: 27%). Notably, the prevalence of cognitive and behavioural symptoms was most the discernible difference between-groups: 41% of patients dying at the diagnosis admission, compared to 19% of patients who lived. Accordingly, the strongest predictor of death during the diagnosis admission was cognitive or behavioural symptoms, such that patients with these difficulties were 3.1 times more likely to die during the diagnostic admission. This supports previous research which suggests early cognitive function, particularly executive functioning and attention, are closely associated with poor prognosis, and may be a useful clinical indicator alongside global measures of patient function[15].

Referral to palliative care

This study revealed several missed opportunities for timely palliative care input for short-term PMG survivors. Only 12% of Group 2 patients surviving the diagnosis admission, but subsequently dying within less than 120 days, had a palliative care consultation whilst in hospital. Given only 46% of this cohort had their tumour resected at diagnosis (compared to 75% of the longer surviving cohort[17]), this is seemingly a group whose poor prognosis is recognised in the clinical setting. Despite this clinical recognition, most of these patients (88%) leave hospital without being referred to palliative care for appropriate planning, and support, yet they die shortly thereafter and 30% die in an acute hospital bed. Arguably, referral to palliative care at their initial point of discharge may have facilitated death at home or in a more appropriate, and cost-efficient hospital setting.

For Group 1 patients who are diagnosed, deteriorate quickly, and then die in hospital there are also missed opportunities for palliative care involvement. Again it seems that these patients are recognised clinically, since an even smaller proportion (28%) has their tumour resected. Yet surprisingly 38% still die in an acute bed, and 22% die without any palliative care consultation. Despite the brevity of survival for this cohort; patients have a mean stay of 40 days, providing sufficient time for palliative care input. Indeed palliative care expertise seems pertinent to ensure patients and their families receive appropriate information, support and spiritual care as death approaches.

Previous studies have indicated health care professionals perceive substantial barriers when assessing appropriate timing of palliative care in the setting of PMG[2] and more broadly[21-23]. In particular, difficulty formulating prognosis and discomfort in discussing palliative care, death and dying with newly diagnosed patients may limit or

delay discussions and goal setting from occurring[24, 25], leading to potentially futile treatment, unnecessary cost and burden[26]. A focus on the ‘here and now’ may also be the preferred stance of PMG patients, who are hoping for disease control[27].

The benefits of timely referral for patients with advanced cancer have however been demonstrated in terms of quality of life, patient and carer experiences, and in some settings, survival estimates[28, 29]. While to our knowledge, no prospective studies of palliative care outcomes in the setting of PMG have been conducted, we would expect similarly favourable outcomes such as those demonstrated for advanced cancer patients. Existential and supportive components of palliative care provision are particularly valued as death nears[30]. A model whereby palliative care is embedded in routine neuro-oncological care may allow discussions and future goal setting to occur more readily. Importantly, pre-emptive referrals to palliative care may more broadly acknowledge a transitional process, rather than simply handing over the patient to a different group of health professionals[23].

A future prospective study should seek to determine the direct benefits (or otherwise) of palliative care, and the economic implications of this practice. In turn, future work may establish a guide for clinicians of optimal targets indicating quality end-of-life care for patients with PMG. Formulating a prognostic score in this setting that could assist in identifying patients for a prompt referral to palliative care units would also be beneficial.

Limitations

This study was limited by the absence of community data, which is necessary to form a complete picture of the care that is provided following discharge to those patients who survived the diagnosis admission. Given community supports are frequently facilitated through the palliative care consultancy team and only 12% of those discharged who died within four months accessed this service, it is plausible that these shorter survivors had limited community supports in place. Nonetheless, we are unable to discern this from our data.

As a retrospective cohort study, the reliance on hospital coded data likely underestimates the true burden of symptoms experienced by these patients since the coding relies upon the symptoms documented in the medical record. This is particularly relevant for more commonly experienced complications such as cerebral oedema, which were documented in only seven and three percent of the Group 1, and 2 patients at diagnosis respectively. Additionally, we are unable to comment on other factors which may be relevant to predicting shorter survival, such as tumour mass or volume, extent of estimated resection, initial response to steroids, and performance status.

Conclusions

This study has revealed that 42% of patients in a large Australian population cohort with high-grade PMG died rapidly within 120 days, many of whom miss out on timely palliative care referral. Our data confirms that whilst patients who die within the diagnosis admission may have a discernible clinical presentation up front, particularly involving cognitive and behavioural symptoms; those who survive the admission and deteriorate rapidly in the months thereafter may present some

difficulties for prognostication. Significant differences in rates of resection between patients surviving in the shorter and longer term indicate that physicians are able to clinically recognise the group who will do poorly. Accordingly, patients who are observed to have cognitive and behavioural difficulties or who do not have the tumour resected should therefore be considered for palliative care referral during their diagnosis admission, to enable additional family and community supports to be increased as necessary. Alongside regular, periodic, multi-disciplinary review, such an approach may facilitate timely communication, existential support, and assist patients and their families over this time of rapid change.

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Table 1. Characteristics of primary malignant glioma cases, stratified by survival

Characteristics	Shorter survivors (Survive < 120days from diagnosis)			Longer survivors ^a (Survive > 120days from diagnosis)	
	Group 1 n = 218	Group 2 n = 264	p value ^b	Group 3 n = 678	p value ^c
Age group n (%)					
<54	27 (12)	38 (14)	0.015	213 (31)	0.000
55-64	45 (21)	57 (22)		184 (27)	
65-74	45 (21)	81 (31)		176 (26)	
≥75	101 (46)	87 (33)		105 (16)	
Sex n (%)					
Male	118 (54)	151 (57)	0.500	408 (60)	0.403
Female	100 (46)	113 (43)		270 (40)	
Country of birth n (%)					
Australian born	142 (65)	182 (69)	0.376	447 (66)	0.378
English-speaking country of birth	161 (74)	208 (79)	0.203	500 (74)	0.108
Married n (%)	127 (58)	181 (69)	0.019	471 (69)	0.786
Rurality n (%)	68 (31)	104 (39)	0.061	239 (35)	0.235
Histology at diagnosis n (%)					
Glioblastoma	194 (89)	228 (86)	0.385	569 (84)	0.351
Astrocytoma	26 (12)	26 (10)	0.464	94 (14)	0.097
Oligodendroglioma/ependymoma/glio	2 (1)	9 (3)	0.068	21 (3)	0.807
Location of tumour at diagnosis n (%)					
Frontal	77 (35)	78 (30)	0.177	217 (32)	0.465
Temporal	45 (21)	59 (22)	0.650	181 (27)	0.169
Parietal	41 (19)	50 (19)	0.971	145 (21)	0.405
Multifocal	98 (45)	81 (31)	0.001	137 (20)	0.001
Occipital	11 (5)	16 (6)	0.630	48 (7)	0.577
Brain stem/cerebellum	5 (2)	0 (0)	0.041	11 (2)	0.125
Symptom profile					
Paresis	35%	20%	0.000	15%	0.068
Speech and swallowing difficulties	32%	17%	0.000	14%	0.394
Seizures	21%	13%	0.020	14%	0.692
Cognitive or behavioural difficulties	41%	19%	0.000	12%	0.004
Visual Disturbance	6%	5%	0.920	5%	0.709
Cerebral Oedema	7%	3%	0.030	4%	0.552
Poor physical function	10%	6%	0.143	4%	0.066
Incontinence	33%	12%	0.000	4%	0.000
Vomiting	9%	3%	0.004	3%	0.752
Headache	0%	0%	0.363	0%	0.482
Total number of symptoms					
0	17%	45%	0.000	54%	0.000
1	25%	28%		28%	
2+	59%	27%		18%	

Charlson comorbidity	0	72%	84%	0.001	89%	0.048
	1+	28%	16%		76%	

Group 1 - Died during diagnosis admission; Group 2- Survived diagnosis admission but died within 120 days; Group 3 - Survive > 120days from diagnosis. ^a Referenced from prior work [17]; ^b Between-group differences comparing groups 1 and 2; ^c Between-group differences comparing groups 2 and 3.

Table 2. Hospital utilisation during diagnosis admission of patients with primary malignant glioma, stratified by survival

Characteristics	Shorter survivors (Survive < 120days from diagnosis)			Longer survivors ^a (Survive > 120days from diagnosis)	
	Group 1 n = 218	Group 2 n = 264	p value ^b	Group 3 n = 678	p value ^c
Total beddays per patient, mean (median)	40 (33)	17 (11)	0.000	17(9)	
Emergency admission, %	80%	66%	0.001	60%	0.123
ICU, %	14%	5%	0.001	6%	0.548
Private health insurance used, %	14%	10%	0.005	49%	
Surgery					
Biopsy	31%	28%	0.516	16%	0.000
Resection	28%	46%	0.000	75%	0.000
Supportive care utilisation					
Social Work	71%	50%	0.000	48%	0.671
Occupational therapy	64%	63%	0.841	63%	0.977
Physiotherapy	85%	82%	0.374	79%	0.395
Speech pathology	60%	35%	0.000	29%	0.095
Psychology	1%	2%	0.899	4%	0.100
Pharmacy	19%	11%	0.007	13%	0.292
Total supportive care					
0	7%	13%		16%	
1	7%	16%	0.001	15%	0.480
2+	85%	71%		70%	
Palliative care utilisation					
Palliative care consult, %	78%	12%	0.000	5%	0.000
Palliative care bed, %	62%	3%	0.000	2%	0.295
Total pal care beddays per patient, median	15 (1-108)	9 (1-46)		84 (15-174)	
No palliative care, %	22%	88%		95%	
Place of death					
Out of hospital	0%	32%		26%	
Hospice/palliative care bed	62%	38%	0.000	49%	0.013
Acute bed	38%	30%		25%	

Group 1 - Died quickly during diagnosis admission; Group 2- Survived diagnosis admission but died within 120 days; Group 3 - Survive > 120days from diagnosis. ^a Referenced from prior work [17]; ^b Between-group differences comparing groups 1 and 2; ^c Between-group differences comparing groups 2 and 3.

Table 3. Likelihood of death for patients with high-grade primary malignant glioma, multivariate logistic regression analysis

Determinant	Death during diagnosis admission ^a (N=482)		Death during first 120 days ^b (N=942)	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age (years)				
<54	1.00		1.00	
55-64	1.03 (0.50 – 2.12)	0.936	1.62 (1.00 – 2.62)	0.048*
65-74	0.72 (0.35 – 1.46)	0.355	2.46 (1.54 – 3.91)	0.000*
≥75	1.49 (0.77 – 2.87)	0.231	4.27 (2.65 – 6.88)	0.000*
Gender				
Male	1.00		1.00	
Female	1.20 (0.78 – 1.84)	0.410	1.05 (0.76 – 1.46)	0.771
Marital status				
Unmarried	1.00		1.00	
Married	0.85 (0.54 – 1.33)	0.481	1.16 (0.81 – 1.66)	0.407
Relevant clinical features/symptoms ^c				
Multifocal Tumour	1.75 (1.14 – 2.70)	0.011*	1.30 (0.91 – 1.85)	0.150
Tumour Excision	0.37 (0.23 – 0.59)	0.000*	0.31 (0.22 – 0.42)	0.000*
Paresis	1.71 (1.04 – 2.81)	0.036*	1.18 (0.77 – 1.80)	0.448
Seizures	1.33 (0.75 – 2.37)	0.330	0.91 (0.57 – 1.44)	0.679
Cognitive and behavioural difficulties	3.07 (1.91 – 4.95)	0.000*	1.30 (0.83 – 2.01)	0.248
Incontinence	2.15 (1.27 – 3.65)	0.004*	2.24 (1.22 – 4.13)	0.010*
Mobility	1.08 (0.51 – 2.31)	0.840	0.97 (0.48 – 1.95)	0.936
Speech and swallowing difficulties	2.14 (1.27 – 3.60)	0.004*	1.06 (0.68 – 1.67)	0.789
Cerebral oedema	1.64 (0.62 – 4.37)	0.158	0.75 (0.31 – 1.80)	0.521
Vomiting	2.97 (1.15 – 7.63)	0.024*	1.16 (0.46 – 2.95)	0.754
Comorbidity	2.10 (1.26 – 3.50)	0.004*	1.36 (0.86 – 2.13)	0.186

CI: Confidence interval; OR, odds ratio; *indicates a significant difference;

^a Likelihood of death during the diagnosis admission, compared to the 120 days following;

^b Likelihood of death after diagnostic admission during the first 120 days from diagnosis, compared to longer survivors;

^c Selected based on factors significant at the between-group level.

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