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Original Article

Functional Independency in Patient with Brain Glioblastoma in King Chulalongkorn Memorial Hospital

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Abstract

Background: Glioblastoma is the most common primary malignant brain tumor. Glioblastoma prognosis is poor with average life expectancy about 10-15 months. Many modalities of treatment (i.e., surgical tumor resection, chemotherapy, radiation therapy) are used for prolong the patient's life. However longer survival may not mean better quality of life. The aim of this study is to assess and compare the quality of life and duration of Functional Independence in patient with Brain glioblastoma after tumor resection and non-resection group.

Methods: We conducted a retrospective cohort study. 87 adult patients (>18 years old) with glioblastoma WHO grade IV from pathological diagnosis who underwent surgery (tumor resection, biopsy) during 2007 – 2023 in King Chulalongkorn Memorial Hospital were included. Exclusion criteria were patient with incomplete information, spinal glioblastoma, poor pre-operative KPS. Defined functional independent was KPS >70. Patient's medical record was reviewed for pre-operative Kanofsky score (KPS), post-operative KPS at 1 week, 1 month, 3 months, 6 months, duration which patient had functional independent, complication of surgery.

Result: The mean time from first diagnosis of brain GBM to dependence status in tumor resection group was 11.60 months and in non-tumor resection group is 3.86 months, no statistically significant (p = 0.087). The KPS in each follow-up time was not different between groups.

Conclusion: The patient with brain GBM, receiving tumor resection treatment tend to had more time in independent than patient receiving non-tumor resection treatment.

Key words: Glioblastoma multiforme, GBM, functional dependency, KPS

Abbreviation: KPS = Karnofsky performance status, GBM = Glioblastoma multiforme

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บทคัดย่อ

ความสามารถในการช่วยเหลือตนเองในผู้ป่วยที่มีเนื้องอกสมองชนิดไกลโอบลาสโตมาที่ได้รับการรักษาในโรงพยาบาลจุฬาลงกรณ์

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หน่วยประสาทศัลยศาสตร์ ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย และโรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย

บทนำ: เนื้องอกชนิดไกลโอบลาสโตมา(GBM; Glioblastoma; High grade glioma WHO2023 grade4) เป็นเนื้องอกชนิดร้ายที่มีต้นกำเนิดจากสมองที่พบได้บ่อยที่สุดและมีการพยากรณ์โรคที่ไม่ดี ผู้ป่วยส่วนใหญ่มีชีวิตอยู่ได้หลังจากการวินิจฉัยประมาณ 10–15 เดือน การรักษามีทั้งการผ่าตัดและไม่ผ่าตัด เช่น การฉายรังสีรักษาหรือการให้ยาซึ่งมีเป้าหมายเพื่อให้ผู้ป่วยมีชีวิตที่ยืนยาวขึ้น แต่การมีชีวิตที่ยืนยาวไม่เท่ากับการมีคุณภาพชีวิตที่ดีหรือสามารถช่วยเหลือตนเองได้ เป้าหมายของการศึกษานี้เพื่อประเมินความสามารถในการช่วยเหลือตนเองโดยเฉพาะในด้านของระยะเวลาที่ผู้ป่วยที่มีเนื้องอก GBM จะสามารถช่วยเหลือตนเองได้อยู่ โดยเปรียบเทียบในกลุ่มที่ได้รับการผ่าตัดเพื่อกำจัดเนื้องอกและผู้ป่วยที่ไม่ได้รับการผ่าตัดเพื่อกำจัดเนื้องอก

วิธีการศึกษา: การศึกษานี้เป็น Retrospective cohort study โดยมี Inclusion criteria เป็นผู้ป่วยอายุมากกว่า 18 ปี ที่ได้รับวินิจฉัยเนื้องอกสมองชนิด glioblastoma WHO grade IV โดยผลตรวจทางพยาธิวิทยา ได้รับการผ่าตัดในโรงพยาบาลจุฬาลงกรณ์ระหว่างพฤษภาคม 2007 ถึงพฤษภาคม 2023 และ Exclusion criteria สำหรับผู้ป่วยที่มีข้อมูลไม่ครบ ผู้ป่วยที่มี spinal glioblastoma และผู้ป่วยที่มี KPS ไม่ดี หรือน้อยกว่า 70 ก่อนการวินิจฉัย ให้นิยามภาวะที่ไม่สามารถช่วยเหลือตนเองได้ด้วย KPS <70 เก็บข้อมูลโดยการทบทวนเวชระเบียนอิเล็กโทรนิกส์ในเรื่อง KPS ก่อนการวินิจฉัย, หลังการวินิจฉัยที่ 1 สัปดาห์, 1 เดือน, 3 เดือน, 6 เดือน, ระยะเวลาที่ผู้ป่วยจะสามารถช่วยเหลือตนเองได้หลังการวินิจฉัยและผ่าตัด และภาวะแทรกซ้อนที่เกิดขึ้นหลังการผ่าตัด โดยแบ่งกลุ่มผู้ป่วยเป็นกลุ่มที่ได้รับการผ่าตัดเพื่อกำจัดเนื้องอกและไม่ได้รับการผ่าตัดเพื่อกำจัดเนื้องอก

ผลการศึกษา: ระยะเวลาเฉลี่ยตั้งแต่การวินิจฉัยถึงผู้ป่วยไม่สามารถช่วยเหลือตนเองได้หรือ KPS <70 ในกลุ่มที่ได้รับการผ่าตัดเพื่อกำจัดเนื้องอกอยู่ที่ 11.60 เดือนในขณะที่กลุ่มที่ไม่ได้รับการผ่าตัดกำจัดเนื้องอกอยู่ที่ 3.86 เดือน ซึ่งไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ (p = 0.087)

สรุป: ในผู้ป่วยที่มีเนื้องอกสมองชนิด GBM ที่ได้รับการผ่าตัดเพื่อกำจัดเนื้องอกมีแนวโน้มมีระยะเวลาที่สามารถช่วยเหลือตนเองได้ยาวนานกว่าผู้ป่วยที่ไม่ได้รับการผ่าตัดกำจัดเนื้องอก

คำสำคัญ: Glioblastoma multiforme, GBM, functional dependency, KPS

Abbreviation: KPS = Karnofsky performance status, GBM = Glioblastoma multiforme

Introduction

The brain glioblastoma multiforme or high-grade glioma WHO grade4 is the most common primary malignant brain tumor. Patients with brain glioblastoma have poor prognosis with average life expectancy about 10-15 months[1-4]. Many modalities of treatment (i.e., surgical tumor resection, chemotherapy, radiation therapy) are used for prolong the patient's life.

The prognostic factors affecting survival included age, Karnofsky performance status (KPS), chemotherapy administration, radiation therapy, tumor location and extent of tumor resection[5-12].

Many studies focused on survival time assessment in patient with GBM, however longer survival may not mean better quality of life. Thus, quality of life should be considered for patient assessment.[13] The patient's functional status after diagnosed as GBM will be progressively worsened with different rate until they are in dependent status and died.[14,15] There are some studies emphasized about quality of life of patient with brain GBM, but no studies that using functional dependency as cut point.

The aim of this study is to assess and compare the duration of functional independence in patient with brain glioblastoma after tumor resection and non-resection group after the diagnosis of brain GBM.

Method

Study design and population

We conducted a retrospective cohort study. 87 adult patients (>18 years old) with brain glioblastoma WHO grade 4 from pathological report who underwent surgery (tumor resection or biopsy) during May 2007 – May 2023 at King Chulalongkorn Memorial Hospital, Thailand were included. Exclusion criteria were patient with incomplete information, spinal glioblastoma, preoperative dependent status (KPS <70). The histopathological diagnosis of glioblastoma was confirmed by neuropathologist. Patients was categorized into tumor resection group and non-resection group (biopsy and receiving other non-surgical treatment for GBM).

Treatment

The patients in both groups received surgical procedure for pathological diagnosis. The patient in tumor resection group underwent craniotomy with tumor resection using safe maximal resection policy. While patient in non-tumor resection group, they underwent either burr hole or craniotomy for tumor biopsy with or without 3D neuronavigation assistance.

After surgery and pathological diagnosis were confirmed, patients were referred to medical oncologist and radiation therapist for further treatment. Some patients received reoperation later during follow-up time if there was recurrent or relapsed tumor.

Data collection

Patient's medical record was reviewed for preoperative Kanofsky score (KPS), post-operative KPS at 1 week, 1 month, 3 months, 6 months, duration

which patient had functional independent, preoperative symptoms and signs, location of brain tumor, treatment i.e., radiation therapy or chemotherapy administration, and complication after surgery.

Functional independency

In order to define functional independency, we use KPS >70 to represent functional independent status of patient.

Ethics and approval

This study was approved by the Ethics Committee for Human Research of Chulalongkorn University.

Statistics

All analyses were performed using SPSS version 29.0 (IBM). The duration of patient to dependent status was showed in median. KPS analysis was performed using linear regression analysis. A p-value of ≤ 0.05 was considered to be statistically significant.

Results

Baseline pre-operative information of patients was summarized in Table 1. There was no significantly different between tumor resection group and non-resection group. The mean age of patients was 55.03 ± 15.91 years, and 43 patients (49.4%) were male. Exception for pre-operative ASA classification that was different between tumor resection group and non-resection group (in non-resection group, there were more patient who were in ASA class 3). The patients had a several presenting symptoms, and the most common were headache and cognitive impairment. The tumor was in eloquent area (which were defined to be Sensory, motor, language, visual cortex, diencephalon, internal capsule, brainstem, cerebellar peduncle and deep cerebellar nuclei) in 58 patients (66.7%).

Table 1 Demographic and clinical characteristics of patient with brain glioblastoma

Characteristics	Total (n = 87)	Tumor resection		p-value
		Yes (n = 80)	No (n = 7)	
Age (years), Mean+ SD	55.03+15.91	54.58+16.00	60.29+14.89	0.366
Min-Max	(18-84)	(18-84)	(41-81)	
< 60	46 (52.9)	43 (53.8)	3 (42.9)	0.702
≥ 60	41 (47.1)	37 (46.3)	4 (57.1)	
Sex				
Male	43 (49.4)	39 (48.8)	4 (57.1)	0.713
Female	44 (50.6)	41 (51.2)	3 (42.9)	
ASA				
1	43 (49.4)	40 (50.0)	3 (42.9)	0.032
2	35 (40.2)	34 (42.5)	1 (14.3)	
3	9 (10.3)	6 (7.5)	3 (42.9)	
Underiying disease	44 (50.6)	40 (50.0)	4 (57.1)	1.000
HT	29 (33.3)	27 (33.8)	2 (28.6)	1.000
DLP	17 (19.5)	17 (21.3)	0 (0.0)	0.337
DM	10 (11.5)	9 (11.3)	1 (14.3)	0.588
Old CVA	3 (3.4)	3 (3.8)	0 (0.0)	1.000
CA	3 (3.4)	2 (2.5)	1 (14.3)	0.225
Others	19 (21.8)	16 (20.0)	3 (42.9)	0.173
Presenting Signs & Symptoms				
Headache	41 (47.1)	40 (50)	1 (14.3)	0.114
Cognitive impair	40 (46.0)	38 (47.5)	2 (28.6)	0.445
Motor weakness	29 (33.3)	25 (31.3)	4 (57.1)	0.215
Seizure	20 (23.0)	18 (22.5)	2 (28.6)	0.658
VF deficit	7 (8.0)	7 (8.8)	0 (0.0)	1.000
Sensory deficit	3 (3.4)	3 (3.8)	0 (0.0)	1.000
Incidental finding	2 (2.3)	2 (2.5)	0 (0.0)	1.000
Cerebellar Impair	1 (1.1)	1(1.3)	0 (0.0)	1.000
Site of tumor				
Non-eloquent	29 (33.3)	27 (33.8)	2 (28.6)	1.000
Site eloquent	58 (66.7)	53 (66.3)	5 (71.4)	
RT	76 (87.4)	70 (87.5)	6 (85.7)	1.000
CMT	51 (58.6)	48 (60.0)	3 (42.9)	0.441

Table 2 The mean time from first diagnosis of brain GBM to dependence status in patient with brain GBM

Mean time to dependence (months)	Tumor resection	Non-tumor resection	Difference	95% CI	*p*-value
Value (months)	11.60	3.86	7.74	(-3.85-19.33)	0.087

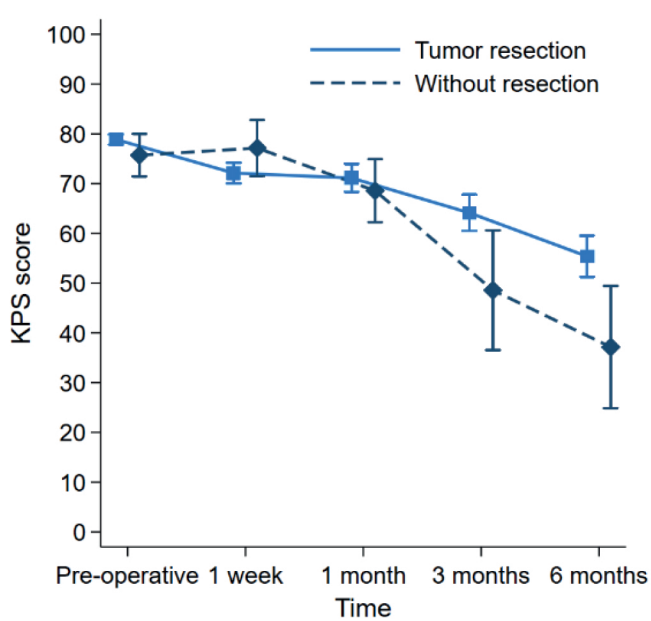
The mean time from first diagnosis of brain GBM to dependence status in tumor resection group was 11.60 months and in non-tumor resection group is 3.86 months, which is no statistically significant.

Table 3 Karnofsky performance status (KPS) of patient with brain glioblastoma by follow-up time

KPS score/Time	Tumor resection (n = 80) Mean ± SD	Without resection (n = 7) Mean ± SD	Mean difference (95% CI)	*p*-value*
Post-operative (Baseline)	78.88 ± 9.00	75.71 ± 11.34	3.16 (-4.04, 10.36)	0.385
Post-operative				
1 week	72.13 ± 18.60	77.14 ± 14.96	-5.02 (-19.41, 9.38)	0.490
1 month	71.13 ± 25.31	68.57 ± 16.76	2.55 (-16.88, 21.99)	0.795
3 months	64.13 ± 32.71	48.57 ± 31.85	15.55 (-10.04, 41.14)	0.230
6 months	55.38 ± 37.04	37.14 ± 32.51	18.23 (-10.56, 47.02)	0.211

*p-value corresponds to independent samples t-test

* Significant at p-value < 0.05



The KPS score of patients was showed in Table3. Preoperative KPS baseline was not statistical different in tumor resection and without resection group (78.88 ± 9.00 and 75.71 ± 11.34, p = 0.385). At 1-week postoperative time, KPS of patients in tumor resection group and without resection group was 72.13 ± 18.60 and 77.14 ± 14.96. At 1-month postoperative time, KPS of patients in tumor resection group and without resection group was 71.13 ± 25.31 and 68.57 ± 16.76. Both 1 week and 1-month postoperative time KPS was not showed statistical different (p = 0.49 and 0.795, respectively).

Although, at 3-month and 6-month postoperative period, KPS of patients in resection and without resection group seemed to be difference, there was no statistical difference (p = 0.23 and 0.21, respectively).

In our study, the median time to dependence (KPS <70) was 11.6 months in tumor resection group vs 3.86 months in without resection group.

The change of KPS from baseline in tumor resection group was significantly presented since 1 week after surgery. Meanwhile, in without resection group, we found significant change in KPS since 3 months after surgery. But, postoperative KPS difference from baseline at 1-month postoperative period showed 7.75 in resection group and 7.14 in without resection group, which was almost same, but still showed not statistically difference from baseline in non-resection group (p = 0.949).

Table 4 Tumor resection on Karnofsky performance status (KPS) in patient with brain glioblastoma (change from baseline)

KPS score/Time	Tumor resection (n = 80)		Without resection (n = 7)		Difference between Groups (95% CI)	p-value
	Change from baseline (95% CI)	p-value	Change from baseline (95% CI)	p-value		
Post-operative						
1 week	-6.75 (-10.51, -2.99)	< 0.001*	1.43 (-11.29, 14.14)	0.826	-8.18 (-21.44, 5.08)	0.227
1 month	-7.75 (-13.00, -2.50)	0.004*	-7.14 (-24.91, 10.62)	0.431	-0.61 (-19.13, 17.92)	0.949
3 months	-14.75 (-21.50, -8.00)	< 0.001*	-27.14 (-49.97, -4.31)	0.020*	12.39 (-11.41, 36.2)	0.308
6 months	-23.50 (-31.85, -15.15)	< 0.001*	-38.57 (-66.79, -10.35)	0.007*	15.07 (-14.35, 44.5)	0.316

Abbreviation: CI, confident interval

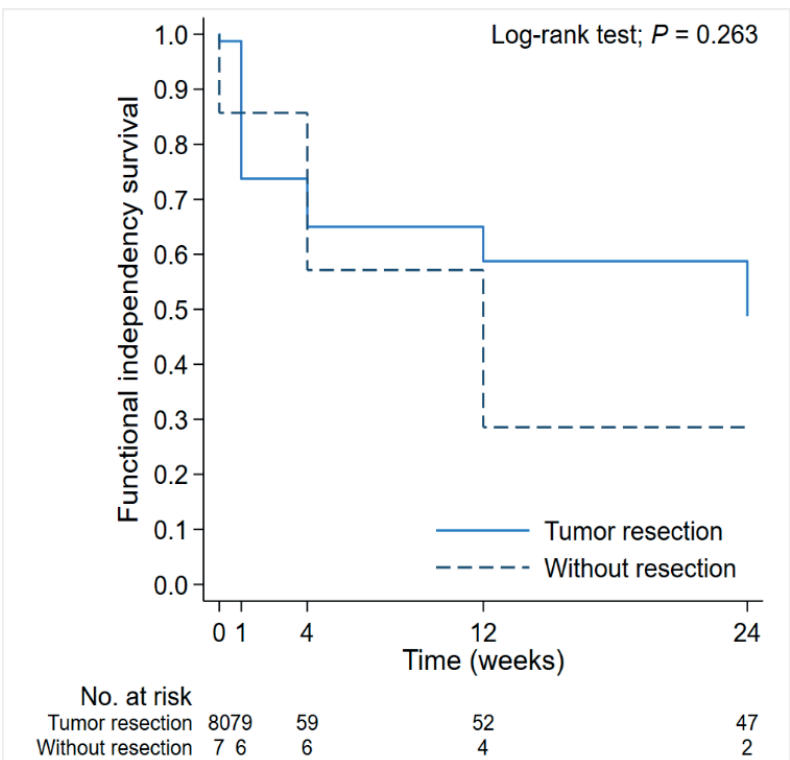
Analyses were conducted with the use of a linear mixed-effects model adjusted for baseline value

* Significant at p-value < 0.05

According to Table 5, the percentage of patient who was still be independent (KPS >70) was 73.75%, 65%, 58.75%, 48.75% in tumor resection group, and 85.71%, 57.14%, 28.57%, 28.57% at 1-week, 1-month, 3-month, 6-month postoperative period. But there was no statistical difference in percentage of patient who was still be independent between groups in each follow-up time up to 6 months (p = 0.263).

Table 5 Univariable analysis for functional independency in patient with brain glioblastoma

Functional independency	Tumor resection (n = 80)		Without resection (n = 7)		*p*-value
	n	SR (95% CI)	n	SR (95% CI)	
Post-operative					0.263
1 week	21	73.75 (62.64 - 82.02)	1	85.71 (33.41 - 97.86)	
1 month	7	65.00 (53.49 -74.34)	2	57.14 (17.19 - 83.71)	
3 months	5	58.75 (47.18 - 68.62)	2	28.57 (4.11 - 61.15)	
6 months	8	48.75 (37.45 - 59.12)	2	28.57 (4.11 - 61.15)	



The multivariate analysis showed only radiation therapy reception was the factor that associated with increased survival with functional independency in these patients.

Table 6 Multivariable analysis for Tumor resection on functional independency in patient with brain GBM by Cox proportional hazard model

Factors	Univariable analysis			Multivariable analysis		
	HR	95% CI	*p*-value	HR_{adj},	95% CI	*p*-value
Tumor resection	0.62	(0.24 - 1.57)	0.311	1.02	(0.33 - 3.18)	0.967
Age (years)						
< 60	1.00	Reference		1.00	Reference	
≥ 60	1.39	(0.78 - 2.48)	0.265	1.28	(0.68 - 2.43)	0.448
Sex						
Male	1.52	(0.85 - 2.74)	0.161	1.49	(0.80 - 2.75	0.205
Female	1.00	Reference		1.00	Reference	
ASA						
1	1.00	Reference		1.00	Reference	
2	1.28	(0.69 - 2.38)	0.434	1.07	(0.54 - 2.12)	0.851
3	1.89	(0.76 - 4.71)	0.172	1.52	(0.51 - 4.58)	0.455
Underlying disease	1.38	(0.77 -2.48)	0.276	-	-	NA
Site eloquent	0.81	(0.45 - 1.48)	0.501	0.66	(0.35 - 1.26)	0.205
RT	0.32	(0.16 - 0.66)	0.002*	0.40	(0.17 -0.95)	0.038*
CMT	0.47	(0.26 - 0.85)	0.012*	0.62	(0.31 - 1.24)	0.177

Abbreviations: NA, data not applicable; HR, Hazard Ratio; HR_{adj} Adjusted Hazard Ratio; CI, confident interval

There were several complications after surgery for GBM in both resection and without resection group. The most common complication was motor weakness, which was occurred only in patients underwent tumor resection.

Table 7 Complication of patient with brain glioblastoma

Complications	Total (n = 87)	Tumor resection		*p*-value
		Yes (n = 80)	No (n = 7)	
Overall Complication	57 (65.5)	54 (67.5)	2 (28.6)	0.228
New Motor weakness	11 (12.6)	11 (13.8)	0 (0.0)	0.588
UTI	8 (9.2)	8 (10.0)	0.(0.0)	1.000
Pneumonia	7 (8.0)	7 (8.8)	0 (0.0)	1.000
VTE	7 (8.0)	7 (8.8)	0 (0.0)	1.000
Ishemic Stroke	7 (8.0)	7 (8.8)	0 (0.0)	1.000
Edema brain	7 (8.0)	6 (7.5)	1 (14.3)	0.456
Wound complication	6 (6.9)	5 (6.3)	1 (14.3)	0.405
Seizure	5 (5.7)	5 (6.3)	0 (0.0)	1.000
Cognitive impair	5 (5.7)	5 (6.3)	0 (0.0)	1.000
Hydrocephalus/Leptomeningeal metastasis	3 (3.4)	3 (3.8)	0 (0.0)	1.000
New VF Defect	2 (2.3)	2 (2.5)	0 (0.0)	1.000
UGIB	1 (1.1)	1 (1.3)	0 (0.0)	1.000

Discussion

This study aimed to assess time that patients with brain GBM had, since the diagnosis until they were functionally dependence. Using KPS <70 as indicator of functional dependence, we conducted retrospective cohort study in our institute to assess the survival time with functional independence in these patients. In the previous study in 2015 by Sacko, et al.[16] the patient in their study who undergone tumor resection surgery had the longer survival time with functional independency (KPS >70) about 15.9 months vs. 6.7 months in non-tumor resection group (p = 0.006). In our study we found that patients underwent tumor resection surgery for brain GBM tend to had more survival time with functional independency (11.60 months) than in non-tumor resection group (3.86 months), but there was no statistically significant (p = 0.087), which may be from small number of samples used in this study.
Our study was the first study in Thailand that emphasized the functional independency (KPS >70) as the indicator of GBM treatment quality, and assessed tumor resection, which was an important method of treatment in brain GBM.

Post-operatively, there was declination of mean KPS in both groups of patients. There was no statistically significant difference in post-operative KPS score in each follow-up time of patient with GBM underwent tumor resection and non-tumor resection (biopsy then RT or CMT) treatment after diagnosis of GBM until 6 months after diagnosis (or operation). But, after 3-month postoperative time, the deterioration rate of KPS in non-tumor resection group tended to be more than in tumor resection group (without statistically significant). This may be explained by the small sample size in non-resection group causing low power of statistic to detect the difference.

Postoperative KPS difference from baseline at 1-month postoperative period in both groups was almost same, but still showed no statistically difference. This may be explained by the small sample size in non-resection group causing low power of statistic to detect the difference.

This may imply that in tumor resection group, the patient tended to have more time in independent status than in non-tumor resection group.

There were several complications after surgery for GBM which was not different between tumor resection and non-resection group. The most common complication from glioblastoma tumor resection in our institute was new motor deficit (while there was none in the non-resection group).

However, in some groups of patients who have GBM that considered to be unresectable or not optimal condition for surgery i.e., other poor medical conditions or preoperative poor KPS score, the result of this study cannot be used and no patient in this study who was not undergone tumor resection due to this reason.

There are several limitations of this study. First, the study design is retrospective study, causing selection bias. Moreover, there was a number of the patient, who was excluded from study because of incomplete information. Second, the very small number of patients in non-tumor resection group, causing low power of statistic to detect the difference

in multiple parameters. Third, there was confounding factor i.e., location of tumor, which affect the outcome of treatment, and our study did not categorize the patient.

The study in the future should be done using other measurements i.e. European Organization for Research and Treatment of Cancer Core Quality-of-Life Questionnaire (EORTC QLQ-C30)[17], EORTC brain cancer module (EORTC QLQ-BN20)[18] which was better for the reliability, validity, responsiveness and sensitivity in quality of life assessment in patient with brain glioblastoma.[19] In addition, multi-center setting and prospective study design should be considered in order to maximize statistical power.

Conclusion

The patient with brain GBM, receiving tumor resection treatment tend to had more time in independent than patient receiving non-tumor resection treatment. However, this result could not be used in patient who was not suitable for tumor resection due to other condition. Furthermore, future study should be done using larger number of patients and using more objective parameter representing functional independence.

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