Middle Black Sea Journal of Health Science / Mid Blac Sea J Health Sci
November 2022; 8(4):592-602

RESEARCH ARTICLE
DOI: 10.19127/mbsjohs.1143930

Effect of Sodium Fluorescein Use on Surgical Outcomes and Survival in Cases with High-Graded Glial Tumor: A retrospective study

Tamer Tunçkale[1(ID)], Tezcan Çalışkan[1(ID)]

[1]Department of Neurosurgery, Tekirdag Namik Kemal University, Tekirdag, Turkey,

Received: 18 July 2022, Accepted: 09 September 2022, Published online: 30 November 2022

Abstract

Objective: The most effective factor on malignant glioma (MGs) treatment affecting overall survival is the extent of resection. The use of sodium fluorescein (FL) staining in order to increase the amount of resection, is applied more effectively and safely at lower doses with the aid of 560nm filtered surgical microscopes. Our aim was to investigate the effects of the use of FL in MGs surgery on the gross total resection rate (GTR), duration of surgery, length of hospital stays, and survival time.

Methods: A retrospective study was conducted on 17 patients whose histopathological evaluations were reported as MGs and operated under surgical white light (Group 1), and 23 patients who were operated under FL560 module surgical microscope (Group 2) with a low dose of (3mg/kg body weight) FL dye. The blood loss in the course of surgery, GTR, surgical time, and hospital stay were compared for both groups with the student-t-test. Kaplan-Meier method was used for the survival time analysis.

Results: GTR rates were found to be 82.3% for patients operated under surgical white light, and the percentage for FL-utilized patients was 91.3%. There was no significant difference in blood loss or hospital stay between the two groups; however, the surgical time for FL-utilized patients was found to be significantly low in comparison to the other group. The overall survival time for patients who were operated under surgical white light was found to be 64 weeks (448 ± 64 days) while it was determined as 84.7 weeks (593±55 days) for patients operated with the use of FL, however, the difference between them was not found out to be statistically significant. The use of FL enabled the surgeon to determine the cortical incision area in 13 cases, where the location of the tumor was close to the cortex.

Conclusions: While the use of FL shortens the surgical time in contrast-enhancing MGs, it increases the GTR rate. FL also functions well with the determination of the location of the surgical site for tumors close to the cortex.

Keywords: Sodium Fluorescein, High-Grade Glioma, Surgical Resection

Suggested Citation: Tamer Tunçkale T, Çalışkan T. Effect of sodium fluorescein use on surgical outcomes and survival in cases with high graded glial tumor: a retrospective study Mid Blac Sea J Health Sci, 2022;8(4):592-602.

Address for correspondence/reprints:
Name and Surname: Tamer Tunçkale
Telephone number: +90 (505) 373 71 03
E-mail: ttunckale@hotmail.com

INTRODUCTION

When a patient is diagnosed with a brain tumor, a great challenge begins in order to maximize the life span of the patient as well as to protect the present neurological competence. MGs are the most prevalent primary brain tumors and are unfortunately very invasive, and rapidly progressive tumors, which are surgically hard to resect totally (1). Today, survival time for patients with MGs is quite short despite standard microsurgery, radiotherapy, and chemotherapy (2). While the American Society of Clinical Oncology issued the overall survival time as 7.7 months for patients undergoing radiotherapy after surgery, the overall survival time for patients undergoing chemotherapy after radiotherapy was determined as 13.5 months (3). One of the most effective treatments for disease-free survival and overall survival is the maximum resection of the tumor (4). Therefore, the main objective of the treatment should be the total excision of the tumor without leading to neurological deficit. For this purpose, there are many techniques such as navigation systems, brain mapping, fluorescein guide, intraoperative ultrasound, and magnetic resonance images (MRI), which are used in order to enhance surgical safety, and also resection (5,6). Intraoperative fluorescent dye, which aimed to determine the edges of the tumor and thus, provides safe and maximum resection, was used first in 1948 by Moore et al. (7) FL stains the contrast-enhancing areas and it is useless in non-contrast lesions. It had been used at high doses such as 15-20 mg/kg for many years in order to determine the edges of the tumor macroscopically; however, many side effects including anaphylactic shock were reported (8,9). Lower doses such as 5-10 mg/kg were used safely and effectively with a special operative microscope module with excitation and observation filters (10,11). Recently, there have been numerous published reports indicating that the tumor edges can be identified much more clearly with the new generation 560nm filtered surgical microscopes with low level (2-4 mg/kg) FL, and thus, enable surgery (10,12-14). Fluorescein-guided surgery, which is conducted with extremely cheap and safe at low doses, has become a considerable alternative to 5-Aminolevulinic acid. The efficacy of low-dose FL use on surgery, which has recently been used in brain tumor surgeries via specially filtered microscopes, and its effect on long-term survival time is not known. In this study, patients with high-grade glial masses for whom FL was used in surgery were investigated in terms of GTR rate, length of hospital stay, duration of surgery, blood loss, and survival at three-year follow-up.

METHODS

A retrospective study was conducted at Namık Kemal University, School of Medicine on 40 patients with high-grade glial tumors. 17 patients who were operated on under white light before receiving the FL560 filter in our hospital between June 2015 and November 2016 were accepted as group 1, and 23 patients who were operated on with the help of FL after having the FL560 filter between December 2016 and November 2018 were accepted as group 2. Data were collected and analyzed in January 2021. The approval for this study was granted by the Namık Kemal University Ethics Committee (date: 28.07.2020 number: 2020.189.07.22).

Inclusion and Exclusion criteria:

Patients between the ages of 39-85 with significant contrast enhancement on their MRI reports were evaluated by a neuroradiologist, who were evaluated by a neuropathologist according to the WHO criteria, (15) diagnosed with glioblastoma multiforme, operated and also treated according to Stupp protocol, which means applying radiotherapy plus concomitant and adjuvant temozolomide, were included in our study (16).

Patients whose performance status was deteriorating due to tumors passing to the other hemisphere, who have tumors located in the brainstem, basal ganglia, or posterior fossa, or due to postoperative radio necrosis, patients with no contrast enhancement on their MRI, those who are contraindicated for contrast administration, and those with renal failure, liver failure, and those who have other malignancies in other organs were excluded from the study.

Patients treated with FL were asked to fill out an informed consent form about the side effects.

All patients were operated on under general anesthesia. For the operations of both groups, ultrasound (Siemens Acuson X300) was utilized in order to determine the location of the tumor and differentiate the residue tumor. Group 1 (n=17) patients were operated on via a surgical microscope under surgical white light. Group 2 patients (n=23) were given 3 mg/kg FL 10% as bolus following anesthesia induction from the central catheter before skin incision. Leica M530 OHX microscope, which is an FL560 fluorescein module, was utilized for the operation of the patients. Tumor parts, which could not be differentiated clearly under white light, and those being highlighted in yellow color under FL560 were excised. Every surgical procedure was recorded and stored digitally.

Residue tumor volumes in the first month of post-operation via contrast-enhanced MRI were evaluated using open-source software (Sectra UniView,https://medical.sectra.com/product/sectra-uniview), and were calculated. While those with contrast enhancement of 0.175cm3 were evaluated as GTR, those with contrast enhancement above 0.175cm3 were determined as subtotal resection (STR).

The hospital stays, surgical time, and amount of blood loss of patients, which were taken from the patient files, were recorded. Surgery notes and videos were analyzed in order to assess the utility of FL in the course of surgery. The time of death of patients was taken from the national recording system, and their life span after their first diagnosis was calculated accordingly.

Statistical analysis

While general survival time was determined as the period between the time of diagnosis and the date of their death, the general survival time of living patients was determined as the period between the time of diagnosis and their last control date on the national online health system.

Pearson's chi-squared test (or if it was not appropriate Fisher's Exact Test) was used for the comparison of categorical variables. Student-t-test were used for the comparison of continuous variables. Kaplan-Meier method was used for the survival time analysis, and the Log-Rank test was used for the comparison of groups. Data, in which the P value was found to be below 0.05, and error performance Type 1 was found out to be below 5%, were determined as statistically significant. All statistical analyses were carried out via SPSS 24 (SPSS Inc., Chicago, III) program.

RESULTS

The study comprised 40 patients with total 50 operations. For patients, who have operated again for recurrence, information of their first operation was evaluated. The median age of patients was 61.5 (min.39-max.85). The average age of patients in Group 1 (n=17) was 63.5± 8.3 (range 50 to 80 years, 9 males, 8 females), and in Group 2 (n=23), it was 59.6 ± 12.3 (range 39 to 85 years, 13 males, 10 female), and no difference in the average of age was found between these two groups (p= 0.269) (Table 1). There was also no difference determined between the groups in terms of the amount of bleeding and hospital stay duration (p=0.247, p=0.155, respectively) (Table 1).

In Group 1, 3 patients had a STR, and 14 patients had a GTR. The percentages of resection for 3 patients who had a STR in Group 1 were determined as 73.2%, 81.3%, and 92.3%. While patients who had a STR in Group 1 were reoperated within the first two months, one patient underwent surgery in the 8th and 20th months, which is for three times in total. In patients who had a GTR, 2 of the patients who had a recurrence underwent a second operation (Table 2).

In Group 2, 2 patients had a STR while 21 patients had a GTR. The resection percentages of STR-receiving patients were 87.6 and 89.1%. In Group 2, while 2 patients, who had a recurrence after the 6th month, underwent 2 operations, 1 patient underwent three operations in total in the 7th and 10th month (Table 3). The age, symptoms, size of the tumor and its location, amount of resection, and number of operations are given in Table 2 for Group 1; whereas these data were given in Table 3 for Group 2.

When survival was analyzed in Group 1 and Group 2, it was found that the overall survival time in Group 1 was 64 weeks (448±52 days), while it was 84.7 weeks (593±55 days) in Group 2, and when it was evaluated via long-rank test, it was found out that the survival time in both groups was similar (p=0.125) (Fig 1).

In 13 cases, the use of FL was beneficial for

Table 1. Characteristic features of both patient groups

		Group1		Group2		
		Mean ± s.s / n	**Median**	**Mean ± s.s / n**	**Median**	**p**
Age		63.5± 8.3	66.0	59.6 ± 12.3	61.0	0.269 ^{t}
Sex	Male	9 (%41)		13 (%59)		
	Female	8 (%44)		10 (%56)		0.822 ^{x2}
Resection	Total	14(%82.3)		21(%91.3)		
	Subtotal	3(%17.7)		2(%8.7)		0.634 ^{f}
Blood loss (cc)		308.2 ± 94.0	290.0	274.1 ± 88.3	270.0	0.247 ^{t}
Surgical time(min)		270.3 ± 44.6	260.0	241.1 ± 37,9	230.0	**0.031** ^{t}
Tumor volume(cm³)		33.4 ± 27.1	23.5	52.5 ± 38.2	47.1	0.086 ^{t}
Hospital stay (day)		9.2 ± 2.6	9.0	8.2 ± 1.9	8.0	0.155 ^{t}

Table 2. Clinical summary of patients operated under surgical white light (Group 1)

Number	Age/Sex	Symptoms/Signs	Localization	Tumor size (cm³)	% of resection	Number of operations
(1)	55/F	Seizure, headache	RP	14,6	100	2
(2)	59/M	Left hemiparesis	RF	5,8	100	1
(3)	58/M	Seizure	LF	19,6	100	2
(4)	70/M	Left hemiparesis	RT	12,2	100	1
(5)	56/F	Right hemiparesis	LF	40,1	100	1
(6)	70/F	Seizure, somnolence	LP	94,8	92,3	2
(7)	61/F	Visual field defect, headache	LO	86,6	100	1
(8)	75/F	Headache, dizziness	RP	11	100	1
(9)	66/M	Headache, left hemiparesis	RF/I/T	45,8	73,2	2
(10)	67/F	Aphasia, headache	RF/T	3,9	100	1
(11)	50/M	Amnesia, headache	RF	50,5	100	1
(12)	68/M	Right hemiplegia	LF	34,4	100	1
(13)	67/M	Headache, right hemiparesis	LP	7,1	100	1
(14)	67/M	Headache, agraphia	RP	42,8	100	1
(15)	80/F	Seizure, headache	RO	23,5	100	1
(16)	59/M	Headache	RF/T	19,7	100	1
(17)	51/F	Left hemiparesis, headache	RF	54,8	81,3	3

patients with a tumor close to the cortex in terms of determining the cortical incision area (Fig 2A-2B-2C). There was no side effect observed against FL given at 3mg/kg in Group 2.

Table 3. Clinical summary of patients operated via Na Flourescein dye (Group 2)

Number	Age/Sex	Symptoms/Signs	Localization	Tumor size (cm³)	% of resection	Number of operations
(1)	39/M	Left hemiparesis, headache	RF	61,7	100	1
(2)	61/M	Headache	RP	31,9	100	2
(3)	51/F	Seizure, dysarthria	LT	3,1	100	1
(4)	62/F	Headache	RO	47,1	100	1
(5)	68/M	Left hemiparesis, headache	RP	27,2	100	1
(6)	66/M	Halusination	RF	16,8	100	1
(7)	66/M	Headache	LP	77,3	100	1
(8)	71/M	Headache	LF	9,5	100	1
(9)	60/F	Seizure, somnolence	LT/P	85,1	87,60%	1
(10)	44/F	Headache	RP	24,6	100	1
(11)	42/M	Seizure, headache	LF	172,2	100	1
(12)	57/F	Left hemiparesis	RF	75,4	100	3
(13)	62/F	Right hemiparesis	LF	30,3	100	1
(14)	52/M	Headache	RO	51,2	100	1
(15)	47/M	Headache	LT	33,9	100	1
(16)	52/M	Dysarthria	LT	65,2	100	2
(17)	51/F	Headache	LP	41,1	100	1
(18)	68/M	Left hemiparesis	LP	22,8	100	1
(19)	48/F	Visual field defect	LO	98	100	1
(20)	74/M	Headache	LO	19,4	100	1
(21)	83/F	Somnolence, shift	RF	105,5	89,10%	1
(22)	85/F	Aphasia, headache	LT	52,7	100	1
(23)	62/M	Seizure	RF	55,9	100	1

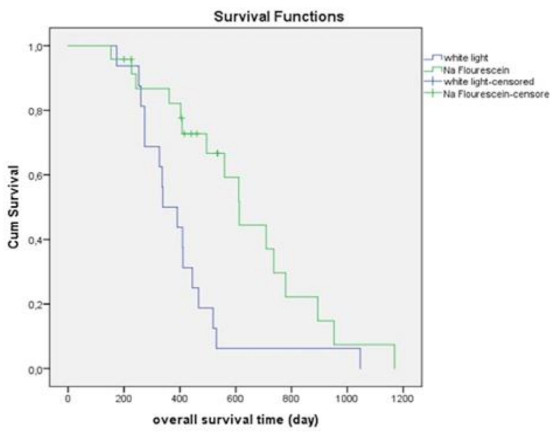

Figure 1. Kaplan-Meier plot stratified by using NA Fluorescein for overall survival (OS).

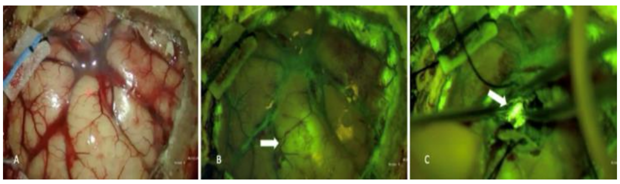

Figure 2A. Image of brain tissue before cortical incision under white light. **2B.** In masses close to the cortex, a yellow highlight is seen in the cortex under FL staining. **2C.** Arrow shows the FL stained tumor tissue after cortical incision.

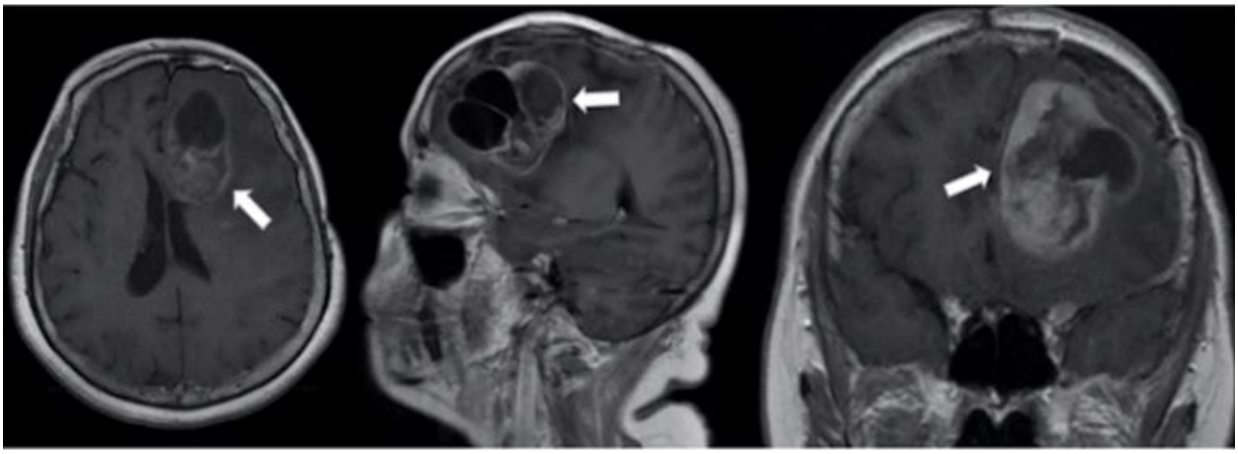

Figure 3. Left frontal cystic heterogeneous contrast-enhancing high-grade glial tumor.

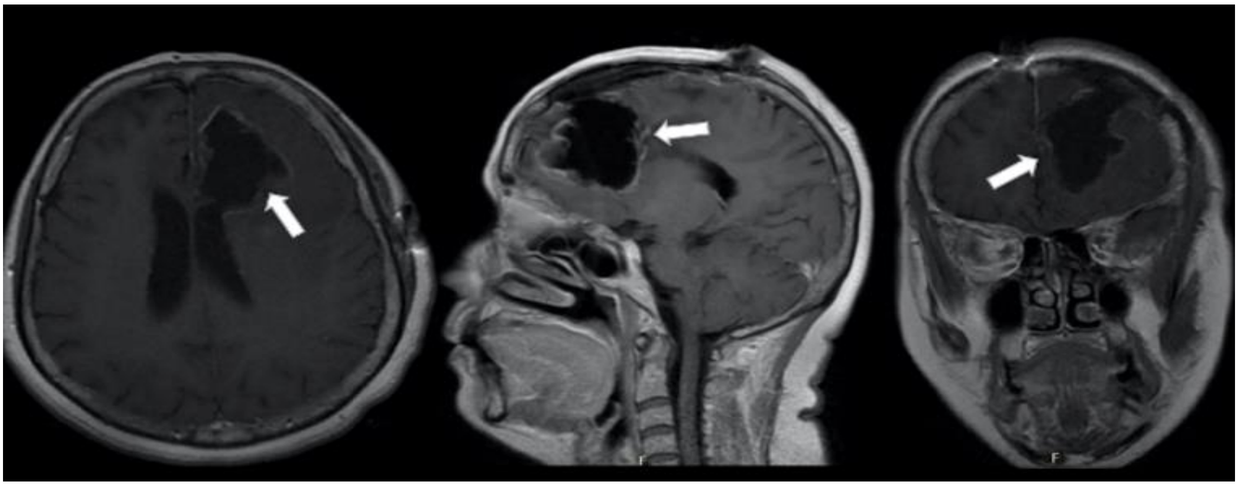

Figure 4. Total excision in the postoperative 24th hour MR image of the patient in whom FL staining was used.

DISCUSSION

Comparing the patients who were operated on for high-graded glial masses with and without the use of FL, it was found that the use of FL reduced the surgical time significantly. While there was no significant difference between the groups in terms of length of hospital stay and amount of bleeding, we found that the use of FL provided some improvement in GTR and survival rates, although there was no statistically significant difference. We experienced that the use of FL was considerably beneficial in 21 patients out of 23. We have observed that the two patients, in which the use of FL was not useful, the contrast enhancement was also relatively less. We can also say that during the surgery, as contrast enhancement in preoperative MRI increases FL highlighting ability becomes more effective.

Like other authors, we have also determined that the utilization of FL gives yellow highlights in the dura and contused brain tissue (11,12,14). The question is whether there is a tumor in the yellow highlighted areas during operation except for these areas, or it is possible that there is a false positivity. Many pathologically confirmed studies have been designed in order to find an answer to this question. Acerbi F et al. stated that by using FL at 5-10 mg/kg in high-graded glial masses, the specificity, sensitivity, and GTR percentages of staining were determined as 89.5%, 94%, and 80%, respectively (10). There were similar results stated in many studies (8,14,17).

The fact that the maximum resection of the tumor is the most important factor affecting the overall survival in high-graded glial masses has led to the improvement of methods aiding the surgeon in tumor surgeries. The biggest handicap in the surgery of intra-axial mass surgeries is that it is sometimes impossible to differentiate the edges of the tumor from the normal brain tissue. In tumors, which lead to contrast enhancement due to the blood-brain barrier the use of fluorophores such as 5-Aminolevulinic acid, FL, or indocyanine green has become promising in the differentiation of brain tissue and tumor tissue (11,18-21). It has been stated that the utilization of FL in primary MGs and recurrent MGs, metastases, lymphomas, and spinal intramedullary lesions are extremely significant (10,22-24). Also, it has been approved that the use of FL dye increases the GTR rate, and in this study, this rate was found to be 91.3%, whereas the rate in those with no FL use was determined as 82.3%. (Fig 3-4) The GTR rate being high in our study may be due to the exclusion criteria we used in order to homogenize the two groups.

We can say that we have experienced that the FL dye provides confidence to the surgeon and that it decreases confusion during operation. This resulted in the surgical time being shortened in the group in which we used FL (p=0.031).

We found out that together with the surgical time, there was also a decrease in the amount of bleeding, and hospital stay; however, these decreases were not found to be significant. (Table 1) In particular, the amount of bleeding in Group 1 was determined as 308.2 ± 94.0 cc while it was found to be 274.1 ± 88.3 cc in Group 2. Although this difference is slight, we assume that this is due to the confidence of the surgeon knowing that he/she is in the tumor and acting quickly in the course of surgery. It is known that the low-dose FL use in a 560 nm filter microscope reduces the side effects of FL and is even used safely in pediatric cases (25). In our study, we did not encounter any side effects related to FL.

Another important point in tumor surgery is the determination of the entry point of the tumor. In tumors close to the cortex, they are reached through cortical incisions from non-eloquent areas (26). In our cases, we performed the operations with the help of ultrasound from the region closest to the cortex. In all of the 13 patients whose lesions were close to the cortex, the yellow highlight at the beginning of the surgery assisted us in finding the entry point (Fig 2B).

Apart from this, there are several studies reporting the effect of the use of FL on survival, and Koc K et al. first mentioned that in their series where they used high doses of FL, the overall survival was determined as 43.9 weeks, whereas it was 41.8 for the control group, and stated that there was no significant difference between the two groups (27). Katsevman et al., however, stated that in their series, in which they used 3-4 mg kg of FL, the median survival was better at 78 weeks compared to the control group, which was 60 weeks (28).

We have found a similar result in this study. The median survival was found to be 84.7 weeks for the group in which we used FL while it was determined as 64 weeks for the group in which no FL was used. (p= 0.634) (Fig 1) The median survival time in which we used FL improved; however, there was no statistical significance. We believe that this difference was parallel to the increase in GTR rate and that it should be studied on a larger series of MGs with different immunohistochemical classifications. This result can be explained through the impact of other factors affecting the limited number of patients as well as the overall survival. We can still say that the result found out on overall survival is promising.

Although the use of low-dose FL in 560 nm filter microscopes in glial tumor surgeries has only recently entered the surgical practice, it has been welcomed excitedly among surgeons, and its use has become prevalent. We have presented our experience in this short period of time in patients treated with the use of FL through observational and statistical data. As the use of FL becomes widespread, which in our opinion is a considerably beneficial technique, we think that the surgical efficacy in different tumor types and its effect on progression-free survival and overall survival should be investigated in larger series.

Limitations

The limitation of this study is the small number of tumors with different contrast enhancement features in this series. Studying in larger series in cystic tumors and MGs with less contrast enhancement will reveal the efficacy of FL more clearly.

CONCLUSION

The use of FL aids to determine the entry point during surgery on tumors close to the cortex, and also shortens the surgical time by helping to differentiate the tumor from the normal tissue. Since the GTR rate increases in MGs patients, it is necessary that its impact on progression-free survival and overall survival be studied on larger series.

Ethics Committee Approval: Ethics committee approval was received for this study from Tekirdağ Namık Kemal University Clinical Research Ethics Committee (ethics committee date 28.07.2020 and no: 2020.189.07.22)
Peer-review: Externally peer-reviewed.
Author Contributions: Concept, Design TT, TÇ, Literature search, Data Collection and Processing TT, TÇ, Analysis or Interpretation, Writing – TT, TÇ

Conflict of Interest: The authors have no interests to declare

Financial Disclosure: The authors received no financial support for the research, authorship, and publication of this article.

Acknowledgments: We would like to thank Assist Prof Birol Topçu, for the evaluation of the data

REFERENCES

1- Quinn T Ostrom, Haley Gittleman, Paul Farah, Annie Ondracek, Yanwen Chen, Yingli Wolinsky, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2006–2010. Neuro-oncol. 2013;15(sup 6): p1–56.

2- Sant M, Minicozzi P, Lagorio S, Johannesen T B, Marcos-Gragera R, Francisci S, EUROCARE Working Group. Survival of European patients with central nervous system tumors. Int J Cancer. 2012;131(1):173 – 185.

3- James R. Perry, Normand Laperriere, Christopher J. O'Callaghan, Alba Ariela Brandes, Johan Menten, Claire Phillips, et al. A phase III randomized controlled trial of short-course radiotherapy with or without concomitant and adjuvant temozolomide in elderly patients with glioblastoma (CCTG CE.6, EORTC 26062-22061, TROG 08.02, NCT00482677). J Clin Oncol. 2016;34(18): Abstract. doi:10.1200/JCO.2016. 34.18_suppl.LBA2.

4- Almeida JP, Chaichana KL, Rincon-Torroella J, Quinones-Hinojosa A. The value of extent of resection of glioblastomas: clinical evidence and current approach. Curr Neurol Neurosci Rep. 2015;15(2):517. doi:10.1007/ s11910-014-0517-x.

5- Nancy Ann Oberheim Bush, Susan M Chang , Mitchel S Berger . Current and future strategies for treatment of glioma. Neurosurg Rev 2017;40:1–14 DOI 10.1007/s10143-016-0709-8.

6- Michael Weller, Martin van den Bent, Jörg C Tonn . European Association for Neuro-Oncology (EANO) guideline on the diagnosis and treatment of adult astrocytic and oligodendroglial gliomas. Lancet Oncol 2017;18(6):e315-e329. doi: 10.1016/S1470-2045(17)30194-8.

7- Moore GE, Peyton WT, French LA, Walker WW. The clinical use of fluorescein in neurosurgery; the localization of brain tumors. J Neurosurg 1948;5(4):392–8.doi:10.3171/jns.1948.5.4.0392.

8- Chen B, Wang H, Ge P, Zhao J, Li W, Gu H, Wang G, Luo Y, Chen D:. Gross total resection of glioma with the intraoperative fluorescence-guidance of fluorescein sodium. Int J Med Sci. 2012;9(8):708-714.

9- Dilek O, Ihsan A, Tulay H. Anaphylactic reaction after fluorescein sodium administration during intracranial surgery, J. Clin. Neurosci. 2011;18:430–431.

10- Francesco Acerbi, Morgan Broggi, Marica Eoli, Elena Anghileri, Lucia Cuppini, Bianca Pollo, et al. Fluorescein- guided surgery for grade IV gliomas with a dedicated filter on the surgical microscope: preliminary results in 12 cases. Acta Neurochir. 2013;155(7):1277–86.doi:10.1007/s00701-013-1734-9.

11- Kuroiwa T, Kajimoto Y, Ohta T. Development of a fluorescein operative microscope for use during malignant glioma surgery: A technical note and preliminary report. Surg Neurol. 1998;50(1):41- 48; discussion 48-49.

12- Acerbi F, Broggi M, Eoli M, Anghileri E, Cavallo C, Boffano C, et al. Is fluorescein-guided technique able to help in resection of high-grade gliomas? Neurosurg. Focus 36 (2014) E5.

13- Schebesch KM, Proescholdt M, Höhne J, Hohenberger C, Hansen E, Riemenschneider MJ, et al. Sodium fluorescein-guided resection under the YELLOW 560 nm surgical microscope filter in malignant brain tumor surgery- a feasibility study, Acta Neurochir. (Wien) 2013;155:693–699.

14- Hamamcıoğlu MK, Akçakay MO, Göker B, Kasımcan MÖ, Kırış T. The use of the YELLOW 560 nm surgical microscope filter for sodium fluorescein-guided resection of brain tumors: Our preliminary results in a series of 28 patients. Clinical Neurology and Neurosurgery. 2016;143:39–45. doi: 10.1016/j.clineuro.2016.02.006.

15- Wesseling P, Capper D. WHO 2016 Classification of gliomas. Neuropathol Appl Neurobiol, 2018;44(2):139-150. doi: 10.1111/nan.12432.

16- Stupp R, Mason Van Den Bent WP, Weller MJM, Fisher B, Taphoorn MJB, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N. Engl. J. Med. 2005;352:987–996.

17- Rey-Dios R, Hattab EM, Cohen-Gadol AA. Use of intraoperative fluorescein sodium fluorescence to improve the accuracy of tissue diagnosis during stereotactic needle biopsy of high- grade gliomas. Acta Neurochir. 2014;156(6):1071-1075.

18- Cavallo C, De Laurentis C, Vetrano IG, Falco J, Broggi M, Schiariti M, et al. The utilization of fluorescein in brain tumor surgery: a systematic review. J Neurosurg Sci. 2018;62:690–703. doi: 10.23736/S0390-5616.18.04480-6.

19- Stummer W, Pichlmeier U, Meinel T, Wiestler OD, Zanella F, Reulen HJ. Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial. Lancet Oncol. 2006;7:392–401.doi: 10.1016/s1470-2045(06)70665-9.

20- Acerbi F, Vetrano IG, Sattin T, de Laurentis C, Bosio L, Rossini Z, et al. The role of indocyanine green videoangiography with FLOW 800 analysis for the surgical management of central nervous system tumors: an update. Neurosurg Focus. 2018;44:E6. doi: 10.3171/2018.3.FOCUS1862.

21- Kuroiwa T, Kajimoto Y, Ohta T. Surgical management for supratentorial astrocytic tumors. Minim Invasive Neurosurg. 42(4):182-186, 1999.

22- Schebesch KM, Hoehne J, Hohenberger C, Acerbi F, Broggi M, Proescholdt M, et al. Fluorescein sodium-guided surgery in cerebral lymphoma. Clin Neurol Neurosurg. 2015;139:125–8. doi: 10.1016/j.clineuro.2015.09.015.

23- Höhne J, Hohenberger C, Proescholdt M, Riemenschneider MJ, Wendl C, Brawanski A, et al. Fluorescein sodium-guided resection of cerebral metastases—an update. Acta Neurochir. 2017;159:363–7.

24- Höhne J, Schebesch KM, de Laurentis C, Akçakaya MO, Pedersen CB, Brawanski A, et al. Fluorescein Sodium in the Surgical Treatment of Recurrent Glioblastoma Multiforme. World Neurosurg. 2019;125:e158-e164. doi: 10.1016/j.wneu.2019.01.024.

25- Göker B, Kırış T. Sodium fluorescein–guided brain tumor surgery under the YELLOW-560-nm surgical microscope filter in pediatric age group: feasibility and preliminary results. Childs Nerv Syst. 2019;35(3):429-435. doi: 10.1007/s00381-018-04037-4.

26- Duffau H. Lessons from brain mapping in surgery for low-grade glioma: insights into associations between tumour and brain plasticity. The Lancet Neurology. 2005;4(8):476– 486.

27- Koc K, Anik I, Cabuk B, Ceylan S. Fluorescein sodium-guided surgery in glioblastoma multiforme: A prospective evaluation. Br J Neurosurg. 2008;22(1):99-103.

28- Gennadiy A Katsevman, Ryan C Turner, Ogaga Urhie, Joseph L Voelker, Sanjay Bhatia. Utility of sodium fluorescein for achieving resection targets in glioblastoma: increased gross- or near-total resections and prolonged survival. J Neurosurg. 2019;132(3):914-920. doi: 10.3171/2018.10.JNS181174.