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Original Article

Prognostic impact of sodium fluorescein-guided microsurgery on cognitive function, neuropeptide dynamics, and short-term outcomes in brain glioma patients

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Abstract: This study conducted a retrospective analysis on 107 brain glioma patients treated from January 2018 to February 2020 to assess the impact of sodium fluorescein-guided microsurgery on postoperative cognitive function and short-term outcomes. Patients were divided into two groups: a control group (n=50 patients) undergoing routine surgery and a research group (n=57 patients) receiving sodium fluorescein-guided microsurgery. The study compared postoperative total resection rates, changes in cognitive scores, and neuropeptide levels in cerebrospinal fluid between the groups. The findings revealed that the research group experienced shorter surgical time and hospitalization duration, reduced blood loss, and higher total resection rates compared to the control group. Furthermore, the research group demonstrated improvements in cognitive scores and an increase in neuropeptide levels after surgery. There was no significant difference in the comparison of the incidence of postoperative complications between the two groups. The WHO classification and preoperative performance scores were independent prognostic factors for the evaluation of 3-year survival, highlighting the clinical significance of sodium fluorescein-guided microsurgery in improving quality of life and cognitive functions of patients without compromising their long-term survival outcomes.

Keywords: Sodium fluorescein, microsurgery, brain glioma, cognitive function, neuropeptide, short-term prognosis

Introduction

Glioma, also known as neuroectodermal or neuroepithelial tumor, arises from the glial cells within the brain and constitutes the most common type of primary intracranial tumors [1, 2]. Gliomas account for as high as 25%-30% of all brain tumors, with 80% of them are malignant [3]. Glioblastoma (GBM) is the most aggressive glioma variant that comprises approximately 47% of all glioma cases [4]. Characterized by poor treatment outcomes, rapid disease progression, and a high mortality rate, the median survival duration of GBM is merely 14 months. GBM patients, particularly those live in regions with high GBM incidence rates but without the conditions to receive proper treatment, often bears significant financial and spiritual burdens, so do their families [5, 6]. According to the glioma classification issued by World Health Organization (WHO) in 2016, gliomas are categorized into grades I to IV, with grades I and II being the low-grade gliomas (LGGs). Among LGG patients, some are curable through surgical interventions, after which the recurrence rate would be relatively low and survival duration high, normally exceeding 5 years [7]. In contrast, grade III and IV gliomas are deemed as high-grade gliomas (HGGs) with a predictable high malignancy degree. HGGs are hard to be cured by surgical intervention alone because of their aggressive nature, typically accompanied by high recurrence rates, poor prognosis, and a general survival duration of only 1 to 3 years, even in addition to chemotherapy and radiotherapy applications [8, 9].

Minimally invasive surgery has become a widely accepted approach for treating brain gliomas. However, the unclear boundary between tumor and normal brain tissues makes it challenging for neurosurgeons to resect the tumor completely. As a consequence, the postoperative prognosis of patients is often poor, with a survival rate not exceeding 9.8% [10]. Nonetheless, this issue could be addressed with the application of fluorescence-assisted microsurgery, which is able to visualize brain tumors in real time. This advanced technique can assist neurosurgeons in achieving tumor resection at full capacity while preserving normal brain function during the surgical process [11]. In recent years, a built-in fluorescent module in surgical microscopes has facilitated the rising of fluorescence-guided microsurgery. Sodium fluorescein, a water-soluble fluorescent imaging agent, features an excitation peak at 460-490 nm and an emission peak at 510-580 nm [12]. During surgery, tumors often present a distinctive yellow-green or bright yellow boundary when observed under a fluorescence-assisted surgical microscope on fluorescence mode, whereas normal brain tissues remain unstained. Sodium fluorescein, therefore, has gained popularity as a fluorescent imaging agent in neurosurgery due to its easy application, affordability, and low occurrence rate of complications [13]. Furthermore, with the advent and advancement of fluorescent surgical microscopes, the recommended dosage of sodium fluorescein has been reduced from 20 mg/kg to 2-5 mg/kg. This reduction in dosage has little impacts on the intraoperative effectiveness of fluorescence and the surgical resection process [14]. However, the benefits of sodium fluorescein-guided microsurgery for evaluating postoperative cognitive function and the short-term outcomes of patients with brain glioma remain a subject of interest. For instance, a study by Wang et al. [37203814] assessed the clinical efficacy of sodium fluorescein-guided microsurgery on HGG patients, and their findings suggested that the gross total resection rates of patients following sodium fluorescein application in the study group were markedly enhanced in comparison to those in the control group, with a notable shorter surgical duration and improved overall survival rates, indicating that utilizing sodium fluorescein in tumor resection was advantageous. However, the insights presented in an article by Schupper et al. [34220688] merit consideration. This article reviewed the application of sodium fluorescein-guided microsurgery in brain tumor surgeries and explored various facets of sodium fluorescein usage. While sodium fluorescein proves effective in delineating HGGs owing to its capacity to traverse the blood-brain barrier, the concerns over its non-optional nature still exist. Sodium fluorescein could possibly accumulate in the normal brain parenchyma in adjacent to tumor tissues, resulting in false-positive outcomes.

Therefore, this study was designed to address the false-positive outcome issues of sodium fluorescein and gain a growing understanding of its advantages and disadvantages in the application of neurosurgery through evaluations of the postoperative cognitive function and short-term outcomes of patients with brain gliomas undergoing sodium fluorescein-guided microsurgery.

Methods and data

Clinical data

A retrospective analysis was conducted on a cohort of 141 patients with brain glioma treated at the First Affiliated Hospital of Guangxi Medical University from January 2018 to February 2020. This study has gained approval from the Medical Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Ethics Approval No.: 20215846).

Inclusion and exclusion criteria

Inclusion criteria: patients were eligible if they met the established diagnostic standards for brain glioma [15]; their diagnosis was confirmed through three-dimensional cranial magnetic resonance imaging (MRI) and electroencephalogram (EEG); their vital signs were stable; their projected survival time exceeding 3 months; and their clinical records were complete. Patients who had undergone relevant surgical and anesthetic procedures because of their clinical manifestations were included as well, only if they met the above criteria.

Exclusion criteria: patients were ineligible if they were diagnosed with brainstem gliomas; they were unfit to undergo surgery because of the presence of comorbidities such as coagula-

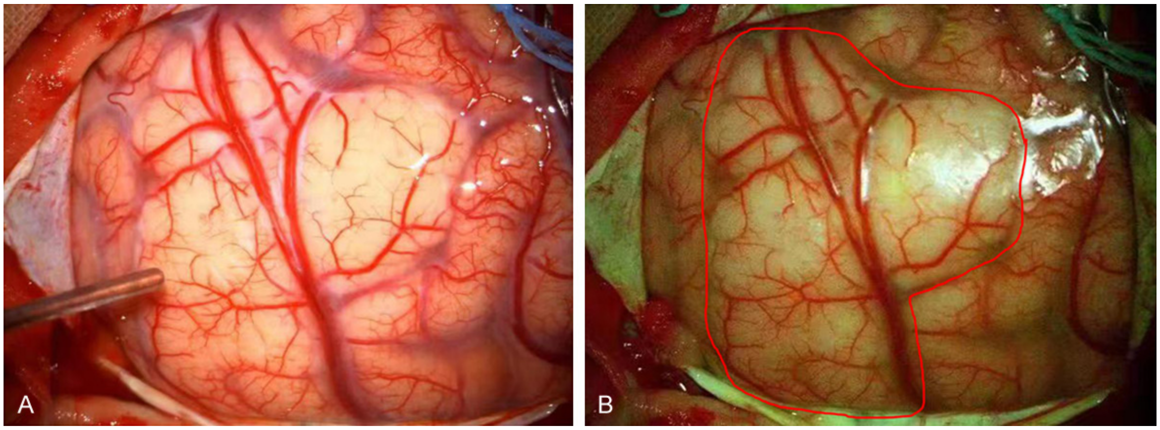

Figure 1. Sodium fluorescein-guided surgery. A: Normal white light mode; B: YELLOW 560 fluorescence mode. Note: Red marks are high fluorescent areas and also tumor margin.

tion dysfunction or severe dysfunctions in the heart, lungs, liver, or kidneys; they had received preoperative adjuvant therapies like radiotherapy or chemotherapy; their clinical data were incomplete; they had documented adverse reactions to fluorescein sodium or severe reactions to other contrast media.

Sample screening

A total of 107 patients were considered eligible in accordance with the inclusion and exclusion criteria, among which, 50 patients who received routine surgeries for brain glioma treatment were grouped as the control, and the remaining 57 patients who underwent sodium fluorescein-guided microsurgery were grouped as the research subjects. The introduction of sodium fluorescein-guided microsurgery to the Department of neurosurgery of the First Affiliated Hospital of Guangxi Medical University between the years 2019 and 2020 marked a pivotal transition from traditional surgical approaches to an advanced fluorescence-based surgical approach. After the year 2019, the selection of surgical approach was based on the availability of the fluorescein-guided technique as well as on the discretion of neurosurgeons', which emphases on tumor characteristics and the overall health of patients. This novel surgical approach for glioma resection added feasibility of systematic evaluations on postoperative outcomes in comparison to the routine surgical approach.

Therapeutic regimen

Surgical method: The preoperative MRI scanning were applied to figure out the location, the extent of invasion and the maximum diameter of the tumor, as well as how the tumor was connected with the surrounding cerebral lobes, the brain stem, blood vessels, and nerves. Sophisticated surgeons operated on patients in both the research and control groups. Patients in the research group had undergone a sodium fluorescein allergy test prior to surgery. Those who exhibited stable vital signs without the presence of red rash were considered not allergic and received an intravenous injection of sodium fluorescein at a dose of 1 mg/kg, 30 minutes before the surgery commenced. After anesthesia, a routine craniotomy was performed, followed by the incision of the dura mater. When the normal white light mode and the YELLOW 560 fluorescence mode were turned on in the microscope, the surgeons could discern the tumor's boundary, differentiate between edematous and normal brain tissue, and identify the relationship between the tumor and functional areas. **Figure 1** shows two images of the tumor and its surrounding tissues under the surgical resection microscope on different modes. The YELLOW 560 fluorescence mode was primarily utilized to observe the fluorescent area of the tumor and delineate its boundary, while the normal white light mode was predominantly employed for tumor removal. In the YELLOW 560 fluorescence mode, the tumor parenchyma exhibited a bright yellow or normal yellow hue, suggesting a strong fluorescent reaction. HGG patients that presented significant enhancement on preoperative cranial MRI showed a color of bright yellow, whereas LGG patients without the presence of enhancement a normal yellow color. The marginal tissue surrounding the tumor displayed a color of light yellow, signifying a weak fluorescent reaction. The normal brain tissue did not exhibit any fluorescence at all. The fluorescent degree in the tumor tissue was correlated with the level of enhancement observed on preoperative cranial MRI, with more pronounced MRI enhancement translating to more distinctive tumor fluorescence staining. During the surgical procedure, surgeons meticulously switched the two modes on the microscope, aiming to excise all fluorescence-stained tissues. This process was repeated until no fluorescent tissues were observed. Additionally, a small portion of the tissue that did not display fluorescent staining was carefully removed from the anterior, posterior, medial, and lateral cranial areas of patients for thorough pathological examinations. Following the meticulous removal operation on target tissues, routine procedures for achieving hemostasis and closing the cranium were executed. Subsequently, the patient was transferred to the ward, where they were closely monitored during their recovery from anesthesia. The collected pathological samples were categorized as "non-fluorescent tissue", "weak fluorescent tissue", and "strong fluorescent tissue" based on the intensity of yellow fluorescent staining observed under the microscope's fluorescence mode during the surgery. These samples were then forwarded for standard pathological and immunohistochemical analyses.

Postoperative examination and treatment: After surgery, patients in both groups were subjected to standard vital sign monitoring with comprehensive care. The care encompassed oxygen supplementation, measures to reduce brain edema, strategies for the prevention and treatment of epilepsy, and nutritional support specifically targeted at brain health. Within 24 hours following the surgery, a cranial CT scanning was conducted on each patient to assess the presence and severity of any hematoma and brain edema in the operated area. Furthermore, a cranial MRI with both plain and enhanced scanning was performed within 72 hours post-surgery to evaluate the extent of tumor removal. Patients diagnosed with LGGs who underwent a complete tumor resection were placed under vigilant observation. Patients identified with high-risk LGGs - characterized by factors such as incomplete tumor removal, a maximum tumor size of ≥6 cm, tumor extension across the cranial midline, preoperative neurological deficits, or age ≥40 years - and those diagnosed with HGGs were initiated on concurrent radiotherapy and chemotherapy at the conclusion of the first postoperative week. The radiotherapy regimen consisted of a total dosage ranging from 54 to 60 Gy, administered daily over a period of 42 days. Concurrently, at the onset of radiotherapy, patients were prescribed with oral temozolomide at a dosage of 150-200 mg/m^2, taken daily for 5 consecutive days. Subsequently, each patient underwent 6 cycles of adjuvant chemotherapy, with each cycle spanning 28 days.

Collection of clinical data

Clinical data extracted from patients' electronic medical records encompassed their sex, age, WHO tumor degree classification, maximum tumor diameter, lesion location, the presence of comorbid epilepsy, and the history of diabetes mellitus, hypertension, smoking, and alcohol use. Perioperative indicators included operation time and intraoperative blood loss. The medical records also encompassed key metrics such as the total resection rate, the Karnofsky Performance Scale (KPS) scores [16], the Mini-Mental State Examination (MMSE) scores [17], details of postoperative complications, and the duration of hospital stay. Additionally, laboratory tests measured the levels of oxytocin (OT), β-endorphin (β-EP), and arginine vasopressin (AVP) in the cerebrospinal fluid.

Scoring function

The KPS was employed to assess the health status of patients, with a higher score indicating better health status. The total score was 100 points. The MMSE was applied for the evaluation of patients' cognitive functions before and after treatment, with a score of less than 27 points suggesting the presence of cognitive dysfunction.

Follow-up

The 3-year survival data of patients were compiled from their electronic medical records and telephone follow-up records. Statistical analysis was performed using information gathered from both outpatient follow-up visits and telephone follow-ups. Telephone follow-ups were

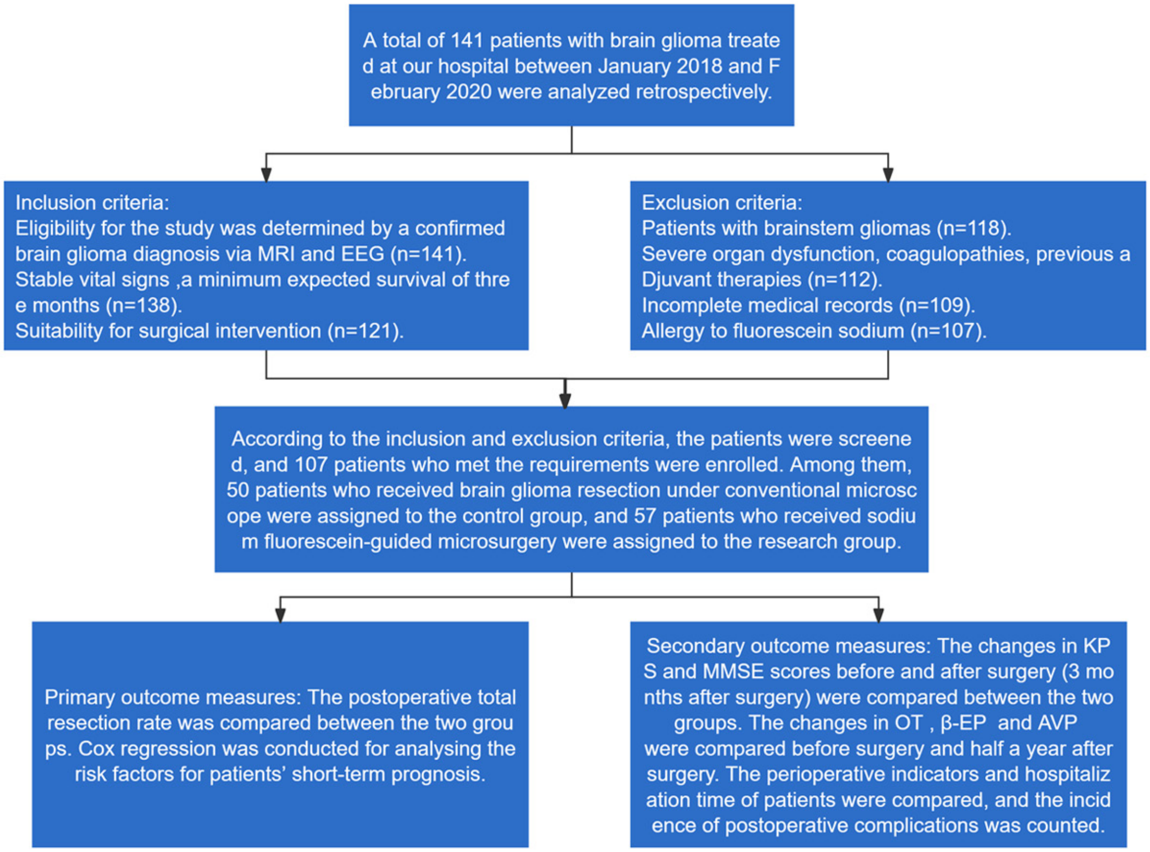

Figure 2. Flowchart of patient inclusion, exclusion, and outcome measures.

scheduled at 4, 8, and 12 months during the first year, and then every 6 months subsequently.

Outcome measures

Primary outcome measures included a comparison of the postoperative total resection rates between the two groups. Cox regression analysis was employed to identify risk factors affecting the short-term outcomes of patients.

Secondary outcome measures included comparisons of changes in KPS and MMSE scores pre- and post-surgery (3 months after surgery) between the two groups. The levels of OT (ml060469), β-EP (ml057845), and AVP (ml058799) were also compared between the two groups before surgery and six months post-surgery. Measurements of AVP, OT, and β-EP were performed using enzyme-linked immunosorbent assay (ELISA) kits provided by Shanghai Enzyme-linked Biotechnology Co., Ltd. Furthermore, perioperative indicators, duration of hospital stay, and the incidence of postoperative complications were evaluated and compared as well. To enhance understanding, a flowchart has been designed and is displayed in **Figure 2**.

Statistical analyses

This study utilized SPSS 26.0 software for statistical analysis. Measurement data underwent a normality test, with the Shapiro-Wilk test applied for analysis. Data that were normally distributed were presented as Mean ± SD, and comparisons between and within groups were performed using the independent-samples T test and the paired t test, respectively. For data not following a normal distribution, representation was in quartiles, and the Mann-Whitney U test was used for statistical evaluation. Categorical data were presented as n (%), with within-group comparisons were conducted using the χ^2 test. Cox regression analysis was utilized to identify factors influencing patients' 3-year survival rate. Furthermore, time-depen-

Table 1. Baseline data

Factors	Control group (n=50)	Research group (n=57)	*P* value
Sex			0.255
Male	20	29	
Female	30	28	
Age			0.571
≥45 years old	28	35	
<45 years old	22	22	
WHO classification			0.935
II	12	12	
III	21	25	
IV	17	20	
Maximum tumor diameter			0.605
≥6 cm	25	26	
<6 cm	25	31	
Focus location			0.668
Two or more sites	22	20	
Frontal lobe	15	20	
Temporal lobe	10	15	
Other	3	2	
History of diabetes mellitus			0.719
Yes	4	6	
No	46	51	
History of hypertension			0.651
Yes	6	9	
No	44	48	
History of smoking			0.605
Yes	25	31	
No	25	26	
History of alcoholism			0.685
Yes	4	3	
No	46	54	

Note: WHO: World Health Organization.

Table 2. Perioperative indicators and hospitalization time

Group	Operation time (h)	Intraoperative blood loss (mL)	Hospitalization time (d)
Control group (n=50)	3.82±0.68	284.6±19.63	15.74±3.59
Research group (n=57)	2.85±0.46	215.26±12.16	9.86±2.71
t value	8.717	22.253	9.630
P value	<0.0001	<0.0001	<0.0001

dent receiver operating characteristic (ROC) curves were employed to assess the value of prognostic factors for the prediction of patients' 1, 2, and 3-year survival rates. A two-sided test was carried out as well for analyses, with P<0.05 indicating the presence of statistical significance.

Results

Baseline data analysis

When comparing baseline data between the two groups, no significant differences were found in terms of sex, age, WHO tumor degree classification, maximum tumor diameter, focus location, history of diabetes mellitus, hypertension, smoking, and alcohol use (P>0.05, **Table 1**).

Comparison of perioperative indicators and hospitalization time

Statistical analysis on operation duration, intraoperative blood loss, and hospitalization time of patients in the two groups revealed that the research group had significantly shorter operation duration and hospitalization time compared to the control group (P<0.0001, **Table 2**). Furthermore, the research group experienced significantly less intraoperative blood loss than the control group (P<0.0001, **Table 2**).

Comparison of total resection rate

The comparison between the two groups showed a significantly higher total resection rate in the research group compared to the control group (P<0.05, **Table 3**).

Comparison of KPS and MMSE scores

Statistical analysis on the KPS and MMSE scores of patients in both groups was conducted before and after surgery. Prior to surgery, there was no significant difference in the KPS and MMSE scores between the two groups (P>0.05, **Figure 3**). However, both groups exhibited a significant increase in KPS and MMSE scores after

Table 3. Comparison of total resection rates

Group	Total resection	Subtotal resection	Most resection	Partial resection	Total resection rate
Control group (n=50)	39	5	4	2	39 (78.00)
Research group (n=57)	53	4	0	0	53 (92.98)
χ^2					4.960
P value					0.025

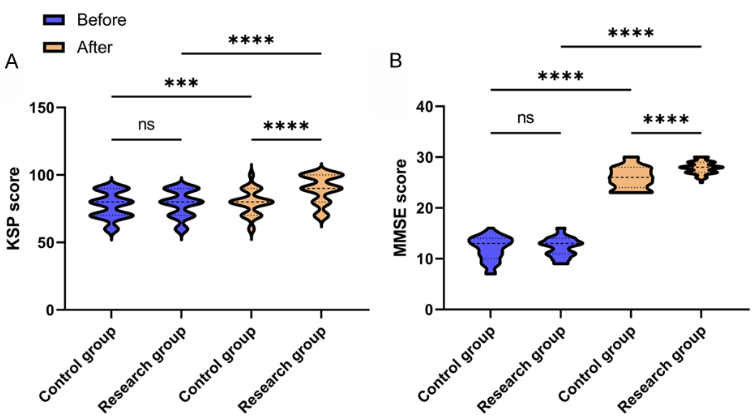

Figure 3. Changes in functional scores of patients before and after treatment. A: Changes in KPS scores of patients in the two groups before and after surgery; B: Changes in MMSE scores of patients in the two groups before and after surgery. Notes: KPS: Karnofsky Performance Scale; MMSE: Mini-Mental State Examination; nsP>0.05; ***P<0.001; ****P<0.0001.

surgery (P<0.001, **Figure 3**), with notably higher KPS and MMSE scores in the research group when compared to those in the control group (P<0.0001, **Figure 3**).

Comparison of neuropeptide indexes

The OT, β-EP, and AVP levels were statistically analyzed in both groups before and after surgery. Prior to surgery, there were no significant differences in the levels of OT, β-EP, and AVP between the two groups (P>0.05, **Figure 4**). However, a significant decrease was identified in the levels of OT, β-EP, and AVP in both groups six months after surgery (P<0.0001, **Figure 3**), with a more notable elevation in the research group than that in the control group (P<0.0001, **Figure 4**).

Comparison of postoperative complication incidence

The comparison of the incidence of postoperative complications showed no significant difference between the control group and the research group (P>0.05, **Table 4**).

Analysis of prognostic factors

Cox regression analysis was utilized to identify factors influencing patients' prognosis. It was identified through initial univariate Cox regression that age, tumor classification, and the preoperative KPS score were significant prognostic factors affecting patients' 3-year survival rates (P<0.01, **Table 5**). The results of subsequent multivariate Cox regression analysis verified again that tumor classification and the preoperative KPS score were independent prognostic factors (P<0.01, **Table 6**). Furthermore, the time-dependent ROC curve analysis demonstrated that WHO tumor degree classification and the preoperative KPS score were of use in predicting patients' 3-year survival outcomes in clinical settings (**Figure 5**).

Discussion

Brain glioma, the most common malignant brain tumor, often inflicts pressure on brain tissues by infiltration, leading to neurological dysfunction in patients [18]. Surgery plays a pivotal role in glioma treatment, particularly microsurgery, which is beneficial because of its minimal invasion nature [19]. However, as brain glioma grows in an invasive manner, making it challenging for neurosurgeons to swiftly and accurately delineate the boundary between normal brain tissue and tumor tissue, often resulting in incomplete tumor resection [20]. Therefore, intraoperative auxiliary technologies have been developed to address the issue.

In 1948, Moore et al. [21] reported the use of sodium fluorescein in brain tumor surgery for the first time, and it was subsequently applied in puncture biopsies for the identification of

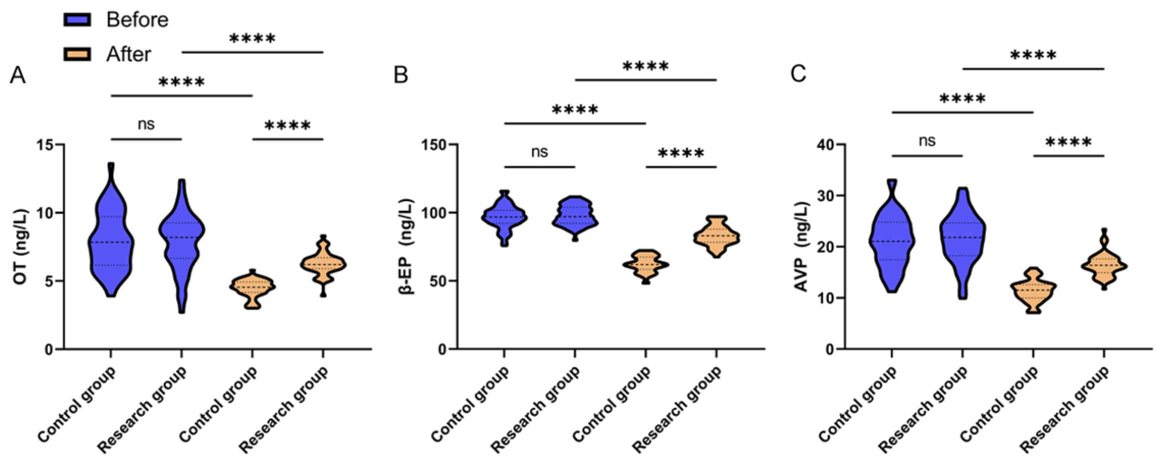

Figure 4. Changes of neuropeptide indexes in patients before and after treatment. A: Changes in OT level of patients in the two groups before and after surgery; B: Changes in β-EP level of patients in the two groups before and after surgery; C: Changes in AVP level of patients in the two groups before and after surgery. Notes: OT: oxytocin; β-EP: β-endorphin; AVP: Arginine vasopressin; nsP>0.05; ****P<0.0001.

Table 4. Postoperative complication incidence

Group	Intracranial infection	Postoperative hemorrhage	Vasospasm	Epilepsy
Control group (n=50)	2	3	1	2
Research group (n=57)	2	2	3	1
χ^2 value	0.017	0.371	0.788	0.492
P value	0.893	0.542	0.374	0.482

Table 5. Univariate Cox regression

Factors	β	SE	Wald	*P* value	HR value	95% CI	
						Lower limit	Upper limit
Sex	0.168	0.265	0.400	0.527	1.182	0.703	1.988
Age	0.959	0.302	10.117	0.001	2.610	1.445	4.714
WHO classification	0.720	0.194	13.749	<0.001	2.055	1.404	3.007
Maximum tumor diameter	0.246	0.265	0.858	0.354	1.278	0.760	2.149
Focus location	0.131	0.270	0.237	0.627	1.140	0.672	1.936
History of diabetes mellitus	-0.377	0.519	0.527	0.468	0.686	0.248	1.897
History of hypertension	-0.324	0.404	0.644	0.422	0.723	0.328	1.596
History of smoking	-0.088	0.265	0.109	0.741	0.916	0.545	1.540
History of alcoholism	0.654	0.469	1.948	0.163	1.924	0.768	4.822
Operation time	-0.006	0.176	0.001	0.974	0.994	0.704	1.405
Intraoperative blood loss	0.005	0.003	1.747	0.186	1.005	0.998	1.012
Preoperative KPS score	-0.058	0.014	18.021	<0.001	0.944	0.919	0.970
Preoperative MMSE score	0.009	0.062	0.023	0.880	1.009	0.894	1.140
Preoperative OT	0.014	0.066	0.042	0.838	1.014	0.890	1.154
Preoperative β-EP	-0.016	0.018	0.790	0.374	0.984	0.951	1.019
Preoperative AVP	0.040	0.028	2.099	0.147	1.041	0.986	1.099
Surgical regimen	0.222	0.265	0.701	0.402	1.249	0.743	2.099

Notes: WHO: World Health Organization; KPS: Karnofsky performance scale; MMSE: Mini-mental state examination; OT: Oxytocin; β-EP: β-endorphin; AVP: arginine vasopressin.

Table 6. Multivariate Cox regression

Factors	β	SE	Wald	*P* value	HR value	95% CI	
						Lower limit	Upper limit
Age	0.591	0.321	3.384	0.066	1.806	0.962	3.389
WHO classification	0.530	0.186	8.107	0.004	1.700	1.180	2.448
Preoperative KPS score	-0.04	0.015	7.645	0.006	0.961	0.934	0.988

Notes: WHO: World Health Organization; KPS: Karnofsky performance scale.

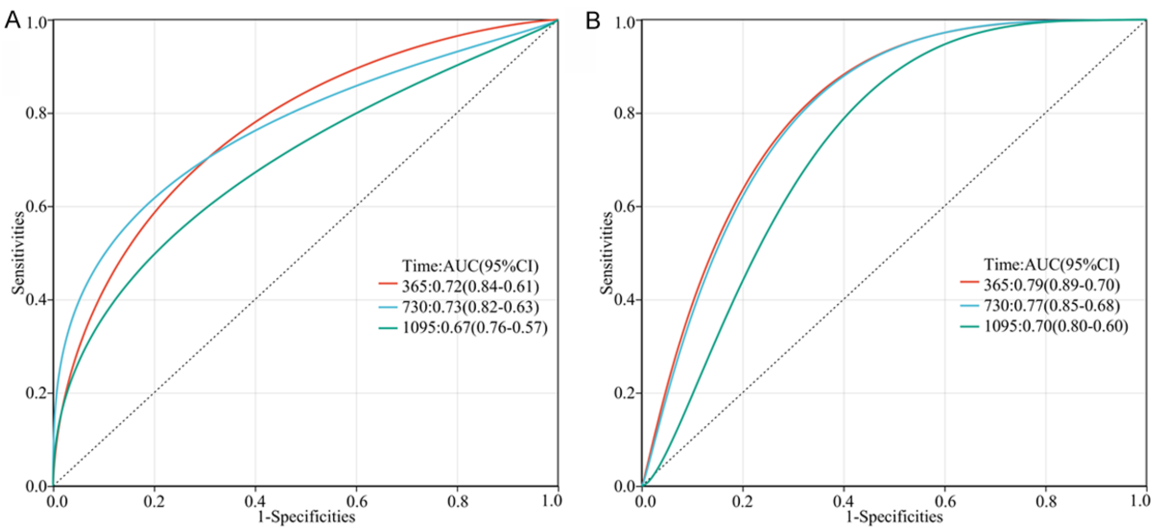

Figure 5. Time-dependent ROC curves of WHO classification and preoperative KPS score for the prediction of patients' 3-year survival. A: Time-dependent ROC curve of WHO classification for the prediction of patients' 3-year survival; B: Time-dependent ROC curve of preoperative KPS score for the prediction of patients' 3-year survival. Notes: ROC: Receiver operating characteristic; WHO: World Health Organization; KPS: Karnofsky performance scale.

meningioma, glioma, brain tumor metastasis etc. However, as the technological development and equipment are not satisfactory, the application of sodium fluorescein in neurosurgery were limited for decades. Recent years have seen a resurgence in clinical interest towards sodium fluorescein, fuelled by advancements in medical technology and widespread adoption of neurosurgical microscopes [22]. The impact of sodium fluorescein-guided microsurgery on postoperative cognitive function, neuropeptide levels, and short-term prognosis in patients with brain glioma is yet to be fully understood. This study demonstrated that sodium fluorescein-guided microsurgery resulted in shorter operation duration and hospitalization time, as well as reduced intraoperative blood loss in comparison to routine surgeries. Additionally, the group undergoing sodium fluorescein-guided microsurgery exhibited a higher total resection rate than the control group. These findings suggest that sodium fluorescein-guided microsurgery could enhance the efficacy of tumor removal in patients with brain glioma and improves their perioperative indicators, thereby potentially elevating the postoperative health status of patients. A study by Wang et al. [23] suggested no significant difference in intraoperative blood loss and hospitalization duration between the HGG group treated with sodium fluorescein-guided microsurgery and the control group. Regardless, patients in the former group experienced a notably shorter operation time than those in the later. These findings are inconsistent with the results in the current study, which may be attributed to the enhanced visualization of tumor boundaries under the microscope in fluorescence mode. This capability could not only reduce blood loss and operation time, but also assist in improving the extent of tumor resection, thereby possibly shortening the hospitalization time of patients.

As microsurgical techniques are constantly evolving, sodium fluorescein-guided microsurgery has shown promising prognostic outcomes in clinical settings [24]. This approach enables surgeons to identify the focal tissue accurately, thereby enhancing the surgical efficacy while maximally preserving normal tissues. It also minimizes collateral damage to blood vessels and functional areas, ensuring unaffected nervous system function. This surgical approach also contributes to the postoperative recovery of neurological functions in patients and enhancement of their quality of life [25]. In this study, sodium fluorescein-guided microsurgery was proved effective in reducing damages to brain functions and improving the postoperative quality of life of patients, accompanied by minimal influences on their cognitive functions. These outcomes are attributed to the precise location of tumor with the use of sodium fluorescein technique, leading to accurate resection. Through the application of sodium fluorescein, the nervous system function could remain integral, damages to the brain tissues minimized and vital blood vessels preserved as many as possible. Therefore, sodium fluorescein-guided microsurgery could reduce patients' cognitive impairment and enhance their postoperative quality of life.

Neuropeptides are active endogenous substances predominantly found in the central nervous system, playing a vital role in the protection and management of the nervous system function [26, 27]. In this study, the levels of OT, β-EP, and AVP in the cerebrospinal fluid of patients in both groups decreased within six months after surgery, with the research group exhibiting significantly higher levels than the control group. This result suggests that tumor resection under microscopic guidance has minimal impacts on the levels of neuropeptides in the cerebrospinal fluid of patients, indicating a relatively rapid recovery of these substances. It is worthy of noting that OT, β-EP, and AVP are valuable neuropeptides in the cerebrospinal fluid whose expressions are closely linked to the recovery of nerve cell functions in the brain [28]. Surgical intervention can impair neurological functions and reduce neuropeptide levels in the cerebrospinal fluid. However, tumor resection performed under microscopic guidance offers precise localization of the target area, minimizing disruption to the surrounding neural functional zones. As a result, the postoperative levels of OT, β-EP, and AVP in the cerebrospinal fluid can swiftly rebound to the preoperative levels. This rapid recovery of neuropeptide levels can produce advantageous outcomes and good prognosis for patients.

Finally, an analysis was carried out to identify factors influencing the 3-year survival rate of patients. The result of regression analysis indicated that the tumor degree classification according to the WHO standards and the preoperative KPS score were statistically significant in predicting patients' 3-year survival rate. The WHO tumor degree classification, based on the pathological characteristics of patients' tumors, denotes for their malignancy levels [29]. A higher tumor degree marks a severer tumor and a poorer prognosis. The KPS score, with its wide application in assessing the quality of life of tumor patients, proves particularly valuable in evaluating their prognostic outcomes when measured preoperatively. A higher KPS score denotes for better health status of tumor patients and a greater capacity in them to endure side effects associated with chemotherapy. Echoing the findings of this study, Thomas et al. [30] also identified a low KPS score as a detrimental factor for the survival and prognosis of patients. The result of time-dependent ROC curve analysis highlighted the clinical significance of tumor degree classification in accordance with WHO standards and the preoperative KPS score in forecasting the 3-year survival and their usefulness in predicting the prognosis of tumor patients. Although multivariate Cox regression analysis recognized the WHO tumor degree classification standards and the preoperative KPS score as independent factors for the prediction of the 3-year survival rate, the primary aim of this study was to evaluate the effect of sodium fluorescein-guided microsurgery on postoperative cognitive function, quality of life, and neuropeptide levels in patients with brain glioma. The results revealed notable enhancements in quality of life (as indicated by KPS score) and cognitive function (as measured by MMSE score) among patients treated with sodium fluorescein-guided microsurgery. These factors play a vital role in the evaluation of the overall well-being and postoperative recovery of patients, offering a holistic view of treatment outcomes that extend beyond mere survival rates. The study further underscores the enhanced surgical efficacy and potential safety advantage, as evidenced by shortened operation time and decreased intraoperative blood loss in patients undergoing sodium fluorescein-guided microsurgery. These improvements are pivotal in patient care, potentially mitigating the risks tied to prolong and intricate surgical interventions. In summary, although the sodium fluorescein-guided microsurgery does not have marked impacts on the 3-year survival rate of patients, its significant contributions to elevating their postoperative cognitive functions, quality of life, and surgical efficacy have highlighted its importance in the comprehensive care and management of patients with brain glioma. In neuro-oncology, it is essential to adopt a novel approach for evaluating treatment outcomes through taking into consideration of various healthcare aspects of patients.

This study has conducted a retrospective analysis on the impact of sodium fluorescein-guided microsurgery on cognitive functions and short-term outcomes of patients with brain glioma, yet it has encountered several limitations. Firstly, the results might be biased because the study was retrospectively carried out with a small sample size. Secondly, this is a single-center study, to apply the findings from this study to a mass population requires verification with data from multiple centers. Lastly, the study focus was placed on the evaluation of the short-term survival rates of patients, further research needs to be carried out to ascertain the effects of surgical interventions on patients' long-term outcomes. Hence, our future endeavors will be directed towards corroborating these findings and offering a more comprehensive understanding of the efficacy of the surgical technique.

In conclusion, sodium fluorescein-guided microsurgery demonstrates promise in enhancing the quality of life of patients with giloma and mitigating their cognitive impairment while realizing a 3-year survival. Nevertheless, further large-scale and multi-center research will be our next plan to substantiate these preliminary findings and explore the long-term prognostic implications of this surgical technique.

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Disclosure of conflict of interest

None.

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