Exp Oncol 2022
44, 4, 307–313

Experimental ONCOLOGY

RADIOSURGICAL TREATMENT OF RECURRENT GLIOBLASTOMA AND PROGNOSTIC FACTORS AFFECTING TREATMENT OUTCOMES

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***Background*: Glioblastoma (GBM) is the most prevalent malignant tumor of the brain in adults with the inherent aggressive behavior and high recurrence rate. The stereotactic radiosurgery (SRS) is currently considered as one of the effective modalities for GBM treatment allowing for the improvement of survival with the acceptable toxicity level. *Aim*: To assess the effects of various factors on the survival of GBM patients following SRS. *Patients and Methods*: We retrospectively reviewed treatment outcomes of 68 patients who received SRS for recurrent GBM treatment in 2014–2020. SRS was delivered with Trilogy linear accelerator (6 MeV). The area of recurrent tumor/continued tumor growth was irradiated. For the treatment of the primary GBM, the adjuvant radiotherapy was provided at the standard fractionated regimen with the total boost dose of 60 Gy divided to 30 fractions (Stupp's protocol) in the setting of the concomitant chemotherapy with temozolomide. 36 patients then received temozolomide as the maintenance chemotherapy. SRS for the treatment of recurrent GBM was provided at a boost dose of 20.2 Gy on average being delivered into 1–5 fractions with average single dose of 12.4 Gy. The survival was analyzed by the Kaplan—Meier method with a log-rank test used for assessing the impact of the independent predictors on the survival risks. *Results*: The median overall survival (OS) was 21.7 months (95% confidence interval (CI) 16.4–43.1), median survival after SRS was 9.3 months (95% CI 5.6–22.7). The majority of patients (72%) were alive for at least 6 months following SRS and about half of patients (48%) survived for at least 24 months following the resection of the primary tumor. OS and survival after SRS depend significantly on the extent of the surgical resection of the primary tumor. The addition of temozolomide to radiotherapy prolongs survival in GBM patients. The relapse time affected significantly OS ($p = 0.00008$), but not survival after SRS. Neither OS, nor survival after SRS were affected significantly by such factors as the age of patients, the number of SRS fractions (one fraction *vs* several fractions), and target volume. *Conclusion*: Radiosurgery improves the survival in patients with recurrent GBM. The extent of the surgical resection and adjuvant alkylating chemotherapy of the primary tumor, overall biologically effective dose and time between the primary diagnosis and SRS affect significantly the survival. The search for the more effective schedules for treating such patients requires further studies with more numerous cohorts of patients and extended follow-up.**

Key Words: **malignant glioma, glioblastoma, neurosurgical procedures, recurrence, radiosurgery, survival.**

DOI: 10.32471/exp-oncology.2312-8852.vol-44-no-4.18920

Glioblastoma (GBM) (glioma of the malignancy grade 4 by the WHO classification) ranks first by its incidence among the primary tumors of CNS in adults [1, 2].

In spite of the thorough studies, the pathophysiological mechanisms of GBM have not yet been elucidated in detail. The effective methods for GBM treatments are lacking, and the appropriate combination of surgery, radiotherapy and chemotherapy (CTX) still fails to produce satisfactory outcomes. The mean overall survival of GBM patients is about 15 months [3]. The unfavorable forecast in GBM is associated mostly with the inherent aggressive behavior of this cancer manifested in tremendously high recurrence rate (about 90%) [4]. The current treatment of the primary GBM is standardized and based on the criteria of evidence-based medicine. The treatment comprises the maximum safe resection of the tumor, adjuvant radiotherapy in the setting of the concomitant CTX with temozolomide followed by the maintenance temozolomide CTX. Contrary to primary GBM, the standards for the treatment of recurrent GBM have not been defined. The treatment strategy for GBM patients is considered based on the previous treatment modalities taking into account the age, Karnofsky performance status, the methylation status of *MGMT*, and the progression of the disease [5]. The stereotactic radiosurgery (SRS) is currently considered as one of the effective options for GBM treatment that could be used as a component of the multimodal treatment or a single modality. The modern precision SRS techniques allow the spatially precise targeted delivery of radiation dose sparing the adjacent areas of intact brain tissue that is of particular importance for repeated irradiation in cases of the local progression of malignant glioma [6–8]. Nevertheless, the number of systematic reviews and meta-analyses as well as clinical studies related to the radiosurgery of GBM is rather scarce. We attempted to assess the effects of various factors on the survival of GBM patients following SRS based on the analysis of our experience in the treatment of such a category of patients.

Submitted: September 16, 2021.

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Abbreviations used: BED – biologically effective dose; CI – confidence interval; CTX – chemotherapy; GBM – glioblastoma; IDH – isocitrate dehydrogenase; MRI – magnetic resonance imaging; OS – overall survival; PTV – planning tumor volume; SRS – stereotactic radiosurgery.

PATIENTS AND METHODS

We retrospectively reviewed patients who received SRS for GBM treatment at the State Institution "Academician Romodanov Institute of Neurosurgery, the National Academy of Medical Sciences of Ukraine" between 2014 and 2020. A total of 68 patients (37 males and 31 females, aged 18–81, mean age 50.7) were included in the study. SRS was delivered with Trilogy linear accelerator (Varian, USA). The study was approved by the Institutional Ethics Committee (record № 3 of June 6, 2016). All patients gave the informed agreement prior to SRS. In all cases, the diagnosis of GBM grade 4 according to the WHO classification was confirmed by a pathologist after the surgery of the primary tumor. According to the volume of the resection of primary tumor, the patients were distributed as follows: total resection with perifocal zone — 54 (79.4%), subtotal resection — 5 (7.4%), partial resection — 6 (8.8%), stereotactic biopsy — 3 (4.4%). Besides the maximal safe tumor resection, the primary treatment protocol included postoperative chemoradiotherapy with the total boost dose of 60 Gy in 30 fractions and temozolomide 75 mg/m^2 7 days a week during the course of radiotherapy.

After a 4-week break following postoperative chemoradiotherapy, patients received 6–12 cycles of adjuvant temozolomide as maintenance CTX. In the study group, only 36 (52.9%) patients received such maintenance CTX with temozolomide. The patients were followed up at the Department of Adjuvant Therapy of CNS Tumors and the Radioneurosurgery Department of the Acad. AP Romodanov Institute of Neurosurgery of the NAMS of Ukraine. The control magnetic resonance imaging (MRI) (with i/v paramagnetic contrast enhancement) was performed in two months following the completion of radiotherapy and thereafter every 3 months or upon neurological deterioration. In case when progression should be differentiated from pseudoprogression, perfusion neurovisualization techniques (MRI or multislice computed tomography) were applied.

Most patients in our study have been treated prior to the 2016 revision of WHO classification of central nervous system tumors prompting the wide-scale molecular genetic testing in neurooncology. For that reason, the mutations of isocitrate dehydrogenase (*IDH*) gene and methylation status of *MGMT* gene [9] were assessed only in 14 out of 68 patients. All 14 cases were of *IDH* wild type; in 9 cases *MGMT* promoter was unmethylated.

In most cases (59 patients), GBM was diagnosed based on the complex of clinical-and-radiological data and neurovisualization findings taking into account the dynamics of the clinical status. The diagnostic decision making involved a multidisciplinary team comprising neurosurgeon-oncologist, radiologist and radiation oncologist. In 8 (11.8%) patients, the diagnosis of GBM was confirmed upon pathohistological study of surgically resected specimens of the recurrent tumor (5 cases of subtotal resection of recurrent GBM and 3 cases of partial resection).

The patients were assigned to SRS when their Karnofsky performance status score was not less than 70.

The recurrent tumor or residual part of recurrent tumor and postoperative area (in case of former surgical resection of GBM) was irradiated using Trilogy (Varian, USA) linear accelerator at the energy of 6 MeV. SRS planning was based on the superimposed MRI and multi-slice computed tomography findings obtained for delineating gross tumor volume according to the margins of the recurrent tumor assessed by paramagnetic accumulation. Planning tumor volume (PTV) represented gross tumor volume and surgical cavity (in case of resection of recurrent tumor) with added 2–5-mm safety margin. To select the dose schedule, the following parameters were taken into account: the dose regimen of the first radiation course, the time since the first radiation course, the volume and localization of the irradiated target, the total biologically effective dose (BED_{11}) for the overall RT courses, the radiation load onto the critical brain structures (brainstem, optic chiasm, etc.) according to the calculation of normal tissue complication probability [10]. The patients were irradiated in supine position. Thermoplastic mask was used for immobilization. The concomitant systemic therapy was not added. The boost dose to PTV was from 12.0 Gy to 42.0 Gy (20.2 Gy on average) being delivered in 1–5 fractions with a single boost dose from 4.8 Gy to 20.0 Gy (12.4 Gy on average). The mean PTV was 34.4 cm^3 (2.5–616.7 cm^3). The combined intensity-modulated radiotherapy + multi-leaf collimator Dyn ARC technique was used representing the combination of the intensity modulated radiation with dynamic conformal rotation allowing for the maximally homogeneous dose distribution within the irradiated target with maximally shortened irradiation time, reduction of radiation load and providing more comfortable treatment conditions.

The primary end-points of the study were overall survival (OS) and survival after SRS. OS was defined as time from the first surgery to the death of the patient (event) or the date of the last observation (censored observation). Besides, the survival rate for 3, 6, 12, 18, and 24 months was assessed.

As the secondary end-points of the study, we analyzed the association between the survival and such independent factors as time between the primary diagnosis and SRS, the extent of the radical surgical treatment of the primary tumor, the patient's age and gender, the dose schedule (overall BED for the courses of radiation and BED of SRS, the number of SRS fractions (single fraction *vs* several fractions), the volume of irradiated target, the absence/presence of surgical resection of recurrent tumor, CTX. For assessing how the survival depends on the time between the primary diagnosis and SRS, our study cohort was divided into three independent groups differing by the recurrence-free time (< 10 months; 10–20 months; > 20 months).

The survival was analyzed by the Kaplan—Meier method. The log-rank test was used for assessing the impact of the independent predictors (covariates) on the survival risks (for comparing Kaplan—Meier survival curves for different groups). The effects of the quantitative covariates on survival was assessed by regression analysis based on Cox proportional-hazards model. For taking the decisions as to the statistical significance of the results, obtained p values were compared with the assumed critical level of statistical hypothesis adoption/rejection $\alpha = 5\%$. STATISTICA 64 ver. 10.0.1011.0 StatSoft Inc. was used for statistical calculations.

RESULTS

Survival in cohort under study. During the follow-up period, 53 out of 68 patients (77.9%) died. The death of two patients was not directly related to GBM. The median OS was 21.7 months (95% confidence interval (CI) 16.4–43.1), median survival after SRS was 9.3 months (95% CI 5.6–22.7). The OS at 12 months amounted to 91% (95% CI 84–98%), at 18 months — 64% (95% CI 52–75%), and at 24 months — 48% (95% CI 36–60%). For survival after SRS, the percentages at 3, 6 and 12 months were (95% CI 79–95%), 72% (95% CI 61–83%), and 34% (95% CI 22–46%), respectively. Therefore, the majority of patients (72%) were alive for at least 6 months following SRS and about half of patients (48%) survived for at least 24 months following the resection of the primary tumor (Fig. 1, 2).

Survival according to predictive factors. OS and survival after SRS depend significantly on the extent of the surgical resection of the primary tumor. The median OS was 16 months in combined group of patients with partial resection (N = 6) and stereotactic biopsy (N = 6) as compared to 28 months in the combined group of total resection with perifocal zone (N = 54) and subtotal rejection (N = 5) ($p = 0.00934$) (Fig. 3). The difference in median survival after SRS between these groups was also significant ($p = 0.01592$) (Fig. 4).

The median OS was 20 months in males *vs* 33 months in females ($p = 0.04799$). The median survival after SRS in males and females was 7 months and 10 months, respectively ($p = 0.02168$). Meanwhile, neither OS, nor survival after SRS were affected significantly by such factors as the age of patients, the number of SRS fractions (one fraction *vs* several fractions), and target volume. Analysis of dose effects on survival by Cox model revealed the significant difference for the overall BED_{11} for all courses of radiation ($p = 0.030891$). The longest OS was in cases when overall BED_{11} was not less than 145 Gy while the worse OS was

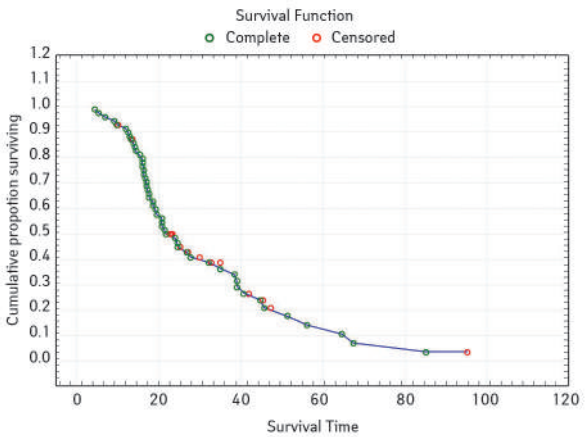

Fig. 1. Kaplan—Meier OS curve for retrospective analysis of 68 patients with recurrent GBM

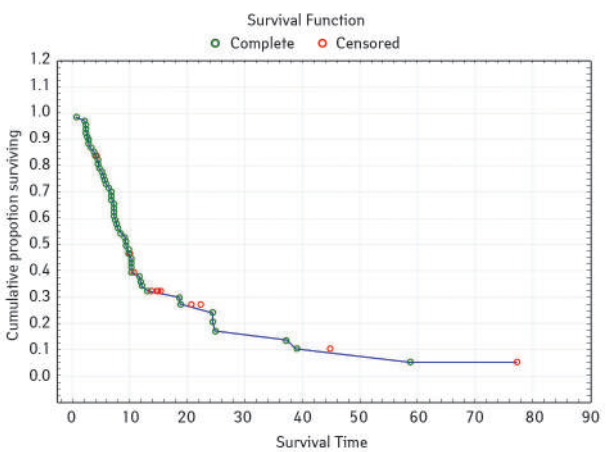

Fig. 2. Kaplan—Meier curve of survival after SRS for retrospective analysis of 68 patients with recurrent GBM

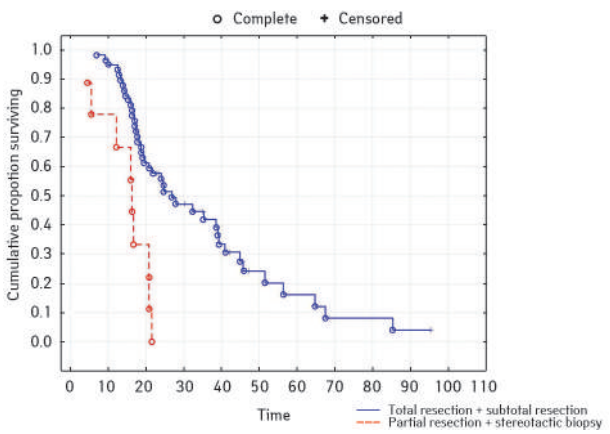

Fig. 3. Kaplan—Meier OS curve for retrospective analysis of 68 patients with recurrent GBM stratified according to the extent of surgical resection of the primary tumor

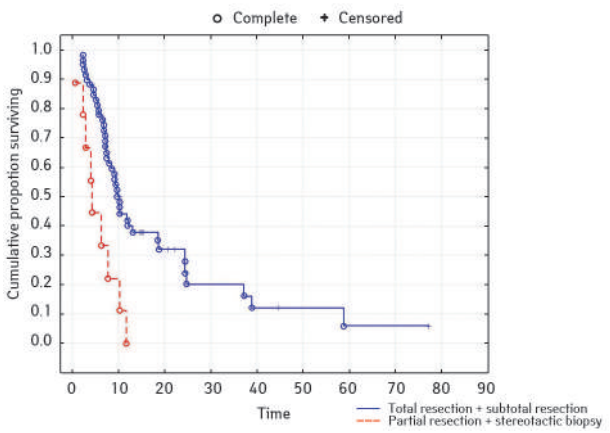

Fig. 4. Kaplan—Meier curve of survival after SRS for retrospective analysis of 68 patients with recurrent GBM stratified according to the extent of surgical resection of the primary tumor

recorded when overall BED_{11} was 85 Gy and less. Adjuvant CTX with temozolomide had a positive effect both on OS and survival after SRS (p = 0.03538 and p = 0.02411, respectively). The surgical resection of the recurrent tumor affects OS (p = 0.02105) but not survival after SRS (p = 0.56657). Such findings are rather contradictory, which seems to be due to the inhomogeneity of our cohort as to the surgical resection of the recurrent tumor (only 9 patients of 68).

We have also analyzed the survival of patients stratified according to the relapse time. In groups with the relapse times < 10 months, 10–20 months and > 20 months, median OS is 17, 22 and 45 months, respectively (Fig. 5). Kaplan—Meier curves for these groups demonstrate significant differences verified by log-rank test (p = 0.00008).

Nevertheless, medians of survival after SRS for the same groups are about the same (p = 0.70568 by log-rank test) amounting to 9.5 months (Fig. 6).

The regimen for the accompanying therapy early post-SRS was chosen by the radiation oncologist individually. When required, steroids (dexamethasone) were used with the strict rule — the possibly least dose for the possibly short time. In our group under study, no SRS-related adverse reactions grade III–IV were observed within the observation period. In no case, radiosurgery did not result in the complications requiring neurosurgical intervention such as hydrocephaly, intracerebral hemorrhage, symptomatic radiation-related edema that was resistant to steroid therapy.

DISCUSSION

The treatment of recurrent GBM remains one of the most complicated tasks in neurooncology. Since in most patients the tumor progresses locally followed by advanced growth and a death, the improvement of the local control plays the key role in GBM therapy. In 2021, several systematic reviews and meta-analyses on the treatment outcomes of recurrent GBM (both systemic and locoregional) were published [11–13]. For certain categories of patients, locoregional treatment, SRS in particular, is the best treatment approach. Nevertheless, it should be stressed that the overall studies point to unsatisfactory results of recurrent GBM whichever is the variant of therapy.

In our opinion, several recently published systematic reviews and meta-analyses are the most attractive from the point of SRS efficacy in recurrent GBM treatment. In 2019, Kazmi *et al.* [8] analyzed the results of re-irradiation of 2095 patients with recurrent GBM based on 50 clinical trials. Following irradiation of recurrent GBM, 6-month survival was 73% (95% CI 69–77) and 12-month survival — 36% (95% CI 32–40). It was interesting that shorter irradiation schedules (⩽ 5 fractions) were associated with higher levels of 6-month progression-free survival testifying to the favor of hypofractionated radiosurgical irradiation over the conventional fractionation schedules in SRS. In general, the study by Kazmi *et al.* [8] demonstrated that re-irradiation provides the acceptable control of the disease and suitable level of survival. The toxicity of the repeated radiotherapy was low.

The systematic analysis by Minniti *et al.* [12] demonstrates the current state and the recent advancements of GBM treatment using re-irradiation schedule. The detailed analysis of 16 clinical series published in 2005–2020 encompassing 901 patients with recurrent GBM demonstrated that in the average radiation dose 15–18 Gy delivered to the target of 4–10 mL, OS from the date of SRS of recurrent GBM ranged from 7.5 to 13 months and the progression-free time was 4.4–6 months with the acceptable toxicity level.

It is impossible to ignore the recent systematic review and meta-analysis by Schritz *et al.* [13] presenting the data of 308 studies from various databases and 271 clinical trials. Meta-analysis demonstrated that median OS after the treatment of the GBM relapse is 2.9–18.3 months and median of progression-free survival — 0.7–6.0 months.

The problem of the treatment toxicity is certainly one of the most significant concerns when the re-irradiation is considered, especially in neurosurgery. There is still no consensus on several questions. The brain is highly sensitive to the radiation load, especially brainstem, optic nerves and chiasm. Therefore, the ra-

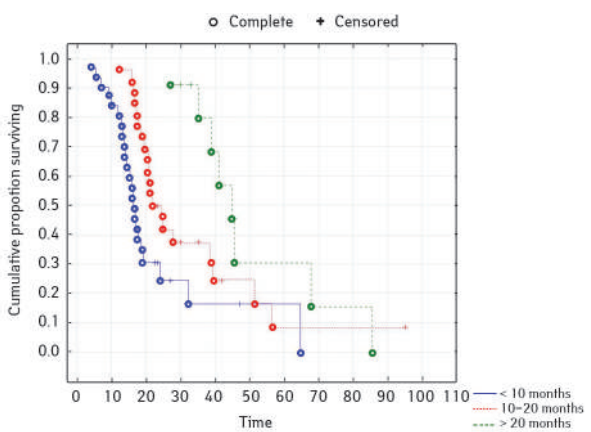

Fig. 5. Kaplan—Meier OS curve for retrospective analysis of 68 patients with recurrent GBM stratified according to the relapse time

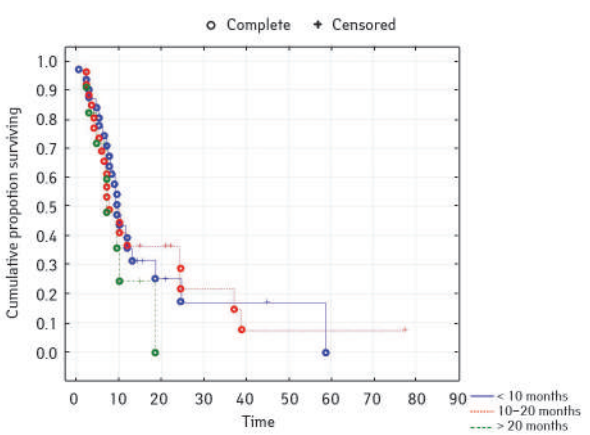

Fig. 6. Kaplan—Meier curve of survival after SRS for retrospective analysis of 68 patients with recurrent GBM stratified according to the relapse time

diation oncologist faces a dilemma whether the toxicity risks of re-irradiation are acceptable relative to the potential treatment benefits. The decision making in such cases is very difficult since the local recurrence of GBM develops earlier than in one year following completion of the first radiation therapy. Furthermore, the correctness of the technique for calculating the total radiation dose could be questionable in the setting of accounting for the irradiation schedules varying by the single doses. The problem of the individual radiosensitivity of patients and the heterogeneity of tumor structures also should not be ignored. As a result, one could not give a strict prognosis for the response to radiotherapy and the survival of the most resistant populations of tumor cells. Although the fundamental long-term studies are required to solve these questions, there is a compelling need to make decisions in current clinical practice.

According to the literature, the rate of the radiation necrosis following SRS of recurrent GBM varies from 4% to 31.3 [8, 14]. Nevertheless, the authors do not clarify the dynamics of the neurologic disorders and steroid therapy that is principal for assessing the grade of radiation toxicity.

Our findings on both survival and SRS toxicity in GBM patients are in line with the current studies on the subject confirming the expediency of such treatment strategy in treating recurrence (continuous growth) of malignant glioma.

The assessment of the impact of various factors affecting treatment outcome following SRS in recurrent GBM patients is an urgent demand of time considering the personalized treatment approach in modern neurooncology. Such analysis provides a basis for the stratification of patients allowing for selecting the most effective treatment schedule and realizing the personification strategy with maximal benefits both for patients and for the medical system as a whole. In this context, several recent studies are worthwhile to pay attention to [6, 8, 15, 16]. These studies demonstrate the positive effect of several factors on survival. Among them are single-fraction and hypofractionated irradiation (SRS) in comparison with the standard irradiation schedules, lesser volume of irradiated target, younger age, the extent of the resection of the primary tumor, the concomitant use of temozolomide, the presence of methylated *MGMT* promoter.

Our analysis of the impact of various factors on survival following SRS in recurrent GBM demonstrated the significant effects of the extent of the primary surgical resection, overall biologically effective dose, alkylating CTX and the age of patients.

In our opinion, our findings demonstrating the association between the relapse time and survival deserve particular attention (Fig. 5 and 6). While relapse time significantly affected OS ($p = 0.00008$), we could not find out the effect of such a factor on survival after SRS ($p = 0.70568$). Earlier, we obtained similar results in our study on the radiosurgical treatment of the recurrent GBM in 59 patients with radically resected primary tumor [17] wherein the relapse time affected OS ($p = 0.00066$) while survival after SRS did not depend on relapse time ($p = 0.47992$). The patients in our previous study were stratified according to relapse time in the same way as in present paper (< 10 months, 10–20 months, > 20 months). Nevertheless, contrary to the current study, the previous cohort encompassed only patients with radical resection of the primary tumor (since the extent of the resection of primary tumor is generally accepted as the factor influencing the survival of patients). In fact, both our studies demonstrated the positive effect of the radical resection of primary tumor on survival.

Our findings as well as the findings of other authors suggest that the recurrent and primary tumors could be regarded as being identical in their biological behavior. The relapse time factor could contribute significantly to OS of patients. These facts seem to reflect dissimilarity between “early relapsing” and “relapsing late” GBM as the tumors with different molecular-genetic profiles. Re-irradiation apparently aligns the survived patients in groups that differ by relapse time. On the other hand, SRS gives a chance to the patients at higher relapse risk (i.e. shorter relapse time) for the same survival as attained in patients with intrinsically longer survival (GBM with “late relapse”). Such results deserve further analysis in more numerous samples taking into account molecular-genetic profiles of both the primary and recurrent tumors.

Certainly, our present study has some limitations. First, the study was retrospective by its design, while prospective randomized studies on re-irradiation for treatment of recurrent malignant gliomas are urgently needed. The analysis of the effects of different combinations of systemic therapy and radiotherapy, in particular immunotherapy and targeted therapy are also of great importance. The most effective schedules of multimodal therapy specifying the optimal dosage regimen and the sequence of the treatment stages should be defined for different subtypes of tumors depending on their biology and molecular features (status of *MGMT* promoter methylation; 1p/19q codeletion; *IDH* mutation; *EGFR* amplification; *TERT* promoter mutation; +7/–10 cytogenetic abnormality, etc). The assessment of the quality of life of patients is equally important since the increased survival without providing the acceptable quality of life could not be considered as the satisfactory treatment outcome. Besides, the radiation oncologists should not be outside the recent developments in the assessment of the individual radiosensitivity while the experimental radiobiological studies on this subject become increasingly more clinically friendly.

Although the prognosis for recurrent GBM remains unpromising, the signs of progress in recurrent GBM treatment could not be overlooked. Radiosurgery is considered as one of the effective therapeutic strategies for treatment of patients with recurrent/continued tumor growth allowing for improving patients’ survival.

To sum up our findings, the majority of patients with GBM progression (local recurrence) (72%) were alive for at least 6 months following SRS and about half of patients survived for at least 24 months following the resection of the primary tumor. OS and survival after SRS depend significantly on the extent of the surgical resection of the primary tumor. The addition of temozolomide to radiotherapy prolongs survival in GBM patients. The OS was the longest in cases when overall BED_{11} was not less than 145 Gy while the worst OS was recorded when overall BED_{11} was 85 Gy and less. Furthermore, our findings demonstrate the association between the relapse time and OS but not survival following SRS.

Our data confirm the suitability of SRS in recurrent GBM. The search for the more effective schedules for treating such patients requires further studies with more numerous cohorts of patients and extended follow-up for the analysis of the complex multimodal treatment accounting for the biology and molecular genetic patterns of the tumors.

CONFLICT OF INTERESTS

Authors declare no conflict of interest.

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РАДІОХІРУРГІЧНЕ ЛІКУВАННЯ ХВОРИХ НА РЕЦИДИВНУ ГЛІОБЛАСТОМУ ТА ПРОГНОСТИЧНІ ФАКТОРИ, ЩО ВПЛИВАЮТЬ НА ЙОГО РЕЗУЛЬТАТИ

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Стан питання: Гліобластома (ГБ) — це найбільш поширена злоякісна пухлина головного мозку в дорослих із вкрай агресивною біологічною поведінкою та високим ризиком рецидивування. Стереотаксична радіохірургія (СРХ) розглядається як ефективний метод, що підвищує виживаність хворих на рецидивну ГБ та має прийнятний рівень токсичності. ***Мета***: Оцінити вплив різних факторів на показники виживаності пацієнтів з рецидивною ГБ після радіохірургічного лікування. ***Хворі та методи***: Дослідження базується на ретроспективному аналізі результатів лікування 68 хворих на ГБ, яким проводили СРХ на ділянку рецидиву/продовження росту ГБ (LINAC «Trilogy», 6 MeV) за період 2014–2020 рр. в Державній установі «Інститут нейрохірургії ім. акад. А.П. Ромоданова НАМН України». Усім пацієнтам з первинною ГБ після операції було проведено курс ад'ювантної променевої терапії в стандартному режимі фракціонування (сумарна вогнищева доза (СВД) 60,0 Гр за 30 фракцій (відповідно до протоколу Stupp)) на тлі конкомітантної хіміотерапії алкілуючим препаратом темозоломідом. 36 (52,9%) хворих у подальшому отримували підтримувальну хіміотерапію темозоломідом. Після встановлення діагнозу рецидиву ГБ, при радіохірургічному лікуванні СВД на мішень опромінення становила 12,0–42,0 Гр (середня 20,2 Гр) і підводилася за 1–5 фракцій з разовою вогнищевою дозою (РВД) 4,8–20,0 Гр (середня 12,4 Гр). Середній об'єм мішені опромінення становив 34,4 см^3. Метод Каплана — Майера, логарифмічний ранговий тест, регресійний аналіз Кокса використано для статистичного аналізу. ***Результати***: Медіана загальної виживаності (ЗВ) становила 21,7 міс (95% довірчий інтервал (ДІ) 16,4–43,1). Рівень

12-місячної ЗВ становив 91% (95% ДІ 84–98), 24-місячної ЗВ — 48% (95% ДІ 36–60). Медіана виживаності після СРХ становила 9,3 міс (95% ДІ 5,6–22,7). Ад'ювантна хіміотерапія темозоломідом підвищує показники виживаності. Термін між первинним діагнозом та СРХ значуще впливав на ЗВ (p = 0,00008), але не мав впливу на виживаність після СРХ (p = 0,70568). Виживаність жінок була вищою, ніж у чоловіків. Не зафіксовано впливу на показники виживаності таких коваріат, як вік хворих, кількість фракцій СРХ та об'єм мішені опромінення при радіохірургічному лікуванні. ***Висновки***: Радіохірургія покращує показники виживаності хворих на рецидивну ГБ. Значущий вплив на виживаність мають такі фактори, як радикальність хірургічного лікування первинної пухлини, ад'ювантна хіміотерапія темозоломідом, сумарна біологічно ефективна доза, термін між первинним діагнозом та СРХ. Існує нагальна потреба у проведенні подальших досліджень з радіохірургічного лікування хворих зі злоякісними гліомами головного мозку, зі збільшенням вибірки та терміну спостереження.

***Ключові слова*:** рецидивна гліобластома, стереотаксична радіохірургія, виживаність.