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Survival rates in patients with the newly diagnosed glioblastoma: Data from the National Cancer Registry of Ukraine, 2008-2016

Artem V. Rozumenko [1], Valentyn M. Kliuchka [1], Volodymir D. Rozumenko [1], Zoja P. Fedorenko [2]

[1] Neuro-Oncology Department, Romodanov Neurosurgery Institute, Kyiv, Ukraine
[2] National Cancer Registry of Ukraine, National Cancer Institute, Kyiv, Ukraine

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Address for correspondence:
Artem Rozumenko, Neuro-Oncology Department, Romodanov Neurosurgery Institute, 32 Platona Mayborody St., Kyiv, Ukraine, 04050, e-mail: dr.rozumenko@gmail.com

Objective. In the current study, we present the results of the survival analysis of patients with newly diagnosed glioblastoma (GBM) in Ukraine.

Materials and methods. A total of 3763 cases of patients with histologically confirmed newly diagnosed GBM who were treated over a 9-year period (2008 – 2016) were included. All patients were grouped as younger adults (<45 years at diagnosis) – 734 (19.5%) cases, middle-aged (45–64 years) – 2360 (62.7%), and older adults (>64 years) – 669 (17.8%). Clinical parameters and survival rates were defined for every three 3-year periods: 2008-2010, 2011-2013, and 2014-2016.

Results. The overall median survival was 12.2±0.2 months. Higher survival rate was observed in young adults 17.4±1.4 months (p<0.001). The hazard ratio (HR) of middle-aged group was 1.79 (95% CI 1.60-2.00; p=0.017) and for older age – 1.51 (95% CI 1.32-1.72; p<0.001). The patients treated in the second period achieved better prognosis with a median survival in 12.6±0.3 months (p<0.001) with HR 0.75, 95% CI 0.66-0.85; p<0.01). The median overall survival in combined treatment protocol group was 16.3±0.5 months, and the worst prognosis was in surgery alone group – 7.5±0.3 months (p<0.001). The HR for surgery with radiotherapy was 1.36 (95% CI 1.22-1.51; p<0.001), and for surgery alone it raised up to 1.94 (95% CI 1.73-2.17; p<0.001). The HR for a combination of surgery with chemotherapy was 1.18 (95% CI 0.90-1.53; p<0.001), but it was not significant (p=0.25).

Conclusions. The using of combined treatment including surgery and chemoradiotherapy was associated with survival advantage for all age groups and time periods.

Keywords*: glioblastoma; survival; surgery; chemotherapy; radiotherapy; elderly*

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Виживаність пацієнтів з первинно діагностованими гліобластомами: дані Національного канцер-реєстру України (2008-2016)

Розуменко А.В.[1], Ключка В.М.[1], Розуменко В.Д.[1], Федоренко З.П.[2]

[1] Відділ нейроонкології, Інститут нейрохірургії ім. акад. А.П. Ромоданова НАМН України, Київ, Україна
[2] Національний канцер-реєстр України, Національний інститут раку, Київ, Україна

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Адреса для листування:
Розуменко Артем Володимирович, Відділ нейроонкології, Інститут нейрохірургії ім. акад. А.П. Ромоданова, вул. Платона Майбороди, 32, Київ, Україна, 04050, e-mail: dr.rozumenko@gmail.com

Мета: провести аналіз виживаності пацієнтів з первинно діагностованими гліобластомами (ГБ) в Україні.

Матеріали і методи. Проаналізовано 3763 випадки гістологічно верифікованих первинно діагностованих ГБ, виявлених протягом 9-річного періоду (2008–2016). Пацієнтів розподілили на групи залежно від віку: молоді особи (<45 років) – 734 (19,5%), особи середнього віку (45–64 років) – 2360 (62,7%), а також особи похилого віку (>64 років) – 669 (17,8%). Клінічні параметри та показники виживаності аналізували за три періоди: 2008–2010, 2011–2013 і 2014–2016 рр.

Результати. Загальна медіана виживання становила 12,2±0,2 міс. Більшу виживаність відзначено серед молодих осіб – 17,4±1,4 міс (p<0,001). Величина відношення ризиків (ВР) для осіб середнього віку становила 1,79 (95% довірчий інтервал (ДІ) 1,60-2,00; p=0,017), для осіб похилого віку – 1,51 (95% ДІ 1,32-1,72; p<0,001). Пацієнти, які лікувалися в 2011–2013 рр., мали кращий прогноз із середньою виживаністю 12,6±0,3 міс (p<0,001) та ВР – 0,75 (95% ДІ 0,66-0,85, p<0,01). Середня загальна виживаність у групі протоколів комбінованого лікування становила 16,3±0,5 міс. Найгіршим прогноз був у пацієнтів, яким провели лише хірургічне втручання, – 7,5±0,3 міс (p<0,001). ВР для комбінації хірургічного втручання з променевою терапією становило 1,36 (95% ДІ 1,22-1,51; p<0,001), для лише хірургічного втручання – 1,94 (95% ДІ 1,73-2,17; p<0,001), для комбінації хірургічного втручання з хіміотерапією – 1,18 (95% ДІ 0,90-1,53; p=0,25).

Висновки. Високі показники виживаності у хворих з первинно діагностованими ГБ усіх вікових груп і в усі періоди дослідження відзначено при використанні комбінованого лікування (хірургічного видалення і хіміотерапії чи променевої терапії).

Ключові слова: *гліобластома; виживання; хірургія; хіміотерапія; променева терапія; особи похилого віку*

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Выживаемость пациентов с первично диагностированными глиобластомами: данные Национального канцер-регистра Украины (2008–2016)

Розуменко А.В.[1], Ключка В.Н.[1], Розуменко В.Д.[1], Федоренко З.П.[2]

[1] Отдел нейроонкологии, Институт нейрохирургии им. акад. А.П. Ромоданова НАМН Укаины, Киев, Украина
[2] Национальный канцер-регистр Украины, Национальный институт рака, Киев, Украина

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Адрес для переписки:
Розуменко Артем Владимирович, Отдел нейроонкологии, Институт нейрохирургии им. акад. А.П. Ромоданова, ул. Платона Майбороды, 32, Киев, Украина, 04050, e-mail: dr.rozumenko@gmail.com

Цель: провести анализ выживаемости пациентов с первично диагностированными глиобластомами (ГБ) в Украине.

Материалы и методы. Проанализированы 3763 случая гистологически верифицированных первично диагностированных ГБ, выявленных в течение 9-летнего периода (2008–2016). Пациентов распределили на группы в зависимости от возраста: молодые лица (<45 лет) – 734 (19,5%), лица среднего возраста (45–64 лет) – 2360 (62,7%), лица пожилого возраста (>64 лет) – 669 (17,8%). Клинические параметры и показатели выживаемости анализировали за три периода: 2008-2010, 2011-2013 и 2014–2016 гг.

Результаты. Общая медиана выживаемости составила 12,2±0,2 мес. Большая выживаемость отмечена среди лиц моложе 45 лет – 17,4±1,4 мес (p<0,001). Величина отношения рисков (ОР) для лиц среднего возраста составила 1,79 (95% доверительный интервал (ДИ) 1,60-2,00; p=0,017), для лиц пожилого возраста – 1,51 (95% ДИ 1,32-1,72; p<0,001). Пациенты, лечившиеся в 2011-2013 гг., имели лучший прогноз со средней выживаемостью 12,6±0,3 мес (p<0,001) и ОР – 0,75 (95% ДИ 0,66-0,85, p<0,01). Средняя общая выживаемость в группе протоколов комбинированного лечения составила 16,3±0,5 мес. Самым худшим прогноз был у пациентов, которым провели только хирургическое вмешательство, – 7,5±0,3 мес (p<0,001). ОР для комбинации хирургического вмешательства и лучевой терапии составил 1,36 (95% ДИ 1,22-1,51; p<0,001), для только хирургического вмешательства – 1,94 (95% ДИ 1,73-2,17; p<0,001), для комбинации хирургического вмешательства и химиотерапии – 1,18 (95% ДИ 0,90-1,53; p=0,25).

Выводы. Высокие показатели выживаемости у больных с первично диагностированными ГБ всех возрастных групп и во все периоды исследования отмечены при использовании комбинированного лечения (хирургического удаления и химиотерапии или лучевой терапии).

Ключевые слова: *глиобластома; выживание; хирургия; химиотерапия; лучевая терапия; лица пожилого возраста*

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Introduction

Glioblastoma (GBM) is the most common primary brain tumor in adults. With the annual incidence of 3.2–6.1 per 100,000/year, GBM presents approximately the half of newly diagnosed primary brain neoplasms. As all anaplastic gliomas, GBM is characterized by infiltrative growth and rapid proliferation that determines high rates of recurrence and progressing neurological deterioration [1-4].

The present-day approach for brain gliomas aims at the improving quality of life and survival rates of patients. The surgical resection is the initial step in the therapy of anaplastic gliomas that could provide accurate tissue diagnosis; it contributes to rapid clinical improvement and could be followed by adjuvant therapy [5,6]. In patients with GBM, the prognosis is commonly poor, even after the treatment in compliance with modern protocols. The impact of the factors contributing to the survival of patients with gliomas could be accurately estimated when the better neurological and surgical outcomes were assured [5-8].

Objective

In this study, we present the results of population-based survival analysis in patients with GBM. Our aim was to evaluate the impact of demographic factors and treatment protocols on overall survival (OS) in patients with GBM.

Materials and methods

Data Selection

For this study, data about patients with GBM diagnosed between 2008 and 2016 were obtained from the National Cancer Registry of Ukraine (NCR).

The inclusion criteria were as follows: 1) age ≥18 years; 2) newly diagnosed histologically verified GBM (WHO Grade IV); 3) follow up and survival data availability.

Exclusion criteria were as follows: 1) absence of surgery in the treatment protocol.

All patients were grouped as younger adults (<45 years at diagnosis), middle-aged (45–64 years), and older adults (>64 years). Clinical parameters and survival rates were defined for every three 3-year periods 2008-2010, 2011-2013, and 2014-2016.

Statistical Analysis

The descriptive statistics were used for continuous variables. The groups of continuous variables were compared with a two-sample t-test and ANOVA test.

For categorical variables, the standard deviation and frequency of distribution were calculated. The

This article contains some figures that are displayed in color online but in black and white in the print edition

distributions of categorical variables were analyzed using Chi-square test.

Overall survival was estimated by the Kaplan-Meier method. Survival curves for the various subgroups were compared using the log-rank (Mantel-Cox) test. OS was calculated as a function of time for the period from histological diagnosis onset until death or last follow-up if censored.

The multivariable Cox proportional hazards model was used to examine four variables: age, sex, treatment protocol, and diagnosis period. We considered a P-value less than 0.05 as statistically significant.

Statistical analysis was performed with the Deducer package (Java GUI extensions to statistical programming platform R licensed under the GNU).

Results

A total 5005 adult patients with GBM diagnosed between 01.01.2008 and 31.12.2016 were found in the database of the National Cancer Registry of Ukraine. Only 3763 (75,2%) of them had data about surgery added in the treatment protocol and were included in the study ***(Table 1)***.

There were 1963 (52.2%) males and 1800 (47.8%) females with mean age 54.0±11.8 years and prominent prevalence (62.7%) of middle-aged (45-64 years). The distribution of age groups ***(Fig. 1)*** was equal in all time periods (p=0.91).

The most of patients received combined treatment including surgery and radiotherapy (41.1-48.5%), next was the group of surgery alone (30.0-36.6%). The number of patients with adjuvant chemotherapy was only 1.8-3.3% and adjuvant chemoradiotherapy — 19.0-23.6%. The difference of treatment protocols used was not significant in all time periods (p=0.08), but significant (p<0.001) for age groups ***(Table 2)***.

The overall median survival was 12.2±0.2 months with range 0–95 months. The Kaplan-Maier survival analysis showed no difference between the groups of patients, depending on the sex (p=0.29). At the same time, better survival was observed in young adults (<45 years) — 17.0±0.6 months (p<0.001) ***(Fig 2)***.

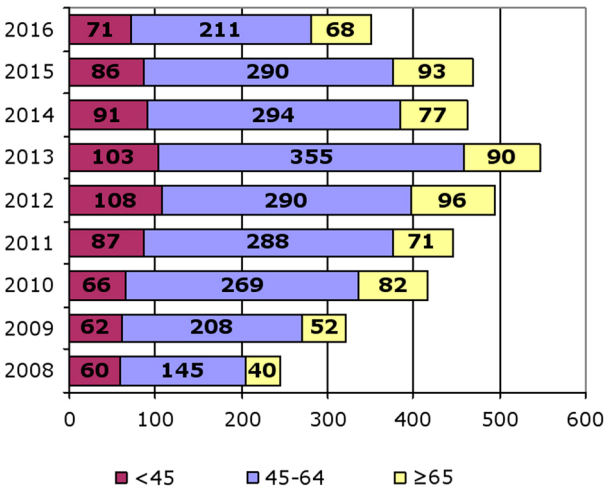

Figure 1. Cases distribution by years and age groups

Table 1. Demographic and clinical characteristics in study groups

Parameter	Total	Time period			p-value
		2008-2010	2011-2013	2014-2016	
No. of patients (%)	3763 (100.0)	984 (26.1)	1490 (39.6)	1289 (34.3)	
Age at diagnosis (yrs.)					
Mean	54.0±11.8	53.9±11.4	53.7±12.0	54.3±11.7	0.38
Range	18-90	18-81	18-87	19-90	
< 45 (%)	734 (19.5)	188 (19.1)	298 (20.0)	248 (19.2)	
45–64 (%)	2360 (62.7)	622 (63.2)	935 (62.8)	803 (62.3)	
>65 (%)	669 (17.8)	174 (17.7)	257 (17.2)	238 (18.5)	0.91
Sex					
Male (%)	1963 (52.2)	531 (54.0)	765 (51.3)	667 (51.7)	
Female (%)	1800 (47.8)	453 (46.0)	725 (48.7)	622 (48.3)	0.42
Treatment protocol					
Surgery (%)	1254 (33.3)	319 (32.4)	494 (33.2)	441 (34.2)	
Surgery + Radiotherapy (%)	1738 (46.2)	431 (43.8)	719 (48.3)	588 (45.6)	
Surgery + Chemotherapy (%)	87 (2.1)	29 (3.0)	29 (1.9)	29 (2.3)	
Surgery + Chemoradiotherapy (%)	684 (18.2)	205 (20.8)	248 (16.6)	231 (17.9)	0.08

Table 2. Cases distribution by treatment protocol and age groups

Treatment protocol	<45	45–64	>64	Total
Surgery (%)	220 (30)	789 (33.4)	245 (36.6)	1254 (33.3)
Surgery + Radiotherapy (%)	319 (43.5)	1144 (48.5)	275 (41.1)	1738 (46.2)
Surgery + Chemotherapy (%)	22 (3.0)	43 (1.8)	22 (3.3)	87 (2.3)
Surgery + Chemoradiotherapy (%)	173 (23.6)	384 (16.3)	127 (19.0)	684 (18.2)
Total (%)	734 (19.5)	2360 (62.7)	669 (17.8)	3763 (100)

The patients treated in the second period achieved better prognosis with median survival of 12.6±0.3 months (p<0.001) ***(Fig 3)***.

The median overall survival in combined treatment protocol group was 16.3±0.5 months, it was significantly lower in the surgery/radiotherapy group (12.7±0.2) and in the surgery/chemotherapy group (13.4±1.3), and the worst prognosis was in surgery alone group – 7.5±0.3 months (p<0.001) ***(Fig 4)***.

Table 3 and ***Table 4*** contain summarized survival data and follow up.

The Cox proportional hazards modeling showed that treatment in the second (HR 0.75, 95% CI 0.66-0.85) and third (HR 0.80, 95% CI 0.73-0.88) period was associated with better prognosis (p<0.001). Younger patients were likely to live longer, then middle-aged (HR 1.79, 95% CI 1.60-2.00; p<0.001) and older adults (HR 1.51, 95% CI 1.32-1.72; p<0.001). The using of full treatment protocol combining surgery with chemoradiotherapy predicted better survival while the HR for surgery with radiotherapy was 1.30 (95% CI 1.17-1.45; p<0.001), and for surgery alone it raised up to 1.94 (95% CI 1.73-2.17; p<0.001). The HR for a combination of surgery with chemotherapy was 1.18, but it was not significant (p=0.25) ***(Table 5)***.

Discussion

The GBM is the most common brain glioma with the likelihood of fast relapse after surgical resection and poor

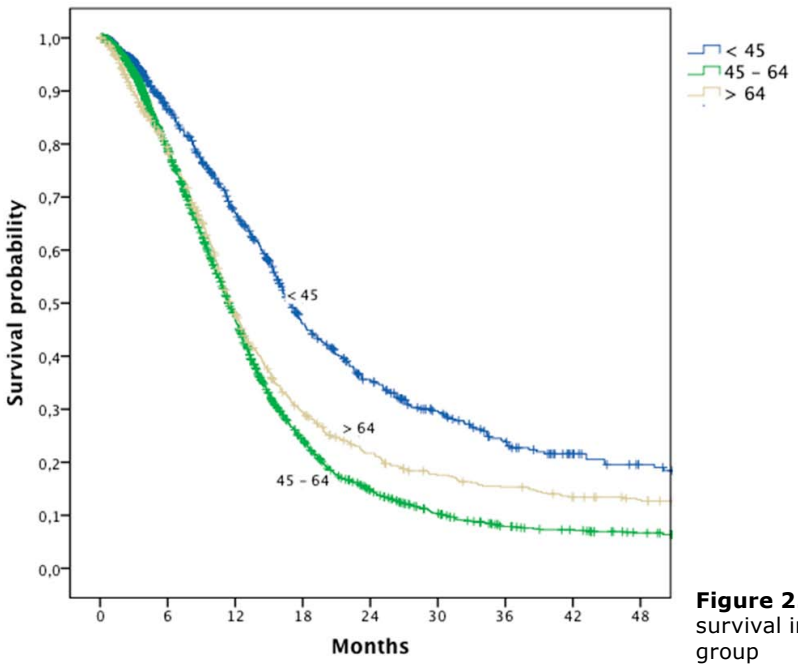

Figure 2. Kaplan-Meier curves showing overall survival in the whole cohort depending on age group

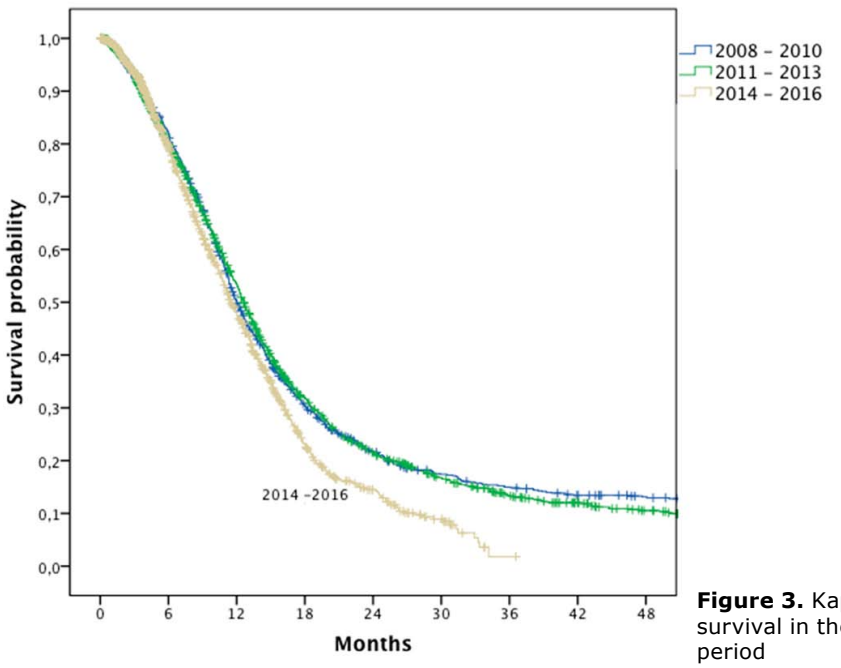

Figure 3. Kaplan-Meier curves showing overall survival in the whole cohort depending on time period

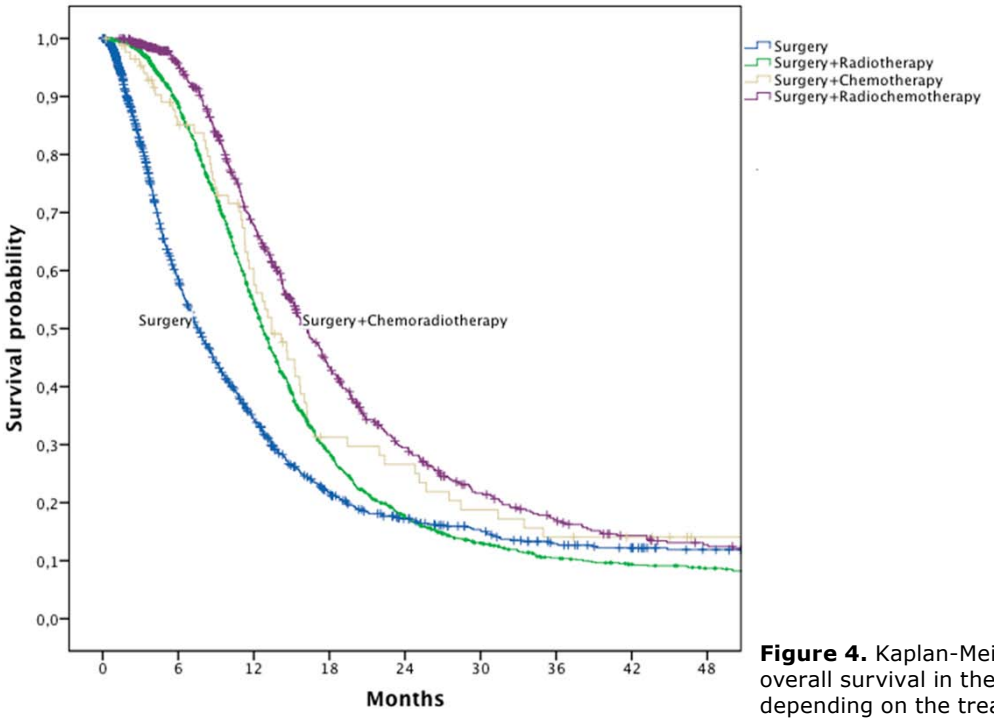

Figure 4. Kaplan-Meier curves showing overall survival in the whole cohort depending on the treatment protocol

Table 3. Survival outcomes of the study

Parameter	Total	Time period			p-value
		2008-2010	2011-2013	2014-2016	
Median overall survival (months)	12.2±0.2	12.0±0.3	12.6±0.3	11.5±0.4	<0.001
Age at diagnosis					
<45	17.0±0.6	21.7±2.8	18.2±1.3	15.6±0.7	
45–64	11.4±0.2	11.6±0.5	11.9±0.3	10.8±0.4	
>64	11.5±0.4	12.0±0.4	9.1±2.4	7.8±1.0	<0.001
Treatment protocol					
Surgery	7.5±0.3	8.3±0.6	8.3±0.6	6.3±0.4	
Surgery + Radiotherapy	12.7±0.2	12.2±0.4	13.4±0.3	12.4±0.5	
Surgery + Chemotherapy	13.4±1.3	14.6±1.7	13.4±2.4	12.0±0.8	
Surgery + Chemoradiotherapy	16.3±0.5	14.6±1.0	16.4±1.2	16.3±0.8	<0.001

Table 4. Follow-up of the study

Parameter	Follow-up (months)				p-value
	6	12	18	24	
Age at diagnosis					
<45	86.4	66.9	46.0	35.4	
45-64	79.2	46.9	24.4	14.7	
>64	79.3	47.9	29.3	21.3	<0.001
Treatment protocol					
Surgery	58.5	34.3	21.7	17.2	
Surgery + Radiotherapy	88.6	54.2	28.7	17.5	
Surgery + Chemotherapy	85.1	60.3	31.3	25.0	
Surgery + Chemoradiotherapy	95.5	67.8	43.2	29.5	<0.001
Time period					
2008-2010, %	82.0	50.1	30.5	21.7	
2011-2013, %	80.3	53.4	31.8	21.3	
2014-2016, %	79.4	47.4	23.2	14.2	<0.001
Total, %	80.6	50.7	29.3	19.%	<0.001

Table 5. Multivariable survival analysis of clinical parameters

Parameter	p-value	HR		95,0% CI	
Period					
2008-2010	<0.001	0.80		0.73-0.88	
2011-2013	<0.001	0.75		0.66-0.85	
2014-2016	<0.001	1			
Age at diagnosis					
<45	<0.001	1		0.51-0.70	
45–64	<0.001	1.79		1.60-2.00	
>64	<0.001	1.51		1.32-1.72	
Treatment protocol		*first*	*last*	*first*	*last*
Surgery	<0.001	1	1.94	-	1.73-2.17
Surgery + Radiotherapy	<0.001	0,699	1.36	0.64-0.76	1.22-1.51
Surgery + Chemotherapy	0.25	0,605	1.18	0.47-0.78	0.90-1.53
Surgery + Chemoradiotherapy	<0.001	0,515	1	0.46-0.58	-

prognosis despite sophisticated surgery techniques and modern adjuvant therapy regimes. The nowadays treatment paradigm in patients with GBM implies combined approach aimed not only at the survival improvement while maintaining high rates of the quality of life. The optimum treatment protocol for brain GBM remains controversial. The individualization of the treatment for GBM supposes the integration of various parameters such as age, performance status, results of molecular analysis etc. [6,9,10,11].

There are very few publications discovering epidemiological aspects of malignant gliomas in Ukraine. Most prominent of them were published during previous decade [12,13].

The current study was an attempt to analyze the results of different treatment protocols application and to show the survival trends in patients with newly diagnosed GBM in Ukraine.

Epidemiological data suggests the progredient increase of GBM incidence mainly due to the wide accessibility of neuroimaging tools and population aging. In Ukraine, it was observed the tendency of GBM diagnosis growth during the first and second period from 2008 to 2013. In the last period (2014-2016) the decrease of patients' number could be associated with social and economic changes in the country. Regardless of the similar treatment protocols, this period also was characterized by the decrease of overall median survival and survival rates.

The results achieved in prior studies have shown that the better prognosis for GBM patients is promoted by the younger age, the greater extent of resection facilitated by image-guided techniques, the absence of postoperative neurological deficit, and application of combined treatment protocols [5,8,14,15].

The patient's age significantly impacted survival, and our study concluded the benefits of any treatment protocol for young patients. At the same time, the similar results in patients in middle age and older groups suggest the same effectiveness of combined approach for elderly patients.

Adjuvant therapy provides better survival in all patients groups. The using of surgery protocol alone has higher risk of dying by 94%, the following radiotherapy reduces it to 36%. The combined adjuvant therapy has almost twice lower risk of dying and raises 2-year survival rate from 17.2% to 29.5% with overall median survival 16.3±0.5.

The available data of recent studies suggest the overall median survival rates as 12.5–15.9 months with HR for age over 65 years 1.88 [16]. Other declares median survival time and 2-year OS being 18.0 months and 38.9% after chemoradiotherapy compared to 12.7 months and 12.6% after radiotherapy [17].

In this study, we could not explore the effect of the resection extent on survival due to the inaccessibility of detailed surgical procedure data for each patient. The data of our previous study and a lot of other single institute research confirms the positive effect of cytoreduction on higher survival rate. As well as using of intraoperative neuroimaging technique facilitates performing of safer and complete resection it also reduces hazard ratios. The using of intraoperative neuromonitoring and neuroimaging tools provides high rates of complete resection with low rates of neurological disorders [6,8,10,18,19].

The emergence of highly effective chemotherapeutic drugs has improved the survival rates in patients (especially the term of non-recurrent survival). The leading clinicians involved in GBM research put increased focus on finding optimal chemical compounds with high tropism to tumor cells. The future breakthrough in the treatment of patients with GBM is conditioned with the development of novel molecular biology, genetics, biochemistry paradigms [20,21].

This research has methodological limitations and could not pretend on full-covering study due to continuing developing of oncological data collecting system in Ukraine. The incompletion of GBM cases collected in the NCR could explain the low incidence of GBMs (0.58-1.30 per 100,000) in contrast to data of other countries: 3.20 per 100,000/year for the US, 4.64 per 100,000/year for the UK [3,4].

The other limitation of the study is in the absence of key prognostic factors in the NCR, such as the extent of resection, a number of reoperations, regimes of radio- and chemotherapy, molecular markers (IDH mutation, MGMT methylation status).

Our data are fully consistent with the data of the biggest registers (regarding the influence of various

factors, the very terms of general and non-recurring survival), which confirms the fact that the specialized neurooncological service to the patients with GBM in Ukraine is at the appropriate level.

Conclusions

The neurooncological service in Ukraine provides different treatment modalities for the patients with newly diagnosed GBMs. In current population-based research, the global survival trends were observed. The better results were found for the combination of surgery with chemoradiotherapy. The unification of treatment protocols associated with survival advantage in GBM patients of all ages.

Disclosure

The authors report no conflict of interest concerning any drugs, materials, devices or methods used in this study or the findings specified in this paper.

Ethical approval

The study was conducted within the guidelines of the institutional review board.

References

1. Jacques G, Cormac O. Central nervous system tumors. Pediatric Neurology Part II. 2013;:931-958. doi: 10.1016/B978-0-444-52910-7.00015-5. PubMed PMID: 23622303.
2. Butowski N. Epidemiology and Diagnosis of Brain Tumors. CONTINUUM: Lifelong Learning in Neurology. 2015;21:301-313. doi: 10.1212/01.CON.0000464171.50638.fa. PubMed PMID: 25837897.
3. Ostrom QT, Gittleman H, Liao P, Vecchione-Koval T, Wolinsky Y, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary brain and other central nervous system tumors diagnosed in the United States in 2010-2014. Neuro Oncol. 2017 Nov 6;19(suppl_5):v1-v88. doi: 10.1093/neuonc/nox158. PubMed PMID: 29117289.
4. Brodbelt A, Greenberg D, Winters T, Williams M, Vernon S, Collins VP; (UK) National Cancer Information Network Brain Tumour Group. Glioblastoma in England: 2007-2011. Eur J Cancer. 2015 Mar;51(4):533-42. doi: 10.1016/j.ejca.2014.12.014. PubMed PMID: 25661102.
5. Hervey-Jumper S, Berger M. Role of Surgical Resection in Low- and High-Grade Gliomas. Current Treatment Options in Neurology. 2014;16(4). doi:10.1007/s11940-014-0284-7. PubMed PMID: 24595756.
6. McGirt MJ, Chaichana KL, Gathinji M, Attenello FJ, Than K, Olivi A, Weingart JD, Brem H, Quiñones-Hinojosa AR. Independent association of extent of resection with survival in patients with malignant brain astrocytoma. J Neurosurg. 2009 Jan;110(1):156-62. doi: 10.3171/2008.4.17536. PubMed PMID: 18847342.
7. Delgado-López P, Corrales-García E (2016) Survival in glioblastoma: a review on the impact of treatment modalities. Clinical and Translational Oncology 18(11):1062-1071. doi: 10.1007/s12094-016-1497-x. PubMed PMID: 26960561.
8. Filippini G, Falcone C, Boiardi A, Broggi G, Bruzzone M, Caldiroli D et al. Prognostic factors for survival in 676 consecutive patients with newly diagnosed primary glioblastoma. Neuro-Oncology. 2008;10(1):79-87. doi: 10.1215/15228517-2007-038. PubMed PMID: 17993634.
9. Gil-Robles S, Duffau H. Surgical management of World Health Organization Grade II gliomas in eloquent areas: the necessity of preserving a margin around functional structures. Neurosurgical Focus. 2010;28(2):E8. doi: 10.3171/2009.12.focus09236. PubMed PMID: 20121443.
10. González-Darder JM, González-López P, Talamantes F, Quilis V, Cortés V, García-March G, Roldán P. Multimodal navigation in the functional microsurgical resection of intrinsic brain tumors located in eloquent motor areas: role of tractography. Neurosurg Focus. 2010 Feb;28(2):E5. doi: 10.3171/2009.11.FOCUS09234. PubMed PMID: 20121440.
11. Keles G, Lamborn K, Berger M. Low-grade hemispheric gliomas in adults: a critical review of extent of resection as a factor influencing outcome. Journal of Neurosurgery. 2001;95(5):735-745. doi: 10.3171/jns.2001.95.5.0735. PubMed PMID: 11702861.
12. Rozumenko VD. Neurooncology: modern state of the problem. Onkologiya. 2006; 8 (2):188-19. Russian. Available from: http://dspace.nbuv.gov.ua/bitstream/handle/123456789/7473/08_561.pdf
13. Rozumenko VD. [Epidemiologiya opukholey golovnogo mozga: statisticheskie faktory]. Ukrainian Neurosurgical Journal. 2002;(3):47-48. Russian. Available from: http://nbuv.gov.ua/UJRN/Unkhj_2002_3_45.
14. Lacroix M, Abi-Said D, Fourney DR, Gokaslan ZL, Shi W, DeMonte F, Lang FF, McCutcheon IE, Hassenbusch SJ, Holland E, Hess K, Michael C, Miller D, Sawaya R. A multivariate analysis of 416 patients with glioblastoma multiforme: prognosis, extent of resection, and survival. J Neurosurg. 2001 Aug;95(2):190-8. doi: 10.3171/jns.2001.95.2.0190 . PubMed PMID: 11780887.
15. Stummer W, Reulen HJ, Meinel T, Pichlmeier U, Schumacher W, Tonn JC, Rohde V, Oppel F, Turowski B, Woiciechowsky C, Franz K, Pietsch T; ALA-Glioma Study Group. Extent of resection and survival in glioblastoma multiforme: identification of and adjustment for bias. Neurosurgery. 2008 Mar;62(3):564-76; discussion 564-76. doi: 10.1227/01.neu.0000317304.31579.17. PubMed PMID: 18425006.
16. Verlut C, Mouillet G, Magnin E, Buffet-Miny J, Viennet G, Cattin F, Billon-Grand NC, Bonnet E, Servagi-Vernat S, Godard J, Billon-Grand R, Petit A, Moulin T, Cals L, Pivot X, Curtit E. Age, Neurological Status MRC Scale, and Postoperative Morbidity are Prognostic Factors in Patients with Glioblastoma Treated by Chemoradiotherapy. Clin Med Insights Oncol. 2016 Aug 17;10:77-82. doi: 10.4137/CMO.S38474. PubMed PMID: 27559302.
17. Seidlitz A, Siepmann T, Löck S, Juratli T, Baumann M, Krause M. Impact of waiting time after surgery and overall time of postoperative radiochemotherapy on treatment outcome in glioblastoma multiforme. Radiat Oncol. 2015 Aug 16;10:172. doi: 10.1186/s13014-015-0478-5. PubMed PMID: 26276734.
18. Kurimoto M, Hayashi N, Kamiyama H, Nagai S, Shibata T, Asahi T, Matsumura N, Hirashima Y, Endo S. Impact of neuronavigation and image-guided extensive resection for adult patients with supratentorial malignant astrocytomas: a single-institution retrospective study. Minim Invasive Neurosurg. 2004 Oct;47(5):278-83. doi: 10.1055/s-2004-830093. PubMed PMID: 15578340.
19. Rozumenko A, Kliuchka V, Rozumenko V, Semenova V, Kolesnyk S, Fedorenko Z. Image-guided resection of glioblastoma in eloquent brain areas facilitated by laser surface thermal therapy: clinical outcomes and long-term results. Neurosurg Rev. 2018 Jan 22. doi: 10.1007/s10143-018-0948-y. PubMed PMID: 29356927.
20. Davis FG, Freels S, Grutsch J, Barlas S, Brem S. Survival rates in patients with primary malignant brain tumors stratified by patient age and tumor histological type: an analysis based on Surveillance, Epidemiology, and End Results (SEER) data, 1973-1991. J Neurosurg. 1998 Jan;88(1):1-10. doi: 10.3171/jns.1998.88.1.0001 . PubMed PMID: 9420066.
21. Li YM, Suki D, Hess K, Sawaya R. The influence of maximum safe resection of glioblastoma on survival in 1229 patients: Can we do better than gross-total resection? J Neurosurg. 2016 Apr;124(4):977-88. doi: 10.3171/2015.5.JNS142087. PubMed PMID: 26495941.