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# Surgical management of periventricular glioma: decision-making and preoperative assessment of resectability

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#### Address for correspondence:

Artem Rozumenko, Department of Intracerebral Tumors, Romodanov Neurosurgery Institute, 32 Platona Mayborody st., Kyiv, Ukraine, 04050, e-mail: dr.rozumenko@gmail.com **Objective.** Periventricular gliomas (PVG) are deep-seated tumors with wide invasion into cerebral core structures accompanied by high rates of postoperative deterioration and early relapse.

The purpose of this study was to define the preoperative neuroimaging signs as the factors determining the early postoperative outcome in patients with high-grade PVG.

**Materials and methods.** The clinical records of 132 (50 females and 82 males) consecutive patients with a mean age 45.9 years (range 21–69) undergoing image-guided surgery for PVG at a single academic institution were retrospectively analyzed. There were 52 (39.4 %) WHO grade III gliomas, and 80 (60.6 %) of patients had WHO grade IV gliomas.

**Results.** Postoperative median KPS score significantly raised from 67.4 to 82.0, as well as a number of patients with the KPS score  $\geq$  70: from 18 (13.6 %) to 109 (82.6 %) with p<0.01. The multivariate regression analysis revealed that poor postoperative functional status was associated with basal ganglia involvement (OR 2.75, 95% CI 0.93–8.09, p = 0.07), the higher EOR grade (OR 3.30, 95% CI 1.15–9.43, p = 0.03), and hydrocephalus (OR 5.08, 95% CI 1.49–17.35, p = 0.09).

Total/subtotal resection was carried out in 84 (63.6 %) cases; in 48 (36.4 %) cases, the partial resection was performed. The multivariate logistic regression analysis revealed that three factors decreased the likelihood of total/subtotal resection in PVG: basal ganglia invasion (OR 0.18, 95% CI 0.06–0.55, p<0.01), minor extraventricular part (OR 0.40, 95% CI 0.17–0.94, p = 0.04), and contralateral side extension (OR 0.38, 95% CI 0.16–0.92, p = 0.03). In contrast, the presence of tumor-associated cyst (OR 3,73, 95% CI 1.32–10.54, p = 0.01) increased odds of total/subtotal resection. The four-tear grading system of PVG integrating statistically identified factors of total/subtotal resection and risks of postoperative neurological deterioration was developed.

The Kaplan-Meier analysis showed that overall median survival was  $17.7 \pm 1.9$  months for patients with high-grade PVG. The survival analysis using Cox regression model revealed that age over 45 years (HR 1.77, 95% CI 1.06–2.99; p = 0.03) and higher tumor WHO grade (HR 2.24, 95% CI 1.27–3.95; p = 0.005) significantly decreased survival rates.

**Conclusions.** The proposed grading system provides the possibility of preoperative evaluation of PVG resectability that in combination with 3D surgical planning and image-guided resection allows performing maximal safe resections and preventing of postoperative neurological deficits.

**Keywords:** *periventricular glioma; grading system; extent of resection; image-guided resection; surgical outcomes* 

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# Хірургічне лікування перивентрикулярних гліом: тактика прийняття рішення та доопераційна оцінка резектабельності

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Надійшла до редакції 04.01.2019 Прийнята до публікації 21.02.2019 Перивентрикулярні гліоми (ПВГ) є глибинно розташованими пухлинами з широкою інвазією, які асоціюються з високою частотою післяопераційних ускладнень і ранніми рецидивами.

**Мета**: визначити чинники доопераційної візуалізації, які дають змогу оцінити ранні післяопераційні результати лікування пацієнтів з ПВГ високого ступеня анаплазії.

Матеріали і методи. Ретроспективно проаналізовано клінічні записи 132 (50 жінок і 82 чоловіків віком від 21 до 69 років (середній вік – 45,9

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Розуменко Артем Володимирович, Відділення внутрішньомозкових пухлин, Інститут нейрохірургії ім. акад. А.П. Ромоданова, вул. Платона Майбороди, 32, Київ, Україна, 04050, e-mail: dr.rozumenko@gmail.com року)) пацієнтів, яким виконано операцію з видалення ПВГ під контролем нейронавігації. Серед віддалених гліом було 52 (39,4%) WHO Gr III та 80 (60,6%) – WHO Gr IV.

Результати. Середній показник за шкалою Карновського у післяопераційний період збільшився з 67,4 до 82,0 балів, а кількість пацієнтів з ≥70 балів – з 18 (13,6%) до 109 (82,6%), (p<0,01). Багатофакторний регресійний аналіз виявив, що низький функціональний статус у післяопераційний період був пов'язаний з інвазією пухлини в базальні ганглії (відношення шансів (ВШ) – 2,75, 95% довірчий інтервал (ДІ) – 0,93–8,09, p=0,07), досягненням більш високого ступеня радикальності (ВШ – 3,30, 95% ДІ – 1,15–9,43, p=0,03) та первинною гідроцефалією (ВШ – 5,08, 95% ДІ – 1,49–17,35, p=0,09).

Парціальну резекцію виконано в 48 (36,4%) випадках, у решти пацієнтів – тотальну або субтотальну. Багатофакторний регресійний аналіз показав, що зниження радикальності пов'язано з інвазією пухлини в базальні ганглії (ВШ – 0,18, 95% ДІ – 0,06–0,55, p<0,01), наявністю у пухлини меншої екстравентрикулярної частини (ВШ –0,40, 95% ДІ – 0,17–0,94, p=0,04) та поширенням на протилежну півкулю (ВШ – 0,38, 95% ДІ – 0,16–0,92, p=0,03). Ступінь резекції був вищім за наявності кіст у структурі пухлинного вогнища (ВШ – 3,73, 95% ДИ – 1,32–10,54, p=0,01).

Розроблена 4-рівнева система градації ПВГ поєднала статистично виявлені чинники, які сприяють досягненню високого ступеня радикальності.

Аналіз результатів за Каплан-Мейером показав, що загальна медіана виживаності становить (17,7±1,9) міс. Використання регресійної моделі Кокса виявило, що вік старше 45 років (відношення ризиків – 1,77, 95% ДІ – 1,06–2,99, р=0,03) і високий ступінь анаплазії (відношення ризиків – 2,24, 95% ДІ – 1,27–3,95, р=0,005) значно знижували показники виживаності.

Висновки. Запропонована система градації дає змогу на доопераційному етапі оцінити резектабельность ПВГ, що разом із застосуванням 3Dхірургічного планування і навігаційного супроводу дає змогу провести максимально безпечне видалення пухлин та запобігти розвитку післяопераційних неврологічних порушень.

**Ключові слова:** перивентрикулярна гліома; система градації; ступінь резекції; нейронавігація; хірургічні результати

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# Хирургическое лечение перивентрикулярных глиом: тактика принятия решения и дооперационная оценка резектабельности

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Розуменко Артем Владимирович, Отделение внутримозговых опухолей, Институт нейрохирургии им. акад. А.П. Ромоданова, ул. Платона Майбороды, 32, Киев, Украина, 04050, e-mail: dr.rozumenko@gmail.com Перивентрикулярные глиомы (ПВГ) являются глубоко расположенными опухолями с широкой инвазией, ассоциируются с высокой частотой послеоперационных осложнений и ранними рецидивами,

**Цель**: определить факторы дооперационной визуализации, позволяющие оценить ранние послеоперационные результаты лечения пациентов с ПВГ высокой степени анаплазии.

**Материалы и методы.** Ретроспективно проанализированы клинические записи 132 (50 женщин и 82 мужчин в возрасте от 21 до 69 лет (средний возраст – 45,9 года)) пациентов, которым выполнена операция по удалению ПВГ под контролем нейронавигации. Среди удаленных глиом было 52 (39,4%) WHO Gr III и 80 (60,6%) – WHO Gr IV,

Результати. Средний показатель по шкале Карновского в послеоперационный период увеличился с 67,4 до 82,0 баллов, а количество пациентов с показателем ≥70 баллов – с 18 (13,6%) до 109 (82,6%), (p<0,01). Многофакторный регрессионный анализ выявил, что низкий функциональный статус в послеоперационный период был связан с инвазией опухоли в базальные ганглии (отношение шансов (ОШ) – 2,75, 95% доверительный интервал (ДИ) – 0,93–8,09, р=0,07), достижением более высокой степени радикальности (ОШ – 3,30, 95% ДИ – 1,15–9,43, р=0,03) и первичной гидроцефалией (ОШ – 5,08, 95% ДИ – 1,49–17,35, р=0,09).

Парциальная резекция выполнена в 48 (36,4%) случаях, остальным пациентам – тотальная или субтотальная. Многофакторный регрессионный анализ показал, что снижение радикальности было связано с инвазией опухоли в базальные ганглии (ОШ – 0,18, 95% ДИ – 0,06–0,55, p<0,01), наличием у опухоли меньшего экстравентрикулярного компонента (ОШ – 0,40, 95% ДИ – 0,17–0,94, p=0,04) и распространением на противоположное полушарие (ОШ – 0,38, 95% ДИ – 0,16–0,92, p=0,03).

Степень резекции была высшей при наличии кист в структуре опухолевого очага (ОШ – 3,73, 95% ДИ – 1,32–10,54, р=0,01).

Разработана 4-уровневая система градации ПВГ, которая объединила статистически выявленные факторы, способствующие достижению высокой степени радикальности.

Анализ по Каплан-Мейеру показал, что общая медиана выживаемости составила (17,7±1,9) мес. Использование регрессионной модели Кокса выявило, что возраст старше 45 лет (отношение рисков – 1,77, 95% ДИ – 1,06–2,99, р=0,03) и высокая степень анаплазии (отношение рисков – 2,24, 95% ДИ – 1,27–3,95, р=0,005) значительно снижали выживаемость.

**Выводы.** Предложенная система градации позволяет на дооперационном этапе оценить резектабельность ПВГ, что вместе с применением 3Dхирургического планирования и навигационного сопровождения позволяет провести максимально безопасное удаление опухоли и предотвратить развитие послеоперационных неврологических нарушений.

**Ключевые слова:** перивентрикулярная глиома; система градации; степень резекции; нейронавигация; хирургические результаты

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#### Introduction

Glioma is the most common primary brain tumor in persons of working age. The social and economic effects of glial tumors in the population are determined by long-term patient disability and loss of performance with the significant decrease in quality of life and life expectancy [1–3].

The appearance of glioma is considering as a result of a neoplastic transformation of stem cells arising mostly from the ventricular-subventricular zone. The periventricular glioma (PVG) itself is characterized by a wide invasion along the white matter fibers, early damage to cerebral core structures, impending anaplastic transformation, and relapse [4, 5]. The functional limits prevent radical surgical treatment, that causes high rates of recurrence and unfavorable prognosis in the vast majority of patients, even after sophisticated combined therapy [6–8].

At the same time, surgery remains a key link in the treatment of patients with PVG that could clarify the histological diagnosis, contributes to clinical improvement and provides additional time for adjuvant therapy application. The improvement of the prognosis for the deep-seated gliomas is associated with the technologies of intraoperative visualization of brain tumors such as the multimodal neuronavigation, intraoperative MRI, intraoperative fluorescence and endoscopic assistance as well as the introduction of the newest methods of adjuvant treatment, in particular, photodynamic therapy, brachytherapy, and radiosurgery [9–16].

In recent studies on high-grade glioma (HGG) patient's survival, the preference to the residual tumor volume estimation instead of the extent of resection is observed. The accumulated data strongly confirms the relation of residual tumor volume with elongation of progression-free period and higher survival rates in operated patients with HGG [17–20].

The **purpose** of the present study was to define the preoperative neuroimaging signs as the factors determining the possibility to achieve survival benefit resection and to assess the early postoperative outcome in patients with high-grade PVG.

# Materials and methods

# Patient population

A retrospective study included patients with supratentorial high-grade PVG operated from February 2009 to December 2017 at the Romodanov Neurosurgery Institute (Kyiv, Ukraine).

The inclusion criteria were as follows: (1) age  $\geq$  18 years, (2) newly diagnosed supratentorial high-grade glioma (WHO III and IV Grade), (3) tumor invades ventricular wall and has both intra- and extraventricular component, (4) image-guided tumor resection, and (5) clinical follow-up and neuroimaging (pre-, intra- and postoperative) data availability. Exclusion criteria were as follows: (1) history of any other malignant tumor and (2) incomplete clinical and neuroimaging datasets.

The functional status of patients was evaluated using the Karnofsky Performance Status Scale (KPS) by a board-certified neurosurgeon or physiotherapist according to clinical observation in the preoperative and postoperative period. All patients received standardized perioperative care.

#### Imaging studies

MRI studies were carried out on 1.5 T Philips Intera (Philips, Netherlands) scanner according to the radiological study protocol for the cranial program of navigation station. The scanning protocol included at least 3D T1-weighted with Gd-enhancement, T2weighted, T2-FLAIR, and DWI sequences.

Postoperative computed tomography was performed on Somatom AR STAR PLUS (Siemens, Germany) or Aquilion ONE (Toshiba, Japan) within 24 hours of surgery for early identification of complication signs. Additionally, MRI with Gd-enhancement performed within 14 days after surgery for radiosurgery planning was helpful to distinguish residual tumor at the period of decreasing edema.

The residual tumor volume was calculated matching the preoperative MRI data with intraoperative data from neuronavigation system and postoperative CT and MRI.

According to previous studies on high-grade glioma patients survival, the residual tumor volume of 5 cm<sup>3</sup> was established as benefit factor for the survival [17].

This residual tumor volume was selected in our study as a threshold between partial and subtotal resection. The cases with radiologically gross total resection (no tumor remains on CT/MRI) were included to subtotal resection group considering wide infiltration pattern inherent to PVG.

## Surgical planning

The surgical planning was performed with a spatial 3D-modeling technique using navigation station software for segmentation and reconstruction of the preoperative MRI series. The spatial location of the tumor to neurovascular structures was defined on 3D models with a reconstruction of basal ganglia, subcortical tracts, deep vessels, and cerebral ventricles. Also, the contouring of tumor invasion areas and perifocal edema was performed. The optimal surgical approach boundaries and the total tumor volume available for the removal were determined preoperatively on the 3D models.

# Surgical procedure

All patients were operated using neuronavigation system StealthStation (Medtronic, USA). The rigid head fixation was mandatory. Preoperative preparations and craniotomy were performed in standard fashion. Image-guidance was utilized for craniotomy and tumor resection to control the EOR and brain-shift monitoring. The standard measures for brain-shift prevention were neutral head positioning, *en bloc* tumor resection, prevention of tissue compression and early opening of intracerebral cavities (cysts, hematomas, and ventricles).

#### Statistical analysis

The methods of descriptive statistics were used for continuous variables. The categorical variables were analyzed using the standard deviation and frequency of distribution. The variables with more than two possible values (age, EOR, tumor location, and size) were dichotomized. The McNemar's test was used to analyze the depending samples.

The multiple logistic regression model with backward stepwise was applied to determine which variables were independently associated with the EOR and postoperative KPS score. All variables were screened for entry into the logistic regression model by using the chi-square test.

A p value of <0.05 was considered significant.

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

#### Results

A total of 132 consecutive patients (50 females and 82 males) with mean age 45.9 years (range 21–69) were retrospectively included in the study.

The periventricular tumors with dominant extraventricular component were in 77 (58.3 %) patients; in other 55 (41.7 %) cases, the intraventricular part was greater or equal to extraventricular one. The tumor extended into the ventricular corpus and/or atrium was found in 36 (27.3 %) cases, the ventricular horns were affected in 96 (72.7 %) cases. The extending of the tumor to contralateral hemisphere was found in 63 (47.7 %) patients, the basal ganglia invading was in 93 (70.5 %) cases, and tumor contact with septum pellucidum was in 58 (43.9 %) cases. The larger diameter of the tumor was over 50 mm in 84 (63.6 %) patients. In 36 (27.3%) patients the tumor-associated cyst was found, and only in 14 (11.6%) cases, hydrocephalus was observed.

The tumors were clinically presented with intracranial hypertension, paresis, and seizures, that prevents the most part of patients to carry normal activity or active work. The average KPS score was 67.4 in the preoperative period, and the number of patients with KPS scores less than 70 was 114 (86.4 %). Demographic and clinical characteristics of patients are presented in **Table 1**.

Total/subtotal resection was carried out in 84 (63.6 %) cases; in other 48 (36.4 %) cases, the partial resection was performed. There were 52 (39.4 %) WHO grade III gliomas, and in 80 (60.6 %) of patients WHO grade IV gliomas were found.

**Table 1.** Demographic and clinical characteristics of patients

Variable	Value (%)	p value				
Patients, N	132 (100.0)					
Age at diagnosis (years)						
Mean	$45.9 \pm 12.8$					
Range	21-69					
< 45	55 (41.7)					
≥ 45	77 (58.3)	0.06				
Sex						
Male	82 (62.1)					
Female	50 (37.9)	< 0.01				
Preoperative KPS score	·					
Median	67.4					
< 70	114 (86.4)					
≥ 70	18 (13.6)	< 0.01				
Tumor extension						
Dominant extraventricular part	77 (58.3)					
Minor extraventricular part	55 (41.7)	0.05				
Ventricular involvement						
Horn	96 (72.7)					
Corpus/Antrum	36 (27.3)	< 0.01				
Septum dislocation						
< 10mm	112 (84.8)					
≥ 10mm	20 (15.2)	< 0.01				
Septum contact						
Present	58 (43.9)					
None	74 (56.1)	0.16				
Contralateral side extension	n					
Present	63 (47.7)					
None	69 (52.3)	0.60				
Basal ganglia invasion						
Present	93 (70.5)					
None	39 (29.5)	< 0.01				
Tumor-associated cyst						
Present	36 (27.3)					
None	96 (72.7)	< 0.01				
Hydrocephalus						
Present	14 (11.6)					
None	118 (88.4)	< 0.01				
Largest diameter of tumor (mm)						
≤ 50	48 (36.4)					
> 50	84 (63.6)	< 0.01				

There was not estimated the reliable relation of the functional status in the preoperative period with tumor size (p = 0.77) and WHO grade (p = 0.13), basal ganglia invasion (p = 0.14), contralateral hemisphere extension (p = 0.42), localization to ventricular wall (p = 0.44) or to ventricular compartments (p = 0.96), septum contact (p = 0.96) and dislocation (p = 0.84), presence of hydrocephalus (p = 0.45), tumorassociated cyst (p = 0.53), patients age (p = 0.19), and sex (p = 0.1).

Postoperative median KPS score significantly raised from 67.4 to 82.0, as well as a number of patients with the KPS score  $\geq$  70: from 18 (13.6 %) to 109 (82.6 %) with *p*<0.01. Twenty-two (17.7 %) patients saved initially low functional status (KPS<70), and one got worse. All surgical complications were hemorrhages in the site of operation — 4 (3.0 %) cases, one of them resulted in fatal outcome. The clinical and surgical outcomes are summarized in **Table 2**.

The multivariate regression analysis revealed the association of poor postoperative functional status with basal ganglia involvement (OR 2.75, 95% CI 0.93–8.09; p = 0.07), the higher EOR grade (OR 3.30, 95% CI 1.15–9.43; p = 0.03), and hydrocephalus (OR 5.08, 95% CI 1.49–17.35; p = 0.09) (**Table 3**).

Multivariate logistic regression analysis revealed that three factors decreased the likelihood of total/subtotal resection in PVG: basal ganglia invasion (OR 0.18, 95% CI 0.06–0.55; p<0.01), minor extraventricular part (OR 0.40, 95% CI 0.17–0.94; p = 0.04), and contralateral side extension (OR 0.38, 95% CI 0.16–0.92; p = 0.03). In contrast, the presence of tumor-associated cyst (OR 3,73, 95% CI 1.32–10.54; p = 0.01) increased odds of total/subtotal resection (**Table 4**).

The follow-up data were available for 103 (78.0 %). The survival analysis using Cox regression model (**Table 5**) revealed that age over 45 years (HR 1.77, 95% CI 1.06–2.99; p = 0.03) and higher tumor WHO grade (HR 2.24, 95% CI 1.27–3.95; p = 0.005) significantly decreased survival rates.

The Kaplan-Meier analysis showed that overall median survival was  $17.1 \pm 1.9$  months for patients with high grade PVG:  $13.4 \pm 0.7$  mos. for glioblastomas and  $44.0 \pm 11.0$  mos. for anaplastic glioma (**Table 6**). The EOR increasing didn't add any benefit to survival for each of WHO grade group (p = 0.71). There was a difference between groups of patients depending on age group and WHO grade (p<0.01). The **Figure 1** presents survival curves.

# Description of grading system

The grading scale evaluation was based on the revealing of statistically verified factors affecting the effectiveness of PVG resection.

Each of statistically verified preoperative neuroimaging sign was considered as a risk factor with the value of 1 score. The absence of risk factors or one of them (0–1 score) matched Grade I, and the cases with 4 risk factors (4 scores) were considered as Grade IV tumors that have lower chances for total/ subtotal resection and increased risk of postoperative neurological deterioration. The proposed grading system and its correlation to surgical outcomes are presented in **Table 7**.

http://theunj.org

Table 2. Clinical and surgical outcomes in study groups

Variable	Total	p value			
Extent of resection					
Total/subtotal resection (%)	84 (63.6)				
Partial resection (%)	48 (36.4)	0.02			
Postoperative KPS score					
Median	82.0				
< 70 (%)	23 (17.4)				
≥ 70 (%)	109 (82.6)	< 0.01			
WHO Grade					
III	52 (39.4)				
IV	80 (60.6)	0.02			

**Table 3.** Multivariate analysis of prognostic factors for postoperative functional status decrease

Variable	p value	OR	95% CI
Hydrocephalus	0.09	5.08	1.49–17.35
Basal ganglia invasion	0.07	2.75	0.93-8.09
Higher EOR grade	0.03	3.30	1.15-9.43

**Table 4.** Multivariate analysis of prognostic factors for total/subtotal resection

Variable	<i>p</i> value	OR	95% CI
Minor extraventricular part	0.04	0.40	0.17-0.94
Basal ganglia invasion	< 0.01	0.18	0.06-0.55
Contralateral side extension	0.03	0.38	0.16-0.92
Tumor-associated cyst	0.01	3,73	1.32-10.54

**Table 5.** Cox regression analysis of survival predicting factors

Variable	Wald	p value	HR	95.0% CI
Age group	6.201	0.03	1.77	1.06-2.99
WHO grade	5.584	0.005	2.24	1.27-3.95

Table 6.	Surv	ival ter	rms in	patier	nts w	ith PVG	
dependin	g on	tumor	WHO	grade	and	patients	age

Age Group	WHO grade	Survival (mos.)	Std. error	95% CI
	III	47.4	3.03	41.4-53.3
< 45	IV	16.2	2.36	11.5-20.8
	Total	44.0	16.54	11.5-76.4
	III	24.5	7.85	9.1-39.8
≥ 45	IV	12.7	1.05	10.6-14.7
	Total	13.4	0.80	11.8-14.9
Total		17.1	1.87	13.4-20.7



**Fig. 1.** Survival functions in patients with periventricular gliomas depending on WHO grade for age group < 45 years (A) and  $\geq$  45 (B)

Grade	Scores	Total/ subtotal resection (%), p<0.01	Postoperative KPS score <70 (%), p = 0.69	Number of cases
Ι	0-1	30 (100)	3 (10)	30
II	2	27 (62.8)	7 (16.3)	43
III	3	21 (55.3)	8 (21,1)	38
IV	4	6 (28.6)	5 (23.8)	21

**Table7.** Proposed grading system for surgical outcomes assessment on our series data

# Discussion

Nowadays approach in surgery for deep-seated brain gliomas reflexes the searching of optimal balance between the EOR maximizing and preserving of functional integrity of surrounding neurovascular structures. Prevention of postoperative neurological deterioration requires individualized surgical strategy considering the tumor location and involvement of eloquent brain structures, as well as the initial neurological deficits and concomitant pathology [3, 8, 12, 13].

Previous studies showed the uniqueness of PVG that could be explained by pathohistological features of subventricular zone as a source of multipotent stem cells. Early malignization and fast relapse are typical for PVG, which predominantly are glioblastomas [6, 21]. The vicinity of basal ganglia and circumventricular organs responsible for metabolic and endocrine function also limits the possibilities of radical resection with high risks of hemorrhage into residual tumor parts [22, 23].

Furthermore, surgical approach to PVG itself is complicated due to hidden subcortical localization of the tumor and high density of surrounding white matter tracts. This requires the mandatory use of image-guided resection techniques, at least multimodal neuronavigation. Also, the fluorescence guidance and intraoperative scanning (MRI and CT) showed their effectiveness and are preferable to routine practice [24–26].

The significant decrease of survival rates for PVG is associated with the incomplete resection, unstoppable tumor cell dissemination, and high levels of postoperative neurological disorders [4–6]. The residual tumor volume was estimated as a significant prognostic factor for survival in patients with high-grade gliomas [17–20].

The grading system for preoperative assessment of outcomes in glioma patients was evaluated together with the ongoing development of surgical techniques and collecting of statistical data in order to analyze their efficacy [27–32].

In our study, we aimed to find out the preoperative neuroimaging prognostic signs for surgical outcomes in patients with PVG. The statistical analysis revealed four factors responsible for maximizing resection and affecting postoperative functional status. The favorable factors were organized in grading system.

In 1998, Vorster et al. published the results of surgery for primary and secondary brain tumors in 204 patients, and proposed a five-tier grading system to assess complication risks and length of hospital stay. Using multivariate regression analysis, the authors defined the following risk factors: patient age over 60 years, preoperative KPS scores of 50 or less, previous radiotherapy, tumor eloquent location, and deep brain structures (ventricles or basal ganglia) invasion. In contrast to our study, it included heterogeneous histological groups and the influence of tumor type was not tested, as well as categories of tumor location (eloquent and deep) were not clearly dissolved [27].

Litofsky et al. (2006). identified patients age and using of image-guided resection as additional factors promoting save resection and decreasing levels of neurological deficits. However, the factor predicting the greater EOR and its association with outcomes was not evaluated by the authors [28].

Our data confirms the value of multimodal surgical planning and image-guided resection that ensure better neurological outcomes in patients with PVG. Preoperative virtual simulation of intervention could help to work out the optimal transcortical approach passing beyond the eloquent structures and to delineate the tumor volume suitable for safe resection. Neuronavigation usage for the entire process of tumor resection helps to control distances to surrounding neurovascular structure and to evaluate achieved EOR when the brain-shift was compensated.

Chaichana et al. in 2010 revealed the relation of preoperative clinical and neuroimaging signs with survival rates in glioblastoma patients. The age, preoperative KPS score, motor and speech deficits, and periventricular location (ventricular wall involvement) were tested with regression analysis and validated in the multicenter study in 2013. The EOR was not included into the grading system, as a factor that could not be revealed preoperatively [29–31].

Statistical analysis of PVG treatment in our series results showed that patents age and tumor WHO Grade influenced postoperative survival rates. At the same time, various neuroimaging signs were statistically tested and used to predict early surgical results (EOR and functional status) in patients with high-grade PVG.

Marcus et al. developed a grading system for preoperative predicting surgical outcomes in glioblastoma surgery. The grading system included the most frequent neuroimaging features that were described in the literature as factors affecting the EOR and/or survival. In this study, each of selected features (1) periventricular or deep location, (2) corpus callosum or bilateral location, (3) eloquent location, (4) tumor size and (5) associated edema had the equal weight of one point in the grading system. The sum of points defined one of three possible grades of complexity. For patient groups with the same grade of complexity, the EOR and postoperative complications rate were calculated. The chi-square test confirmed a correlation of grade score with EOR [32].

In contrast to our study, the criteria for periventricular tumors were wider that lead to the inclusion of tumors without ventricular wall attachment. Also, the prominent limitation in this work was the absence of statistical testing of initially selected preoperative neuroimaging features.

We proposed the grading system with statistically verified neuroimaging features of PVG with influence on surgical outcome: tumor with minor extraventricular part, the tumor-associated cyst, tumor basal ganglia invasion, and contralateral side extension. The small number of included preoperative features makes the grading system more useful for clinical practice. The application of the grading system developed could help to choose surgical tactics of limited resection for complex high-score PVG. Also, we should conclude the absence of statistically significant effect of EOR on survival in our series of high-grade PVG. This fact together with the negative influence of the EOR increasing on postoperative functional status in patients advocates safe resection aimed at the intracranial optimal decompression and achievement of tumor tissue specimens.

The prominent limitation of the study was in its retrospective nature preventing the proper collecting of clinical data and the functional outcome evaluation. This study also did not analyze the influence of prognostic implication of molecular markers and different adjuvant therapy protocols on survival. We suggest that prospective multicenter study is required for further validation of developed grading system to disclose the factors depending on applied surgical techniques and validation of the quality of life and survival data in patients after surgery for PVG.

#### Conclusions

Proposed grading scale provides the possibility of a preoperative evaluation of PVG resectability that in combination with 3D surgical planning and image-guided resection allows performing maximal safe resections and preventing postoperative neurological deficits.

## Disclosure

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

The study was approved and conducted within the guidelines of the Romodanov Neurosurgery Institute review board.

Informed consent

The written informed consent was obtained from each patient or appropriate family member before the surgery.

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