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DETERMINING REHABILITATION PROGNOSIS AND POTENTIAL AFTER REMOVAL OF INTRACRANIAL MENINGIOMAS

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ABSTRACT
The aim of the study is to evaluate the dependence of RP on Ki-67, CD34, Simpson grade, and invasion. Materials and methods. The study included 124 patients who underwent surgery for intracranial meningiomas in the period 2019-2024. The results of the study showed that Low values of Ki-67 and CD34, radical resection and absence of deep invasion serve as reliable markers of high rehabilitation potential. Conclusions. Taking into account the markers we studied will allow us to personalize the postoperative rehabilitation plan and improve recovery rates in patients with intracranial meningiomas.
KEYWORDS: *Meningioma; Ki-67; CD34; Brain Invasion; Simpson Resection; Karnofsky Performance Status; Functional Independence Measure; Rehabilitation Potential.*

INTRODUCTION

Meningiomas account for approximately 30-35% of all primary intracranial tumors in adults, occupying a leading position among benign neoplasms of the brain [5,13]. Women develop meningiomas 1.8-2 times more often than men, which is associated with hormonal influence and expression of estrogen and progesterone receptors in tumor tissues [14]. Although most meningiomas (Grade I) are characterized by slow growth and a favorable prognosis, up to 25% have atypical or anaplastic features (Grade II-III) with an increased risk of recurrence, invasion into brain tissue and worse clinical outcomes [3,4].

Histopathological markers of proliferation (Ki-67) and angiogenesis (CD34) are reliable indicators of meningiomas' aggressiveness and their tendency to recurrence. The Ki-67 index correlates with tumor mitotic activity and prognosis of survival after resection [1,6], and the density of microvessels by CD34 reflects the degree of vascularization and affects the effectiveness of surgical resection and the risk of growth of residual foci [2,15]. The depth of microscopic invasion into the brain is ≥ 3 mm according to Behling et al. (2021) is associated with a three-fold increase in the risk of early recurrence [2], and the degree of radicality of resection according to the Simpson scale remains one of the main controllable prognostic factors [12].

However, data on the impact of these morphological characteristics on the functional recovery of patients after meningioma removal are limited. To date, no unified model has been developed that combines histopathological markers and ΔKPS/ΔFIM indices to predict rehabilitation potential.

THE AIM OF THE RESEARCH

The aim of the research is to evaluate the rehabilitation prognosis and potential depending on Ki-67, CD34, Simpson grade and invasion.

MATERIALS AND METHODS

The study included 124 patients, of which 61% (n=76) were women and 48% (n=39) were men, operated on for intracranial meningiomas, with Grade I patients included in the study amounting to 66.1% (n=82), Grade II - 25.8% (n=32) and Grade III - 8.1% (n=10). According to the results of MRI examination of the tumor localization, the following were detected: convex - 41%, parasagittal - 26%, skull base - 22%, posterior cranial fossa - 11% (Fig. 1).

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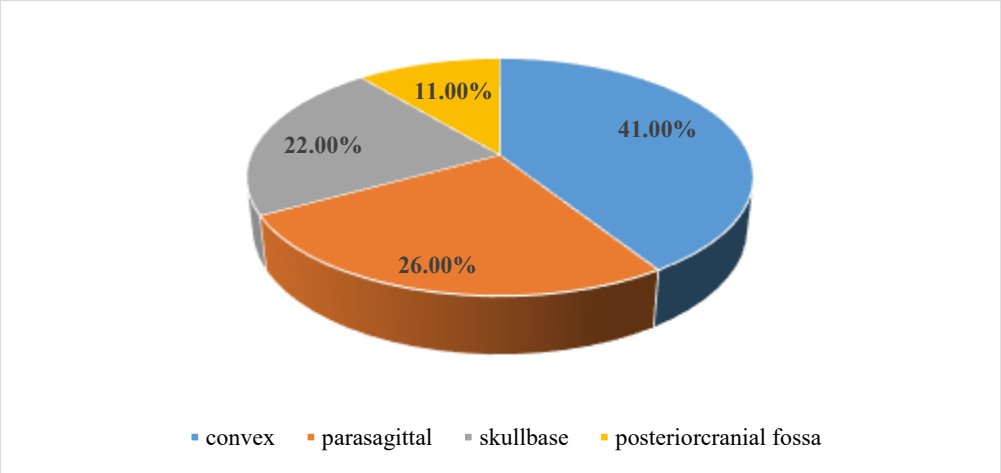


Fig. 1. Localization of Tumors

The assessment of the functional status **(**general ability for self-care and activity) was carried out according to 100 point system Karnofsky Performance Status (KPS) [Mor et al., 1984].

Motor and cognitive functions were assessed using the Functional Independence Measure (FIM) [Keith et al., 1987] on 18 points (18-126 points). The assessment was carried out 3-5 days before the operation and again - 3 months after discharge. The difference ΔKPS and ΔFIM was calculated as "postoperative assessment - preoperative assessment".

Ki-67 was determined using the monoclonal antibody MIB-1. The % of nucleoli of stained cells in five "hot spots" (×400) were counted, the average value. CD34 **is** a marker of vascular endothelium, the antibody QBEnd /10. The average number of vessels per high-power field (HPF, ×400) in five fields was estimated. To assess brain invasion and the radicality of resection, the depth of invasion was studied **:** it was measured microscopically by the greatest penetration of tumor cells into the brain tissue, ≥ 3 mm was considered significant. The degree of resection was classified according to the Simpson IV scale.

Data entry and analysis were performed in SPSS 13.0 (IBM). Quantitative data were tested for normal distribution (Shapiro- Wilk test). Descriptive indicators are presented as mean ± standard error (SE) and range. Comparison of mean values between groups was performed by one-way ANOVA followed by Tukey's test . For qualitative data, χ^2-test or Fisher's exact test were used. Multivariate logistic regression analysis was used to identify independent predictors of high rehabilitation potential (ΔKPS ≥ 15 and ΔFIM ≥ 20), the results are presented as odds ratio (OR) and 95% confidence interval. Cox proportional hazards model was used to assess early relapse (DFS) factors, findings are presented as hazard ratio (HR) and 95% CI. Relapse-free survival was analyzed by Kaplan-Meier method, differences are assessed by log-rank test. Statistical significance was accepted at $p < 0.05$.

THE RESULTS OF THE RESEARCH

The results of the research showed that the postoperative improvement in the KPS scale averaged +11.1 points (from 68.4±1.5 to 79.5±1.4; p <0.001), indicating a clinically significant transition of patients from the “limited independence” category (KPS 60-75) to the “self-care ability with moderate limitations” range (KPS 75-90). The interquartile range before surgery [65; 70] shifted after the intervention to [75; 85], and the range increased from [60; 75] to [65; 90], reflecting both the consistently pronounced progress of the majority of patients and the preservation of variability in individual outcomes (Table 1).

Table 1

Dynamics of the functional status of patients before surgery and after 3 months

Indicator	M ± m	IQR [25%; 75%]	Range [Min ; Max]	p
KPS before surgery	68.4 ± 1.5	[65; 70]	[60; 75]	-
KPS in 3 months	79.5 ± 1.4	[75; 85]	[65; 90]	< 0.001
FIM before surgery	82.0 ± 2.0	[78; 86]	[50; 120]	-
FIM in 3 months	103.0 ± 2.1	[98; 110]	[70; 126]	< 0.001

Similarly, functional independence according to the FIM scale improved by an average of +21 points (from 82.0 ± 2.0 to 103.0 ± 2.1; p < 0.001). Before surgery, the median FIM was in the range of [78; 86], and after 3 months - [98; 110], while the minimum and maximum values shifted from [50; 120] to [70; 126]. Such a significant increase allows us to speak about a significantly higher level of self-care, mobility and social activity of patients after resection. High statistical significance (p < 0.001 for both scales) confirms the reliability of the observed effect and excludes the randomness of the obtained changes.

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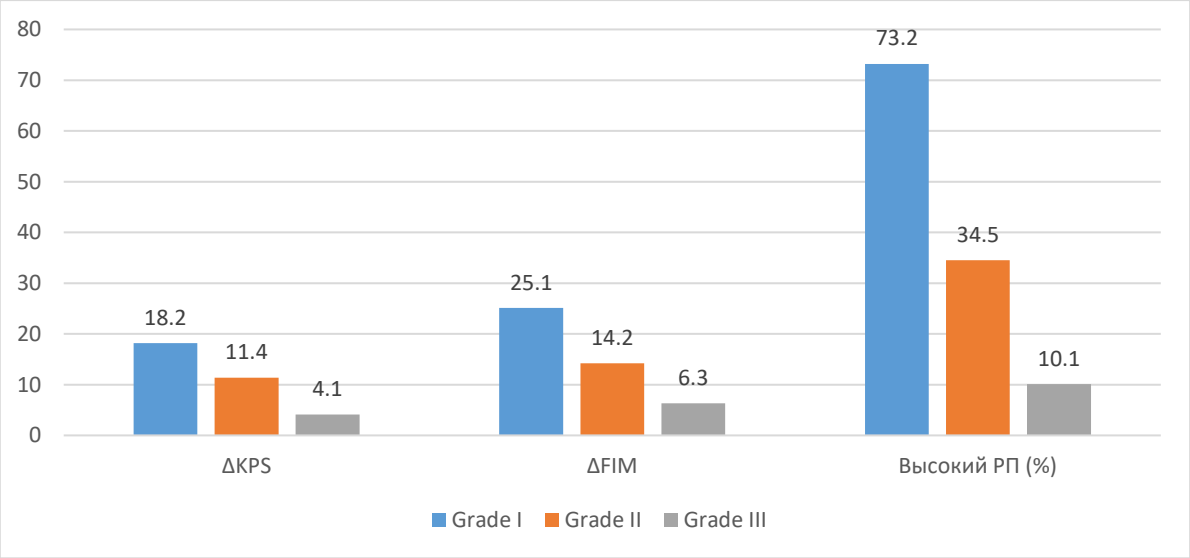


Fig. 2. ΔKPS, ΔFIM and the proportion of patients with high rehabilitation potential by grades

At the further stage of our study, patients after meningioma resection showed a noticeable but variable increase in functional status. The average increase in KPS was 11.1 ± 2.1 points, but the interquartile range [5; 20] indicates that only the upper half of the cohort achieved an improvement of more than 11 points, and 25% of patients improved by less than 5 points. In the range [-10; 30], there were both deteriorations (up to -10) and significant increases (up to +30), which emphasizes the heterogeneity of the recovery process. The threshold ΔKPS ≥ 15 was chosen as a clinically significant criterion of "high RP", since it lies above the median and approximately corresponds to the upper quartile of increases.

On the FIM scale, the average change was 21.0 ± 2.9 points with an IQR of [12; 32], meaning that half of the patients improved within the range of 12–32 points. The range of [-50; 76] reflects that some patients experienced a decrease in functional independence, while the best patients showed an increase of over 70 points. The ΔFIM level ≥ 20 points also proved to be a clinically justified threshold for identifying those who achieved significant recovery of daily skills.

Thus, despite statistically significant average improvement on both scales, only a subset of patients (upper quartile values) have ΔKPS and ΔFIM that cross the established thresholds of high rehabilitation potential. This emphasizes the importance of finding predictors that allow us to predict who exactly will be able to achieve a "high" level of recovery, and who will require more intensive or prolonged rehabilitation measures.

In order to study logistic regression for independent predictors of high rehabilitation potential, the binary indicator "high RP" (ΔKPS ≥ 15 and ΔFIM ≥ 20) was used as a dependent variable in the model.

Table 2
OR of independent prognostic factors of high rehabilitation potential

Predictor	OR	95% CI	p -value
Ki-67 < 4%	4.6	2.0–10.5	0,001
CD34 < 12 vessels/HPF	2.9	1.3–6.4	0,008
Simpson I–II resection	2.5	1.1–5.6	0.027
Absence of diffuse invasion	3.2	1.4–7.2	0,005

As shown in Table 2**,** Ki-67 <4%: patients with low proliferation index have 4.6-fold higher odds of significant functional progress (p = 0.001). CD34 <12 vessels/HPF: moderate angiogenicity increases the odds of high RP by 2.9-fold (p = 0.008). Simpson I-II resection: radical removal increases the odds of recovery by 2.5 times (p = 0.027). No diffuse invasion: no deep brain infiltration is associated with 3.2-fold increased odds of high RP (p = 0.005). All included factors turned out to be statistically significant independent predictors, which emphasizes their prognostic value in planning postoperative management and rehabilitation of patients with meningiomas.

Thus, the integration of morphological markers and functional scales allows not only to predict the outcome, but also to optimize individual rehabilitation protocols, which corresponds to global trends in personalized neurorehabilitation after removal of meningiomas.

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CONCLUSION

Low proliferative index Ki-67 (<4%) and moderate microvascular density CD34 (<12 vessels/HPF) are significantly associated with more pronounced functional recovery (ΔKPS ≥ 15, ΔFIM ≥ 20) and low risk of recurrence after resection of intracranial meningiomas. Depth of brain invasion <3 mm and radical resection according to the Simpson scale I-II are independent predictors of high rehabilitation potential, which emphasizes the importance of the most complete tumor removal with an acceptable neurological risk. Stratification of patients by these morphological markers allows predicting not only survival and the likelihood of relapse, but also the rate and quality of recovery, which is important for planning individual rehabilitation programs. Integration of Ki-67, CD34, invasion and resection extent data into clinical algorithms facilitates optimal resource allocation and more accurate prognosis information for patients.

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