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PERSONALIZED SURGERY IN CHILDREN WITH TEMPORAL LOBE EPILEPSY

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ПЕРСОНАЛИЗИРОВАННАЯ ХИРУРГИЯ ВИСОЧНОЙ ЭПИЛЕПСИИ У ДЕТЕЙ

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Eighty patients with symptomatic drug-resistant temporal epilepsy aged 2–17 years were operated on from 2011 to 2016, the factors that influenced the outcome of surgical treatment were studied. Favorable prognostic factors for the effectiveness of surgical treatment in the long-term period were: male sex ($p<0.01$), children older than seven years ($p<0.01$), disease duration less than three years ($p<0.05$), intake of fewer than three anticonvulsants drugs ($p<0.01$), no history of febrile seizures and epileptic reactions ($p<0.05$), no comorbid conditions ($p<0.05$), serial seizures and statuses ($p<0.01$), no early postoperative seizures ($p<0.01$). The most effective were left-sided resections ($p<0.05$), lesionectomy ($p<0.05$) with removal of epileptogenic foci ($p<0.01$). Thus, rational tactics for surgical treatment of drug-resistant temporal epilepsy in children should be carried out by taking into account the age-related characteristics of the child's development, the nature of the intercurrent pathology, as well as the alleged etiological factor, taking into account the peculiarity of the course of the pathological process.

Keywords: epilepsy, surgery, personalized medicine, children, temporal epilepsy, pediatric neurosurgery

У 80 больных в возрасте 2–17 лет с симптоматической височной медикаментозно-резистентной эпилепсией, оперированных с 2011 по 2016 г., изучены факторы, которые влияли на исход хирургического лечения. Благоприятными прогностическими факторами эффективности хирургического лечения в отдаленном периоде оказались: мужской пол ($p<0,01$), дети старше 7 лет ($p<0,01$), длительность заболевания менее 3 лет ($p<0,05$), прием менее 3 противосудорожных препаратов ($p<0,01$), отсутствие в анамнезе фебрильных припадков и эпилептических реакций ($p<0,05$), отсутствие коморбидных состояний ($p<0,05$), серийных припадков и статусов ($p<0,01$), отсутствие ранних послеоперационных приступов ($p<0,01$). Наиболее эффективными являлись левосторонние резекции ($p<0,05$), проведение лезионэктомии ($p<0,05$) с удалением эпилептогенных очагов ($p<0,01$). Таким образом, рациональная тактика хирургического лечения фармакорезистентной височной эпилепсии у детей должна проводиться с учетом возрастных особенностей развития ребенка, характера интеркуррентной патологии, а также предполагаемого этиологического фактора с учетом своеобразия течения патологического процесса.

Ключевые слова: эпилепсия, хирургия, персонализированная медицина, дети, височная эпилепсия, нейрохирургия детского возраста

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EEG – electroencephalography
MRI – magnetic resonance imaging
PET – positron emission tomography
QOL – quality of life
QOLCE – quality of life in children with epilepsy

Personalized medicine is a rapidly developing field of healthcare based on an individualized way of analyzing the occurrence and course of a disease, as well as the dynamics of the pathological process. This approach to treating drug-resistant temporal lobe epilepsy in children is especially relevant due to the anatomical and functional characteristics of the child population [1].

Given the high prevalence of epilepsy in children (from 0.5 to 0.7 per 1000 persons per year), diagnosis and selection of optimal treatment for epilepsy remain a significant medical and social problem [2]. The temporary form constitutes 25–30 % of all cases of epilepsy and up to 60 % of all cases of its symptomatic focal forms, being the least susceptible medicinal form of the disease [3, 4]. Pharmacoresistant epilepsy is characterized by a progressive course, which has a particularly detrimental effect on the quality of life (QOL) of patients [2, 4]. There is no doubt that surgery is necessary for drug-resistant temporal epilepsy in children [5].

Innovative trends in developing approaches to the surgical treatment of epilepsy consist in eliminating the harmful effects of both the disease and antiepileptic polytherapy. At the same time, the results of surgical therapy remain unsatisfactory in almost half of the cases [5, 6]. On this basis, the feasibility of the study aimed at identifying prognostic factors that influence the results of surgical treatment of temporal epilepsy in children is indisputable.

The importance of predictive factors in the surgical treatment of temporal epilepsy in children remains poorly understood and is often underestimated when planning surgery [7]. Relationship between resection side and temporal epilepsy results, hippocampal sclerosis value, age and duration of disease, the incidence of paroxysms, presence of mental disorders, hereditary load, and perinatal pathology. The effect of pockets of chronic infection and the type of surgical intervention is shown [8–10].

The aim of the study was to evaluate the influence of individual patient factors and surgical methods of treating epilepsy on its outcome in immediate and long periods.

Material and Methods. Retrospective and prospective analysis of the results of surgical treatment of 80 children with resistant temporal epilepsy in the temporal lobe who were treated by prof. A. L. Polenova from 2011 to 2016. Complex clinical and neurological, neuropsychological, electrophysiological (EEG, video-EEG and invasive monitoring, electro-cortico- and subcorticography), neuroimaging (MSCT, MRI, functional MRI, positron emission, and single-photon emission computed tomography) examination. We compared the indicators of preoperative and post-operative studies, as well as data of intraoperative diagnostics with dynamics of clinical manifestations after surgery. When statistically significant dependency was discovered, it was suggested that predictive factors for surgical treatment of temporal epilepsy in the immediate and long term would be reliable.

In this group, boys predominate (51.25 %). In most cases (51.25 percent), the age at the time of the operation was 8–13 years (M (average)=10.5±0.45 years).

All patients in the pre-operative period underwent a comprehensive QOL assessment using a special questionnaire for parents of children aged 4 to 17 years «QOL in children with epilepsy» (QOLCE), in the language and cultural adaptation. A questionnaire on language learning and cultural adaptation was used to assess the anxiety of parents of children with epilepsy.

All patients in the pre-operative period underwent an MRI of the brain (1.5 T and/or 3 T), which revealed structural changes in 75 (93.75 %) children. For the convenience of choosing the optimal tactics of surgical treatment and assessing the results of treatment, MRI data (Fig. 1) were grouped into: local (A) – within one temporal lobe (60 %); widespread (B) – going beyond its limits (34 %); MRI-negative B) – (6 %).

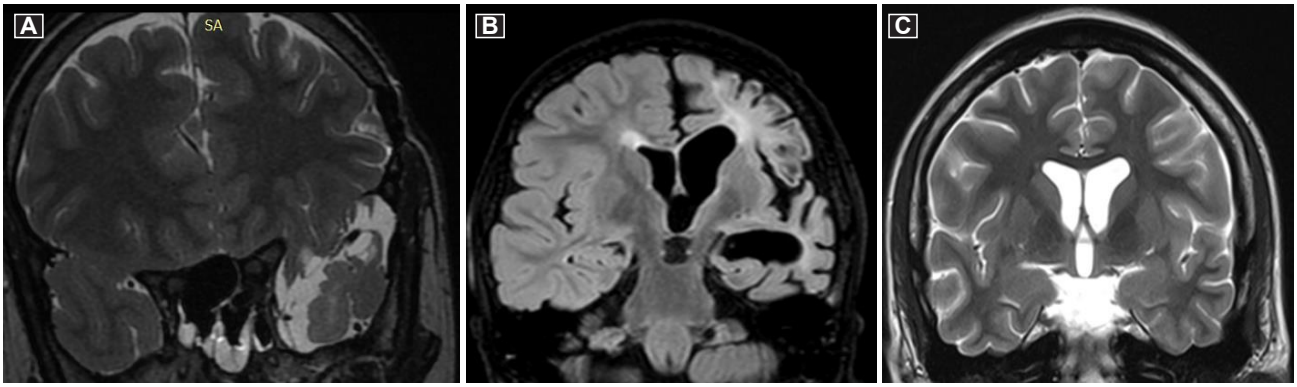

Fig. 1. MP-changes on MRI: A – localized changes in the left temporal lobe; B – diffuse changes in the left hemisphere; C – MR-negative

EEG and video-EEG monitoring in the preoperative and postoperative periods in dynamics was performed in all patients. Electrophysiological examination data, taking into account the degree of involvement of brain structures in the epileptic process, are grouped into four types of EEG variants of temporal lobe epilepsy: 1) single-focal temporal epilepsy – 63 %; 2) bitemporal – 11 %; 3) unilateral temporo-extratemporal (with the formation of 2 foci in one hemisphere) – 10 %; 4) temporo-extratemporal with the formation of more than two foci in both hemispheres – 16 % [11] (Fig. 2).

The surgical treatment of temporal epilepsy was to remove epileptic and/or epileptic lesions. Block resection of the neocortical and/or paleocortical parts of the temporal lobe is performed in 51.25 % of cases, and removal of the zone of structural changes (lesions) – in 32.5 %. Less frequently, 6.25 % of cases were performed by MPC subunits – in 6.25 % of patients and other surgery methods (endoscopic excision of the cyst walls, embolization of arteriovenous malformations, temporotomy) – in 10 %.

Subsequent information refers to periods ranging from 12 months to 5.2 years (average 2.26±0.18 years). Surgical results were evaluated on the Engel scale [12]. In 44 (55 %) of the cases, long-term results, including QOL, were examined using the QOLCE questionnaire, comparing the results in the group of patients with complete cessation of seizures (Engel I) and with stable seizures after surgery (Engel II–IV).

Statistical data. A descriptive analysis was made: absolute and relative frequencies for categorical variables

(n, %) and central inclination parameters (M, Me, Mo) and variance (minimum and maximum values, standard deviation – SD) for continuous variables. The Pearson test χ^2 was used to compare the proportions of the categorical variables, and Bonferroni's correction was used in several comparisons. To compare the results in the short and long term, according to Engel, and to compare the effects of treatment of patients before and after on the QOLCE scale, a non-parametric test was performed with Wilcoxon's signature. A non-parametric analysis of Manna – Whitney was performed to compare the results of the QOLCE treatment with Engel I and Engel II–IV. In addition, a Manna-Whitney test was performed to determine the dependency of the results of surgical interventions during the immediate and long periods of the patient's age, age at manifestation and duration of the disease.

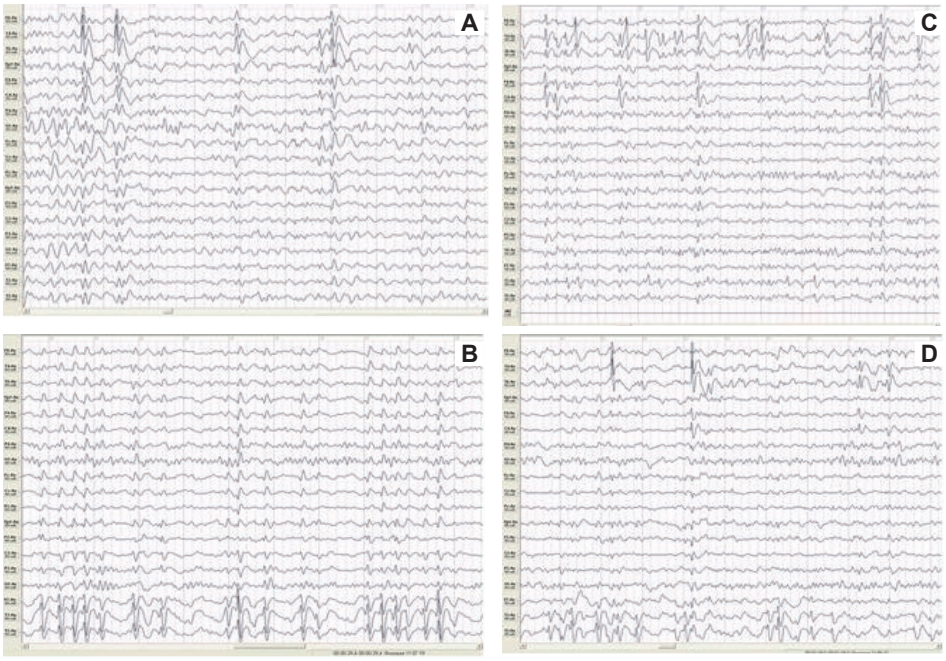

Fig. 2. Patterns of EEG activity: focal changes of paroxysmal character are registered in the temporal part of the right hemisphere (A); paroxysmal activity in the fronto-temporal part of the right hemisphere (B); epileptic activity over the left temporal lobe (C); epileptic activity in the temporal part of both hemispheres (D)

Results and Discussion. In the study group, predisposing etiological factors were aggravated by obstetric and gynecological history in 36 (45 %) cases and premature births in 7 (8.75 %). Comorbid conditions were found in 18 (22.5 %) patients. Hereditary load on epilepsy was found in 5 (6.25 %) children. Epileptic reactions and/or fever convulsions were found in 15 (18.75 %) cases.

The average age was 4.5 years, while in 55 percent of cases, epilepsy was detected before the age of 1. The average duration of the illness was six years. In 2/3 of the period of pathology exceeded three years, and in 32.5 percent of cases, children had epilepsy for seven years or more. Complex partial seizures represented the structure of paroxysms in 1/5 of observations, simple partial seizures – in 5 (6.25 %). Typical temporal epilepsy was complex partial seizures with secondary generalization found in most cases (62.5 %). Seizurepolymorphism was found in 46.25 percent of the cases, and a combination of three or more seizure types was found in 12.5 percent. During hospitalization, seizures were considered temporary in 30 % of cases, temporary in 60 % of cases, and generalized in 10 % of cases. The incidence of paroxysms was very high: 15 percent per week, 2 to 6 per week, 25 percent, 43.75 per day. Epileptic conditions were reported in 20 (25 %) patients.

Neuropsychological testing revealed the presence of psychopathological symptoms in the vast majority (91.25 %) of children, which significantly complicated the course of the pathological process. At the same time, pronounced psychopathological symptoms were detected in 41 cases (51.25 %) with late-onset disease. The average anxiety score for the tested epilepsy-resistant children was 34.76.

The most significant indicators of preoperative QOL were «physical limitations» due to the presence of seizures (20.74±5.53 points), «speech disorders» (31.4±8.9 points), as well as «decreased attention» (31.11±7.85 points). The «final indicator of QOL» in the preoperative period was at the level of 41.71±3.02 points.

Drug resistance in all cases has been established in more than two specialized medical facilities. In most cases, polytherapy using two or three drugs was used in the pre-operative period. At the same time, in 14 patients (17.5 %), the dosage of antiepileptic drugs exceeded the maximum allowed therapeutic dose.

Surgical treatment of temporal epilepsy was unsuccessful or ineffective in 5 cases (6.25 %). In 72.5 % of observations in the nearest period up to 1 year, complete cessation of seizures was achieved (Engel I – result). The remaining 21.25 percent showed a significant decrease in the frequency of attacks.

Long-term surgical treatment of temporal epilepsy showed results for Engel I at only 54.54 %, Engel II at 29.54 %, Engel III at 11.36 %, and Engel IV at 4.54 %. Surgical outcomes were better after lesion and resection of the neocortical and paleocortical parts of the temporal lobe.

The Engel average in the short and long term was 1.34 0.68 and 1.66 0.861, respectively, and the average deterioration was observed over 26.21 15.28 months.

Analysis of QOL performance based on surgical treatment results shows significantly better QOL values («speech impairment», «physical impairment», «energy/weakness», «overall QOL» and «total» (the end point of all subsectors)) in the group of patients with complete cessation of seizures ($p<0.05$).

The study of the most significant prognostic factors influencing the results of surgical treatment of children with symptomatic temporal epilepsy in the near and long term has allowed distinguishing favorable and unfavorable predictors of surgical outcomes.

Good results of surgical treatment were associated with favorable prognostic factors, such as older age (more than seven years) of disease manifestation ($p<0.01$), shorter duration (less than three years) of epilepsy ($p<0.05$), age of the child at the time of surgery more than four years ($p<0.00$), male sex of the child ($p<0.01$), history of taking less than three antie-

pileptic drugs ($p<0.01$), absence of status epilepticus ($p<0.01$), febrile seizures and epileptic reactions in history ($p<0.05$), no comorbid conditions ($p<0.05$), no early postoperative seizures ($p<0.01$), interventions on the left temporal lobe ($p<0.05$), lesionectomy ($p<0.05$).

Adverse prognostic factors were: effects of neuroinfections, scar gliosis and atrophic changes in the brain, arachnoid cysts according to the MRI ($p<0.01$), epileptic leukoencephalopathy manifestation in removed tissue samples ($p<0.05$), multi-focal subunits ($p <0.05$).

The results of surgical treatment of temporal epilepsy, neither in the immediate nor in the long term, were affected: hereditary burden, type of convulsion, polymorphism of seizure, the severity of lateralization following the semiology of seizures, the severity of psychopathological symptoms, Prevalence of changes in the MRI, matching of MRI and EEG data.

Functional magnetic resonance imaging in 9 out of 10 cases has increased hemispheric dominance. PET of the brain with 18F-fluoroxyglucose and methionine in the interictal period helped in the lateralization of the focus of epileptic activity and detection of brain tumors in 67.4 % of cases [13]. Single-photon emission computed tomography was less informative since, in all cases, it was performed during the inter-submarine period and identified areas of reduced perfusion that corresponded to the zone of structural changes on the MRI in 42.7 % of cases.

As our research shows, indicators reflect the age and constitutional differences of the patient, the development of the child, the evolution of the disease, and its dynamics during therapy. The expected results of applying different surgical treatments are predictions of the effectiveness or ineffectiveness of the used treatment tactics, which makes this approach personalized. In our view, the inclusion of established negative and positive prognostic factors of surgical treatment of temporal epilepsy in the algorithm of choosing rational tactics for treatment of drug-resistant forms of the disease in pediatricians will improve the treatment results.

Conclusions. Drug-resistant temporal lobe epilepsy in children is characterized by an early onset of the disease, frequent, polymorphic paroxysms, severe psychopathological symptoms, a progressive course of the disease, a predominantly single-focal temporal type of EEG changes (62.5 %), structural lesions of the brain (93.75 %), predominantly cystic atrophic nature (26.25 %), glioneural tumors (22.5 %) and hippocampal sclerosis (15 %).

The use of a personalized approach to the treatment of drug-resistant temporal lobe epilepsy in children, taking into account the age of the child, the characteristics of its development, the presence and nature of intercurrent pathology, the peculiarity of the course of the disease, the data of introscopy, as well as prognostic factors, made it possible to achieve a complete cessation of seizures in the immediate postoperative period (up to 12 months) in 72.5 % of cases, in the long-term (from 1 to 5 years) in 54.6 % of cases. At the same time, the cessation of seizures was significantly more often associated with an improvement in the QOL of children ($p<0.05$).

Informed consent. The study was conducted in accordance with the requirements set forth in the Federal Law of the Russian Federation of November 21, 2011 No. 323-FZ «On the Fundamentals of Protecting the Health of Citizens in the Russian Federation» and the Helsinki Declaration of the World Medical Association (as amended in 2013, Fortaleza).

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References

1. Wium-Andersen I. K., Vinberg M., Kessing L. V., McIntyre R. S. Personalized medicine in psychiatry. *Nord J. Psychiatry*. 2017;71(1):12-19. https://doi.org/10.1080/08039488.2016.1216163
2. Fine A., Wirrell E. C. Seizures in Children. *Pediatr. Rev*. 2020;41(7):321-347. https://doi.org/10.1542/pir.2019-0134
3. Gataullina S., Dulac O., Bulteau C. Temporal lobe epilepsy in infants and children. *Rev. Neurol*. 2015;171(3):252-8. https://doi.org/10.1016/j.neurol.2015.01.559
4. Kumar G. Evaluation and management of drug resistant epilepsy in children. *Curr. Probl. Pediatr. Adolesc. Health Care*. 2021;51(7):101035. https://doi.org/10.1016/j.cppeds.2021
5. Herta J., Dorfer C. Surgical treatment for refractory epilepsy. *J. Neurosurg. Sci.* 2019;63(1):50-60. https://doi.org/10.23736/S0390-5616.18.04448-X
6. Consales A., Casciato S., Asioli S., Barba C., Caulo M. [et al.]. The surgical treatment of epilepsy. *Neurol. Sci.* 2021;42(6):2249-2260. https://doi.org/10.1007/s10072-021-05198-y
7. Gonzalez L. M., Wrennall J. A. A neuropsychological model for the pre-surgical evaluation of children with focal-onset epilepsy: An integrated approach. *Seizure*. 2020;77:29-39. https://doi.org/10.1016/j.seizure.2018.12.013
8. Jetté N., Sander J. W., Keezer M. R. Surgical treatment for epilepsy: the potential gap between evidence and practice. *Lancet Neurol*. 2016;15(9):982-994. https://doi.org/0.1016/S1474-4422(16)30127-2
9. Mathon B., Bédos Ulvin L., Adam C., Baulac M., Dupont S. [et al.] Surgical treatment for mesial temporal lobe epilepsy associated with hippocampal sclerosis. *Rev. Neurol*. 2015;171(3):315-25. https://doi.org/10.1016/j.neurol.2015.01.561
10. Delev D., Oehl B., Steinhoff B. J., Nakagawa J., Scheiwe C. [et al.] Surgical Treatment of Extratemporal Epilepsy: Results and Prognostic Factors. *Neurosurgery*. 2019;84(1):242-252. https://doi.org/10.1093/neuros/nyy099
11. Jasper H. H. Charting the Sea of Brain Waves. *Science*. 1948;108(2805):343-347. https://doi.org/10.1126/science.108.2805.343
12. Engel J. Jr. Update on surgical treatment of the epilepsies. Summary of the Second International Palm Desert Conference on the Surgical Treatment of the Epilepsie. *Neurology*. 1993;43(8):1612-7. https://doi.org/10.1212/wnl.43.8.1612
13. Sidhu M. K., Duncan J. S., Sander J. W. Neuroimaging in epilepsy. *Curr. Opin. Neurol.* 2018;31(4):371-378. https://doi.org/10.1097/WCO.0000000000000568

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CLINICAL AND EPIDEMIOLOGICAL FEATURES OF THE PREVALENCE OF CONVEXITAL MENINGIOMAS IN THE PREDICTION AND PREVENTION OF THEIR RECURRENT DEVELOPMENT

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КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ РАСПРОСТРАНЕННОСТИ КОНВЕКСИТАЛЬНЫХ МЕНИНГИОМ В ПРОГНОЗИРОВАНИИ И ПРОФИЛАКТИКЕ РАЗВИТИЯ ИХ РЕЦИДИВОВ

И. В. Балязин-Парфенов [1], В. Е. Хатюшин [1], Н. А. Шапран [1], С. С. Тодоров [1], В. Г. Ефанов [2], Ю. Н. Коливашко [2], Г. Л. Резникова [3], Н. Р. Сабуров [4]

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The study assessed the clinical and epidemiological features of the prevalence and dynamics of the incidence of convexital meningiomas in the Rostov region. The incidence of meningiomas among the adult population ranged from 1.12 to 11.51 per 100 000 people. The progressive growth of neurooncological pathology was in areas with high-rise system buildings and highways. In addition, there was a high prevalence of meningiomas among residents of rural areas located within the industrial complex of the Rostov region or in its immediate vicinity. The developed map of an individual system for predicting the detection of meningiomas allows for secondary and tertiary prevention of meningiomas, aimed at their timely prediction, detection and prevention of relapses.

Keywords: meningioma, morbidity, frequency of occurrence, relapses, prognosis, prevention

В исследовании проводилась оценка клинико-эпидемиологических особенностей распространенности и динамики заболеваемости конвекситальными менингиомами в Ростовской области. Заболеваемость менингиомами среди взрослого населения составила от 1,12 до 11,51 на 100 тыс. Прогрессирующим рост нейроонкологической патологии был на территориях с высокоэтажной системной застройкой и транспортными магистралями. Кроме того, отмечалась высокая распространенность менингиом среди жителей сельских районов, находящихся в пределах промышленного комплекса Ростовской области или в непосредственной близости от него. Разработанная карта индивидуальной системы прогноза выявления менингиом позволяет осуществить вторичную и третичную профилактики менингиом, направленные на их своевременное прогнозирование, выявление и предупреждение рецидивов после выбора адекватных методов хирургического лечения.

Ключевые слова: менингиома, заболеваемость, частота встречаемости, рецидивы, прогнозирование, профилактика