Open Access Maced J Med Sci **electronic publication ahead of print,**
published on January 11, 2019 as https://doi.org/10.3889/oamjms.2019.032

ID Design Press, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences.
https://doi.org/10.3889/oamjms.2019.032
eISSN: 1857-9655
Clinical Science

Surgical Treatment of Meningiomas - Outcome Associated With Type of Resection, Recurrence, Karnofsky Performance Score, Mitotic Count

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Citation: Sumkovski R, Micunovic M, Kocevski I, Ilievski B, Petrov I. Surgical Treatment of Meningiomas-Outcome Associated With Type of Resection, Recurrence, Karnofsky Performance Score, Mitotic Count. Open Access Maced J Med Sci. https://doi.org/10.3889/oamjms.2018.503

Keywords: Outcome of surgically treated meningiomas; Simpson; Karnofsky; Mitotic count

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Received: 08-Nov-2018; **Revised:** 17-Dec-2018; **Accepted:** 18-Dec-2018; **Online first:** 11-Jan-2019

Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Meningiomas are the type of central nervous system tumours, derived from the cells of the arachnoid membrane that are well constrained from surrounding tissues, mainly no infiltrating neoplasm with benign features. Meningiomas consist about 15-20% of all primary intracranial neoplasms.

AIM: The evaluation of the outcome of the operatively treated meningiomas in relation with the Karnofsky performance score, survival, recurrence, type of the surgical excision, histological type, mitotic count (MC), localisation and volume of the lesion

METHODS: In this article 40 operatively treated patients are reviewed for the outcome of the operation about the Karnofsky performance score, survival, recurrence, type of the surgical excision, histological type, mitotic count (MC), localisation and volume of the lesion.

RESULTS: Association/interconnection between the mitotic count grade I and the regrowth of meningioma have been verified. Association/interconnection between the mitotic count grade I and the regrowth of meningioma have been verified. Association/interconnection between the mitotic count grade I and the regrowth of meningioma have been established.

CONCLUSION: Gender, age and Karnofsky performance score have predictive value in the treatment of different types of meningiomas. The magnitude of surgical resection is associated with the regrowth of a tumour. The mitotic count in different types of meningiomas presents significant feature in the appearance of meningioma recurrence. The surgical resection and the quality and quantity of patient's survival have a significant relation to the mitotic count of the meningiomas. There is no connection between the size and the localisation of a tumour related to different values of the mitotic count.

Introduction

Meningiomas are slow-growing tumours of the central nervous system that are well-limited from surrounding tissues, mainly non-infiltrative neoplasms with benign characteristics. Among the meningiomas, some of the histologically described are malignant forms, which include 1.7% of all meningiomas, as well as fast-growing variants that act as malignant tumours [1]. The origin of these tumours is derived from the arachnoid cells. Usually, meningioma's are single, solitary, but can also be multiple - up to 8% of cases, which is more common in neurofibromatosis [2]. The growth of meningiomas is expansive, followed with displacement and compression of the surrounding structures, the brain, blood vessels, cranial nerves, etc., but there are also forms of diffusional thickening of the brain membranes, a type of meningioma called meningioma en plaque [3]. Meningiomas can grow everywhere that arachnoid membrane is found (between the brain and the cranium, in the ventricles, down the spinal canal). The ectopic meningiomas may be found growing in the inside of the bone which limits the cranial box-as primary intraosseal meningeomas.4 Meningiomas account for 14.3-19% of all primary

intracranial neoplasms. They are the second most common primary tumour of the central nervous system, just behind the gliomas (43%), and the pituitary adenomas (17%) in the third place. The peak of incidental occurrence of this group of neoplasms is 45 years of age. The gender distribution of meningiomas is almost twice as high in females (men: women = 1: 1.8). Meningiomas in childhood and adolescence account for 1.5% of the total number [3]. Meningioma's most frequent distribution is as follows: parasagittal (20.8%), then convexity (15.2%), and tuberculum sellae (12.8%), followed by localization: sphenoid ridge, olfactory groove, falx, lateral ventriculi, tentorium, the middle fossa, the orbit, the spinal channel, the Sylvian fissure, extracalvarial, multiple localization, the pontocerebral angle, the sphenoidal plane, and the foramen magnum. Around 60-70% of all meningiomas have falcian distribution (including parasagittal distribution), sphenoid wing (including tuberculum sellae), or on the convexity of the brain. Meningiomas rarely occur in the pediatric population, and 28% of them have intraventricular and posterior fossa localisation [4], [5].

Histopathological variables that determine the characteristics of meningiomas include tumour gradient, histological subtype, proliferative index and invasiveness of a tumour to the brain [3], [6], [7]. For our paper, the WHO Classification of Tumours of CNS, 2016 was used:

1. Plain X-ray – Tumor calcifications can be verified (about 10%), then hyper/dysostosis or changes in configuration, the thickness of the skull (including the floor of the anterior cranial fossa in olfactory groove meningioma), an increase in vascular fissures (especially in the middle meningeal artery);

2. Computerised tomography-The presentation of a tumour with this diagnostic tool shows a homogeneous dense mass with a wide base attached to the dura. The presence of psammomatous calcifications can be presumed through the measured 60-70 Hounsfield units in a non-contrast series. Intraventricular meningiomas in 50% of patients produce extraventricular oedema;

3. Nuclear Magnetic Resonance-The signal that a tumour gives in T1WI and T2WI may be isodense, but it is often intensified with contrast gadolinium. The brain's oedema may, but it does not have to be present. Nuclear magnetic resonance provides information about dural venous sinuses (accuracy in the presumption of dural sinus invasion is > 90%). A common sign on NMR is the dural tale;

4. Angiography-The classical finding: "appears rapidly, remains long-lasting" explained that a tumour is visualised in the early arterial phase and remains visible after the completion of the venous phase. It is characteristic that the meningioma's have arteries that arise from the external carotid artery, excluding the olfactory groove meningioma, whose nutrient vessels originates from the internal carotid artery (ICA), or the ethmoidal branches of the ophthalmic arteries, suprasellar meningiomas may be vascularized from the long branches of the ophthalmic artery and parasellar meningioma's that are largely nourished by the internal carotid artery (ICA). The secondary vascular supply may come from the pial branches of the anterior, the middle and posterior cerebral artery. In cases of tentorial meningiomas the artery of Bernasconi & Cassinari or the Italian artery is of interest, or the artery of the tentorium (a branch of the meningohipophysal stem) that is enlarged in lesions, tumours that envelop the tentorium. Angiography gives excellent information on the involvement of the dural venous sinuses and their occlusion, especially in the parasagittal/falx meningiomas. At the same time, angiography may provide preoperative embolisation of a tumour [8].

Surgical treatment is a method of choice for symptomatic meningiomas. Incidental meningiomas without tissue oedema, vascular compromise, or those having clinical presentation only with epileptic seizures that are easily controlled with anti-epileptic medications, can be managed with an expectative approach. In general, the meningioma surgery is very bloody which would imply a great deal of attention to the hemostatic techniques during the intervention, as well as the possible use of autologous blood for transfusion donated preoperatively and also preoperative embolisation of the dominant tumour feeding artery [9]. Radiotherapy is often estimated not to be effective as a primary model of treatment [10].

The outcome in the treatment of meningiomas: 5 years of survival for patients with meningiomas is generally 91.3% [3], [11].

When conducting surgical removal of meningiomas, a system of stratification of the degree of excision is used, and this can describe the radically in the performed surgical treatment. The system for removing meningiomas according to Simpson covers 5 grades:

0) macroscopically complete removal of a tumour, excision of its dural attachment within 2 cm of no-affected dura:

I) macroscopically complete removal of the tumour, with excision of its dural attachment, and of any abnormal bone (including resection of the venous sinus when involved);

II) macroscopically complete removal of the tumour and its visible extensions with endothermic coagulation (Bovie, laser) of the dural attachments;

III) macroscopically complete removal of an intradural tumour, without resection or coagulation of its dural attachments or its extradural extensions (hyperostotic bone);

IV) partial removal, leaving intradural tumour in situ;

V) simple decompression (± biopsy) [12].

The study assesses the outcome through the disability of patients classified according to Karnofsky score, which evaluates psycho-physical (dis)ability as a percentage expressed in dozens starting from 0% (death) to 100% (normal patient, without symptoms and signs of illness) which are grouped into three groups:

0-40% - the patient is not able to care for himself, institutional or hospital care is necessary, in which the patient can progress rapidly;

50-80% - the patient is not able to work, but can live at home and to cope with most individual needs;

80-100% - the patient can continue with everyday activities and work-related obligations, and no special care is required [3].

The most important prognostic factor for treating meningiomas is predicting possible recurrence and survival for malignant or transient types of meningiomas [13], [14]. Negative prognostic factors include non-extensive resection, brain invasion and high mitotic activity which are the most significant predicting factors. The extensiveness of surgical excision is the most important factor in the prevention of recurrent meningiomas. Simpson's grading system [12] is a valuable tool for evaluation for possible tumor recurrence [15], [16]. In addition to this principle, the basic element for the prevention of recurrent meningiomas, the Mitotic index is a factor with great significance for assessment, anticipation, planning of further treatment and outcome in meningiomas [12], [15], [16], [17].

By definition, the mitotic index (MI) is the sum of the mitotic "figures" (MF) in 10 consecutive HPF (High Power Field) in the zone of the highest mitotic activity relative to the remaining cells [18], [19]. This defining factor is dominant in the classification for meningioma’s according to the World Health Organization, with 3 degrees of the mitotic index being defined as a risk factor for local recurrence, according to criteria of histological analysis with prognostic significance [17], [20].

According to Perry et al., [3], [18], [19] and accepted by the World Health Organization, as an objective grading criterion, there are: benign/WHO Grade 1 meningioma’s that do not exceed 4 mitosis per 10 consecutive HPF, atypical/WHO Grade 2, with 5-20 mitoses on HPF and anaplastic/WHO Grade 3, meningioma’s in which mitotic activity exceeds 20 mitoses of 10 consecutive HPFs in the zone of the highest mitotic activity [3], [15], [17], [18], [19].

This classification (determining the mitotic index (MI)) has its weakness. Namely, the selection of zones with the "highest mitotic index" is subjective and subject to bias and the heterogeneity of mitotic activity in various areas of a tumour. Further factors of "error" are variations in the size of the sampled tissue samples, as well as the resected samples and their cellularity, both factors affecting the number of cells that can be evaluated [21].

To specify this method, the mitotic activity can be determined by introducing an immunohistochemical method to objectify this procedure. Protein Ki-67 is a nuclear protein that is closely related and essential in cellular proliferation. This protein is associated with the ribosomal RNA transcription [21], [22].

The H & E (hematoxilyn & eosin) mitotic index, as well as the mitotic indices determined according to immunohistochemistry, can be identified as independent prognostic factors for the poor outcome (recurrent tumor and/or death), adjusted to the patient's age and extensiveness to the tumor resection (with STR (subtotal resection) as an independent factor) [17].

Numerous studies have shown that the mitotic index (in the repeat-MI text) isolated or synchronously, is in harmony with the occurrence of recurrence of meningiomas [15]. Namely, it is one of the most probable prognostic factors in meningiomas. The identification of the mitotic "figures" (MF) [23] and the zone of the most intensive mitotic activity in histological H & E coloured slides is a representative, cost-effective, necessary, but also a subjective task.

The motives were the evaluation of the outcome of the operatively treated meningiomas through objective parameters, to improve the results of the treatment, to reduce the complications, disability, improving quality, and survival, as well as re-socialisation in correlation with the mitotic index.

The purpose of this study is evaluation of the relation of the mitotic index to various groups of meningioma’s and tumour regrowth, assessment of the impact of tumour size over the time of tumour recurrence, assessment of the impact of tumour localization over the time of tumour recurrence, correlation between the mitotic index and the outcome of surgical treatment, followed by disability and survival evaluated according to Karnofsky Score, correlation between the mitotic index and the size and localization of the tumour, and also determination of the time of tumour recurrence in surgically treated subjects with meningiomas.

Material and Methods

In a retrospective study, 40 successive randomly selected patients with an initial diagnosis of intracranial supra- and infratentorial meningioma, treated at the Neurosurgery Clinic-Skopje, were processed.

The subject of the analysis were previously operated patients, without limitation in terms of location, gender, age, which are subject to standard micro-surgical excision, with a tendency to achieve "gross total resection" [12], i.e. maximum, radical surgical excision, Grades 1 and 2 according to Simpson, as well as patients undergoing "subtotal resection", respectively Grade 3, 4 and 5 according to Simpson. For this purpose, the technology for micro-surgical excision was used-microinstumentarium, operative microscope, bipolar coagulation, ultrasonic aspirator.

For surgical excision grading, and the radicality of the operative treatment, the previously mentioned evaluation system for removing meningiomas according to Simpson was used [12].

The study assesses the outcome through the disability of patients classified according to previously mentioned Karnofsky performance status, which assesses psycho-physical condition as a percentage expressed in dozens starting from 0% (death) to 100% (normal patient without symptoms or signs of a disease) that are grouped together into three groups [3].

The pathohistological diagnostics was performed at the Institute of Pathology, Medical Faculty, Ss Cyril and Methodius University of Skopje, Skopje, Republic of Macedonia, using histological and immunohistochemical analyses (diagnosis, mitotic count, subtype-specific immunohistochemistry).

Inclusion criteria were patients of our population with an initial diagnosis of intracranial supra- or infratentorial meningioma and exclusion criteria were patients with meningioma in the spinal canal.

Statistical processing of data is performed in statistical programs STATISTICA 7.1 and SPSS 13.0. The following methods apply: In series with attributive marks percentages per structure (%) are determined; The association, or the differences in the analyzed parameters in relation to the mitotic index, tumour regrowth, Karnofsky score, excision grade according to Simpson, were tested with Pearson Chi-square (χ^2); In series with numerical records determined are: Descriptive statistics (Mean ± Std. Dev., ± 95% CI, Min., Max.); The ratio between the mitotic index and the recurrence period; Karnofsky score; tumour size; Determined with Spearman Rank Order Correlations (R); The influence of size and tumour localization as independent variables on the occurrence of tumour growth as a dependent variable; the influence of the mitotic index and surgical excision as independent variables on the occurrence of tumour recurrence as a dependent variable was determined using Logistic regression analysis (Chi Square, Wald, Exp (B)); The re-emergence of a tumour, tumour size, years, patient age, the time of occurrence of the first symptoms as independent variables, on the independent living as a dependent variable, was determined using Logistic regression analysis (Chi Square, Wald, Exp (B)).

Results

Of the 40 enrolled patients 13 (32.5%) were male, 27 (67.5%) were female. Mean age was 58.58 ± 8.91 years of age, with minimal age of 42 and maximal age of 78.

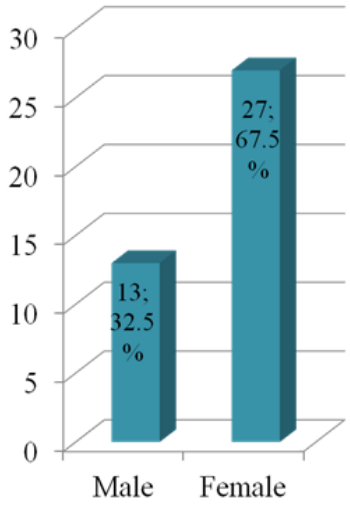

Figure 1: Distribution of the patients according to the gender

Average lesion volume was estimated to be 40.23 ± 16.39 cm, with a minimal volume of 7 ccm and maximal volume of 80.00 ccm.

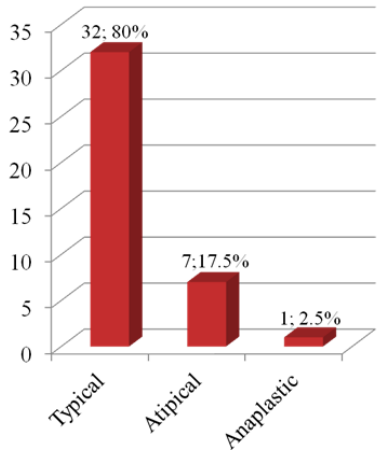

Figure 2: Distribution of the patients according to the histological type

According to the histological type 32 patients or 80% had a typical meningioma, 7 patients or 17.5% had an atypical meningioma, and one patient (2.5%) had anaplastic meningioma.

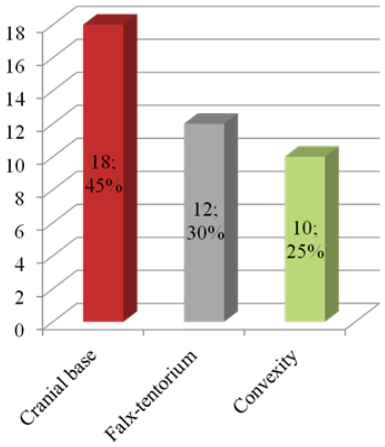

Figure 3: Distribution of the patients according to the localisation of a tumour

The localisation of a tumour was divided into three sections: convexity, cranial base and falx-tentorium. In 18 patients (45%) the meningioma was localised on the cranial base, 12 patients (30%) had a meningioma localised on falx-tentorium, 10 patients (25%) had a convexity meningioma.

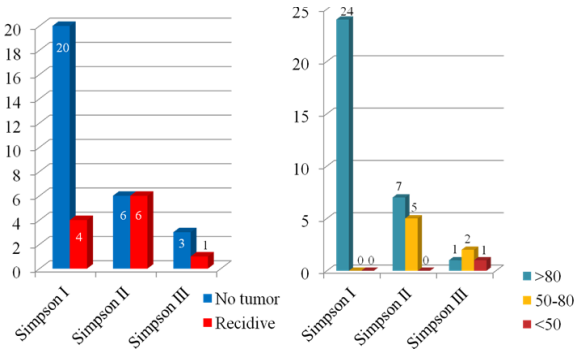

Figure 4: Distribution of the patients according to the surgical excision/tumour recurrence (left); according to the surgical excision/Karnofsky scale (right)

According to the mitotic count 34 patients (85%) had a Grade I, four patients (10%) had a Grade II and 2 patients (5%) had a Grade III mitotic count.

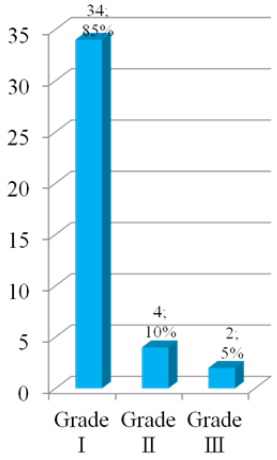

Figure 5: Distribution of the patients according to the mitotic count

Disability and survival were evaluated according to Karnofsky Performance Scale with the following results: 32 patients (80%) had a score of 80% or higher, 7 patients (17.5%) had a score from 50-80% and 1 patient (2.5%) had a score of 50% or lower.

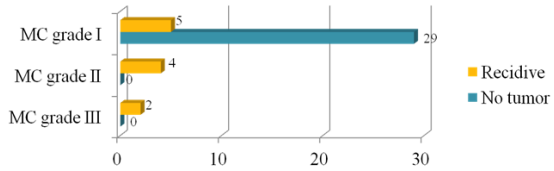

Figure 6: Mitotic count (MC) recidive of a tumour

Simpson scale was used for grading of the degree of excision: 24 patients (60%) had a Simpson I resection, 12 patients (30%) had a Simpson II resection, and 4 patients (10%) had Simpson III resection.

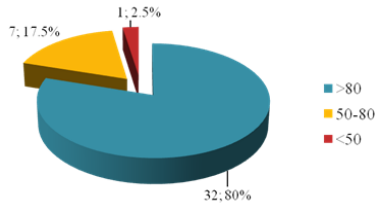

Figure 7: Karnofsky performance scale

In 29 patients (72.5%) no tumour regrowth was noted after the first operation, and in 11 patient (27.5%) tumour regrowth was diagnosed.

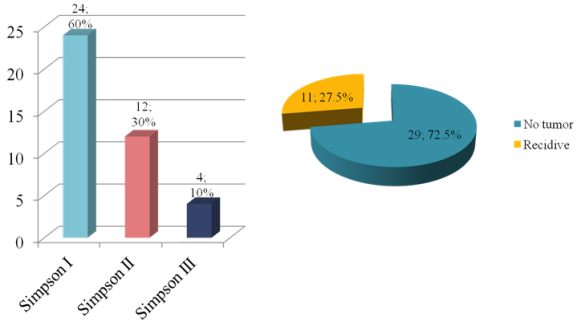

Figure 8: Surgical excision (Simpson) (left); Outcome after the 1st operation (right)

Discussion

Meningiomas represent 13 to 26% of all intracranial tumours with an annual incidence of 6 cases per 100 000 people [24]. Although these tumours behave like benign tumours, they are still associated with significant morbidity and mortality

[18], [25]. In 1993, the World Health Organization (WHO) proposed a classification of meningioma's in three groups: classic or typical (WHO Group I), atypical (WHO Group II) and malignant (WHO Group III) [27]. Depending on the diagnostic criteria used in different studies, the atypical meningiomas are represented with 5 to 17%, whereas the malignant meningiomas range from 1 to 3%, while the rest remains on the classic, typical meningiomas [8], [18], [24], [26].

In this study, according to the use of the mitotic index and the pathophysiological diagnosis, typical meningiomas were represented with 80% (32/40) of cases, atypical meningiomas in 17% (7/40) of cases and one case of anaplastic, malignant meningioma, or 2.5% (1/40), which is in accordance with the representation of the subgroups of meningiomas published in the professional literature [3], [8], [9], [18], [24], [27].

The pathophysiological criteria used for classification of meningiomas include the following estimates: the mitotic index, the presence of atypical mitosis, necrosis, significant pleomorphism, macronucleus, disrupted histoarchitectonics, hypercellularity, the presence of mosaic tissue, the presence of brain invasion, even the minimum presence of a focally clear malignant behaviour (cancer-like, sarcoma or melanoma) [28].

According to the classification of brain tumours published by the World Health Organization in 2007, all meningioma's that exhibit a brain tissue invasion were set in the higher group, WHO Group II [8]. Usability of the brain invasion as a marker of the aggressiveness of the tumour is limited, since the brain tissue can be identified in a small number of surgical specimens, and is rarely recorded by the pathologists [18], [24], [26]. Using these criteria, Andrej Vranic, Mara Popovic, Andrej Cör, Borut Prestor and Joze Pizem published a series of patients with the representation of atypical meningiomas in 76 cases (88%) and 10 patients with malignant meningioma (12%). In this paper, 7 patients had atypical meningioma (17%), and one case of anaplastic meningioma (13%) was enrolled. In the professional literature [26], the ratio of atypical and malignant meningioma's in the interrelated correlation is 1.5:1 to 6:1. In the study of Slovenian authors, this ratio equals 7.6:1, while in our study 7: 1. Benign meningiomas are more common in the female population (female: male ratio is approximately 2:1), while atypical and malignant meningiomas are more common in the male population (the ratio of women to men is 0.8-1.4: 1). In the series of Slovenian colleagues, the ratio of women to men is 1.1:1, while in our study this ratio is 1.6:1, while in the benign form, the ratio according to the gender female: male equals 2.2:1. In the previously cited study of the Slovenian authors, during the patient's follow-up, tumor regrowth was noted in 31 patients (36%), in the period from 4 to 76 months (median of 31), while in our study there were 11 patients, that is, 27.50% without tumour regrowth in the interval of 14.36 ± 7.10, i.e. the minimum re-occurring time from 8 months to the maximum re-occurrence time of 28 months.

The significance of the extensiveness of surgical resection is equally important for all histological subtypes of meningiomas [18], [25]. Sometimes it is difficult to compare the results between studies because the tumour resection in some studies is graded according to Simpson [11], [29] while in the other it is graded as a total or subtotal resection (gross total vs subtotal resection, GTR vs STR) [18], [25], [30]. In the study of Slovenian authors, Simpson I excision was achieved in 47% of patients, and total resection (as GTR) (including Simpson I and II) was achieved at 90%. The non-recurring period of patients with Simpson I excision was longer compared to patients with Simpson II-IV excision, but there were no statistically significant observations.

In the study of Donald Simpson of the Department of Neurological Surgery, Radcliffe Infirmary, Oxford, 90 operations were made according to Simpson I, in which beside tumour extirpation, the dural attachment and extradural extensions were removed so that 8 cases of relapse occur later, or 9% [12]. Of the 114 operations performed according to Simpson II, in which the visible tumour was completely removed, while the dural adherence was coagulated with the endotherm coagulation, 18 relapses or 19% were observed. For operations that are considered incomplete (Simpson III, IV, V), the rate of recurrence is more significant, but it is important to note that a large number of patients treated with limited excision gain a long period of relief [12].

In our study, of the 40 patients with meningioma treated surgically, in 24 patients (60.0%) maximally radical surgical excision was achieved, grade I according to Simpson, of which 4 patients (10.0%) had a tumour recurrence. In 12 patients (30.0%), surgical excision grade II was performed by Simpson, and 6 of them (15.0%) had a tumour recurrence. Four patients (10.0%) performed surgical excision grade III according to Simpson, 1 patient (2.5%) had a recurrence of the tumour, and for all within the defined period of follow-up. There is no significant difference in the reported distribution of data on the degree of surgical excision graded by Simpson and the incidence of tumour regrowth, for $\chi^2 = 4.47$ and $p > 0.05$ ($p = 0.11$).

When patients are grouped according to the histological type of the meningioma, than those with benign form-typical meningioma, have a 5-year survival of 75%, while those with atypical and anaplastic meningioma have a rate of a 5-year survival rate of 70% and 56%, respectively. The prognostic factors for survival in benign tumours

include the patient's age in the time of setting the diagnosis, tumour size, institution (the manner/standard of treatment) in which the patient was treated; for malignant tumours the age at the time of diagnosis is important. The five-year recurrence rate of the symptoms (regardless of the choice of treatment of the disease) equalled 18.2% for benign tumours and 27.5% for patients with malignant meningiomas. In patients with benign meningioma, who were susceptible to complete eradication, the 5-year reappearance rate equalled 20.5%.

It was shown that women have a higher prevalence of all three histological types of meningiomas, compared with men, with no racial difference in the representation of meningiomas. Age is an important predictor of mortality in patients with benign, atypical and malignant meningiomas. As the age of the diagnosis increases, the survival rate decreases dramatically, although the exact cause of death in patients is not taken into consideration, depending on or regardless of the primary illness. Age and race are considered as individual prognostic factors for benign and malignant meningiomas.

According to the study, the 5-year tumour recurrence rate that was previously completely surgically eliminated equalled 20.5%, which is higher than that quoted in the literature [3], [15], [20], [26], [27], [31], [32].

Mirimanoff et al., [32] recognised that the rate of re-emergence of benign meningiomas previously operatively treated was 7% for 5 years and 20% for 10 years. The recurrence rate in the Mirimanoff et al., [20] study accounted for 2% throughout 5 years. In this study, the recurrence time for medium-term time is 14.36 ± 7.10 months, that is, at least 8 months and a maximum of 28 months.

Complete surgical tumour excision is referred to as gross total resection (GTR), which is defined as Simpson grade I or II, which corresponds to a macroscopically performed tumour resection with bipolar coagulation of the dural insertion. Any other type of tumour resection would be understood as subtotal resection (or STR). Pathologists in the study assessed the mitotic activity of the tumour through the determination of the mitotic index with classical H & E colouration, immunohistochemistry with monoclonal anti-PHH3 (phosphohistone H3) antibody and immunohistochemistry technique with a monoclonal anti-Ki-67 antibody [17], [21].

The following results were obtained in the determination of the mitotic index (MI): 251 WHO grade I, 45 atypical meningioma's (WHO grade II) and 5 malignant (anaplastic) meningioma's (WHO grade III). In operative treatment, 238 cases had GTR, while 27 patients had STR. The recurrence rate in the study equaled 12.5% (i.e. 33 patients) with a relative risk for tumor regrowth significantly higher in patients treated with subtotal resection (STR), (10/27; RR = 37%) compared with those treated with radical resection (GTR) (23/238; RR = 9.7%). The average recurrence time was 45 months (48 months after GTR and 36 months per STR). The meningioma recurrence rate with WHO grade I level equalled 6.0% for tumour GTR, or 9.8% in the total cohort. Reproducibility was recorded at 18% for meningiomas with the WHO grade II mitotic index, while for meningiomas with grade III mitotic index, according to the WHO, recurrence equalled 80%. In the pathophysiological assessment of tumours, in addition to cell proliferation and cellular abnormalities, the potential of the tumor for invasion in the brain parenchyma was considered, with the type of tumour being labelled as possibly invasive meningioma. Of the examined series, brain invasiveness was registered in 14 tumours with the following distribution-12 tumours in grade II and 2 in grade III of the WHO (of which, 4 brain tissue-invasive recurrent meningioma's with a relative risk of 29%). The study compares the importance and efficiency of the mitotic index measured by the traditional way of histological preparations according to H&E, as well as the use of monoclonal anti-phosphohistone H3 (PHH3) antibodies and monoclonal anti-Ki 67 antibodies in immunohistochemistry of the preparations. The MI (MI) H & E and MI PHH3 can be identified as independent predictors (predictors) of poor prognosis (recurrence and/or death) adjusted to the age and extensiveness of surgical tumour resection (and STR as an independent variable).

Following the WHO-recommended mitotic indexing guidelines, a lower threshold for mitotic activity, i.e. a mitotic index of 4 and more mitotic figures of 10 large-scale magnifications (HPF) was proposed, at the point of high risk of tumour recurrence and / or death. MI according to H & E is an independent indicator of unfavourable prognosis, as proposed by Perry et al., [18], [33].

In our study, we have the following data on the significance of the mitotic index in the prognosis: out of the total extirpated meningioma's (40 in all), 34 meningiomas, (85%) pathohistologically classified based on mitotic index in grade I according to the WHO, 4 meningioma's (10%) are classified according to the mitotic index in grade II according to the WHO and 2 meningiomas (5%) classified according to the mitotic index in degree III according to the WHO.

As for the examined correlation between the mitotic tumor index and the localization of the tumor, 34 (85, 00%) patients registered a mitotic index of grade I, of whom 15 (37, 50%) patients had a localized tumour on the skull base, 10 (25, 00%) patients had a tumor localized to falx-tentorium, and in 9 (22, 50%) patients the tumor was localized to convexity. In 4 (10.00%) patients a mitotic index of grade II was registered, of which 2 (5.00%) patients had a tumour localized to the skull base, 1 (2.50%) the patient had a tumor localized to the falx-tentorium, and 1 (2.50%) the patient had a localized convexity tumour. Two patients (5.00%) had a mitotic index of grade III, of which 1 (2.50%) the patient had a tumor

localised to the skull base, and 1 (2.50%) patient had a tumor localized to the falx-tentorium. For $\chi^2 = 0.87$ and $p > 0.05$ ($p = 0.93$), there is no significant difference in the displayed distribution between the level of the mitotic index and the localization of the tumour.

Grading of work capacity and disability was done according to the Karnofsky Performance Score, which as an average for patients in Akagami Ryojo's study, Napolitano Mario, Sekhar Laligam equalled 83 ± 10%. Ninety-seven per cent of patients were satisfied with the treatment, expectations were fulfilled in 90%, and according to the Karnofsky index, 83% of patients were labour-efficient. In this study, the comparison is as follows: 40 patients, of which 13 men and 27 women were studied, at a mean age of 58.58 ± 8.91 years. Gross total resection (Simpson grade I) was achieved in 24 patients (60%) and Simpson grade II was achieved in 12 patients (30%) in a total of 90% of patients. The mean tumour volume was 40.23 ± 16.39 cc. The work capacity assessment and the capacity for independent living, conducted according to Karnofsky, 80% of the patients were able to live independently with the possibility of returning to their jobs, 17.5% cannot fulfil their previous working capacity, but can independently function and can fulfil their own individual need, while 2.5%, that is, one patient, is not able to care for himself, that is, he needs an institutional type of care [34], [3].

In conclusion, the results have shown that gender, age and Karnofsky performance score have predictive value in the treatment of different types of meningiomas. Also, the magnitude of surgical resection is associated with the regrowth of a tumour. The mitotic count in different types of meningiomas, as an independent predictor, represents a significant feature in the appearance of meningioma recurrence. The surgical resection and the quality and quantity of patient survival have a significant relation to the mitotic count of the meningiomas. Results have also demonstrated that there is no connection between the size and the localisation of a tumour related to different values of the mitotic count.

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