

REVIEW OF THE OFFICIAL OPPONENT

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to the dissertation of Abdalrahman Nassar " Prognostic factors in
surgical outcomes of sphenoid wing meningioma"

for the degree of Doctor of Philosophy in the field of knowledge

22 Health care in the specialty 222 Medicine

Relevance of the topic

Intracranial meningiomas account for approximately 15-20% of all intracranial tumors. Among all meningioma locations, sphenoid wing meningiomas constitute approximately 20% of all. Due to the anatomical structure of this region, and above all the large size of the wing of the sphenoid bone, extending from the pterion to the area of the sella, these tumors are easy, difficult, and very difficult to be surgically treated and completely removed. It is related to the location of the tumor, its size, the degree of compression on the brain, collateral edema, and the patient's preoperative status (general and neurological). Correct preoperative evaluation is essential to predict whether a complete removal is possible and whether it is safe for the patient. In addition to the size of the tumor in the described location, it is necessary to assess whether the tumor grows through important anatomically and functionally important structures, such as the internal carotid artery with its branches, the optic nerve, the oculomotor nerve, the cavernous sinus, the base of the middle cranial fossa, and whether it propagates towards of the brain stem and the interpeduncular fossa.

The subject of the work undertaken by the Candidate is significant in the tactics of management and treatment of patients with meningiomas of the sphenoid bone. It should be emphasized that in the world literature - although very abundant - the way of dealing with this type of patients is different, and moreover, the preoperative prognosis and treatment approach are sometimes significantly different. Therefore, the possibility of assessing the predictive value based on the most important

parameters is crucial in this case, which method of surgery to choose, and if so, how to optimize it so that the patient gets the maximum benefit.

In the literature, there are many studies devoted to assessing the results of surgical treatment of meningiomas of the sphenoid bone. Nevertheless, there are no studies that comprehensively assess the preoperative risk, taking into account all the most important factors, especially around peritumoral brain edema (PTBE). Comprehensive development of this issue is a difficult challenge, given the different size, location, shape and morphology of the meningiomas of the sphenoid wing.

Assumptions and aims of the study.

The aim of the study was to analyze the effectiveness of various forms of surgical treatment of meningiomas of the sphenoid wing, taking into account various preoperative prognostic factors. Based on the results obtained, the ultimate goal was to further improve the outcomes of surgery for these patients.

The validity of scientific statements, conclusions and recommendations, their probability.

Based on the analysis of the scientific literature, the dissertation of Abdalrahman Nassar managed to single out a new scientific problem, for the solution of which the goals and objectives of the research were methodically correctly chosen. It is emphasized that the need to solve this problem is due to the requirements of practical medicine. The study was performed on a conventional model and on sufficient to obtain reliable results of the materials of 67 patients (senses publication sampling).

The dissertation successfully and reasonably applied a set of modern adequate research methods: general clinical, radiological, histological, operative, measurement methods (treatment proposed the following division of the degree of peritumoral edema), and prognosis. The proper modern methods of the medical statistics were used. This methodological approach allowed the author to obtain objective and convincing data on the laws.

Scientific novelty of the study - the most important achievements.

This research is the first which statistically proved the significant impact of different preoperative predictors on surgical outcome and quality of life in early postoperative period in patients with sphenoid wing meningiomas.

This study is the first of its kind in an extensive study of peritumoral brain edema of sphenoid wing meningiomas. Due to the used formula of evaluation of the peritumoral edema (edema index) it was revealed that PTBE is one of the important negative risk factors in the surgical outcome and complication rate.

Due to the newly proposed classification of tumor size and based on the statistical analysis it was found that tumor volume as factor is independently associated with gender, PTBE, pathological grade and anatomical variants of SWMs, which was not previously known.

It was found that time of sphenoid wing meningiomas recurrence is shorter in patients with PTBE, WHO Gr. II and negligible for Simpson grade.

For the first time it was revealed that extensive PTBE also occur in small medial sphenoid wing meningiomas, these results do not support the prevailing brain parenchyma compression theory.

Practical application of the results of the work

Based on the results, neurosurgeon can predict the extent of tumor resection depending on its location and other risk factors. As it was proved in this study complete tumor resection can be achieved in most of lateral (80.9%), middle (77.8%) and sphenoid-orbital meningiomas (75.0%). Incomplete resection of sphenoid wing meningiomas are strongly related to anatomical location of SWM and tumor volume.

Neurosurgeon can make more precise surgical planning. Newly designed edema index score and classification of sphenoid wing meningioma volume allow to plan surgical approach, tumor removal technique and predict the complications in early postoperative period and surgical outcome in long-term.

In everyday practice neurosurgeon can predict functional and neurological outcome and recurrence of SWM. The research has proven that the functional neurological outcome following surgical resection of SWM is influenced by several factors: extent

of surgical resection, histopathology of the tumor, tumor volume, anatomical location of SWM and presence of PTBE. The pathological grade II, atypical type and Simpson grade III-V are important impact factors for sphenoid wing meningioma recurrence.

Characteristics of the study. Evaluation of the content and design of the dissertation, its completion, analysis of its sections.

The dissertation consists of 178 pages, in which one can find the following chapters: introduction, literature review, material and research methods, evaluation of the correlations of various clinical and diagnostic data, surgery for the medial sphenoid wing meningioma, discussion, conclusion and recommendations for medical practice. The work ends with a reference list of 228 items. There are 39 tables, 24 figures and 33 charts. The structure of the work is like the classical format, with all the chapters mentioned above.

In the introduction the applicant justified the relevance, aim and tasks of the research. The aim is correlated with the topic of the scientific work. The tasks correspond with the aim, help to achieve it. The object of the research is defined correctly. The novelty and practical implication of the scientific work are formulated properly.

The candidate dealt extensively with the topic of meningiomas of the sphenoid wing – in the “Literature review” he presented detailed anatomical and surgical data for these tumors, presenting numerous iconographies. He has analyzed the literature sources on molecular biology, growth factor receptors pathways, risk factors of the meningioma growth, immunochemistry, and meningioma behavior. An attention was drawn to the new molecular, histopathological and surgical classifications of the SWM. Then author shortly described the clinical evaluation and diagnostic options for these tumors. Meticulous care was taken to analyze the variety of possible surgical approaches and special surgical techniques. Scientific articles on the analysis of factors influencing the results of the operation, postoperative course and prediction of possible recurrences are also presented. The researcher has concluded this chapter with the analysis of an unresolved issues of sphenoid wing meningiomas prognosis and management.

In the chapter 2 „Patients and Methods”, the author has presented the research plan in detail, along with a properly selected statistical analysis. He has analyzed the different characteristics of the clinical material. The presented results are consistent and strictly relate to the assumptions of the study. Modern research methods were used, they are described in this chapter.

In the Chapter 3 the author based on tumor characteristics and surgical outcomes evaluated the variety of correlations among them. He has founded that the presence of peritumoral brain edema, tumor volume, preoperative vision impairment and motor weakness and preoperative KPS score were strong-to-moderate statistically significant predictors of worse quality of life in the three-months follow-up. However, the gender and age of patients, PTBE size, tumor location, preoperative symptoms of headache, seizures, III cranial nerve disfunction, aphasia, behavior changes and vertigo were shown to be weak-to-negligible predictors of postoperative outcomes and are not statistically significant.

The novel and important is the study of peritumoral edema in SWM which was found in most of patients. It was found that peritumoral brain edema had an important impact on the incidence of preoperative seizures and motor weakness, whereas no significant effect was found on the preoperative KPS. A strong correlation was revealed between peritumoral brain edema and anatomical location, irregular margin of meningioma, pathological grade. Peritumoral brain edema was one of the important risk factors and significantly correlated with unfavourable short-term surgical outcome and postoperative complications in patients with sphenoid wing meningiomas. It was associated with higher mortality, morbidity and lower KPS in the early postoperative period.

Also, the researcher explored the recurrence rate for the sphenoid wing meningiomas (mean follow-up period 87 months). He has founded important impact factors for tumor recurrence are: pathological grade II, atypical type and Simpson grade III-V. Weak factors included tumor volume, PTBE and anatomical location of SWM. Time to recurrence is shorter in patients with PTBE and WHO Grade II tumors.

Chapter 4 is an analysis of one of the most challenging tumors of brain – medial sphenoid wing meningioma. Only in 37.5% of them the complete tumor resection

was achieved in contrast to most of lateral (80.9%), middle (77.8%) and sphenoidal meningiomas (75.0%). The reasons for incomplete resection of medial sphenoid wing meningiomas were strongly related to anatomical location of SWM and tumor volume. Based on the analysis of the surgical outcome and importance of the different factors on outcome the author has stated that the use of skull base technique with extradural anterior clinoidectomy for surgical resection of medial SWM should be the preferred surgical approach.

The „Discussion” chapter is extensive and includes all the most important references to the world's literature. It logically summarizes the obtained data and results.

The conclusions fully reflect the main content of the scientific work and correlate with the assigned tasks.

Assessing the overall structure of this work, it is basically an exhaustive monograph that could serve as a textbook for neurosurgeons working on meningiomas of the sphenoid bone. It deserves recognition and praise.

Publications and approbation of the results.

The scientific results of the scientific work are fully covered in 4 scientific publications, 3 articles of which are in professional scientific journals recommended by Ministry of Education and Science of Ukraine, one of which is an article in the journal included to Scopus database. The results were presented in Congress and Annual Meeting of the Ukrainian Association of Neurosurgeons.

Taking into account the heterogeneity of the research material (small and very large tumors with variable localization along the sphenoid wing), significant differences between the size of individual groups, it would be advisable to add a short section "Limitations", because the above elements are an important factor in the final interpretation of the research, which I would recommend in the case of publishing the obtained results. It is a valuable material, comprehensively researched and should be announced to a wider group of readers.

The subject of the work undertaken by the Candidate is significant in the tactics of management and treatment of patients with meningiomas of the sphenoid bone. It should be emphasized that in the world literature - although very abundant - the way

of dealing with this type of patients is different, and moreover, the preoperative prognosis and treatment approach are sometimes significantly different. Therefore, the possibility of assessing the predictive value based on the most important parameters is crucial in this case, which method of surgery to choose, and if so, how to optimize it so that the patient gets the maximum benefit. I believe that the most important conclusions from the obtained results are the fact that certain parameters, including mainly peritumoral edema, have a statistically significant value in the preoperative assessment of the patient's prognosis.

The author's original contribution is the multidirectional analysis of the material, which may be the basis for the development of a model of management in these patients. Such data could be helpful in making decisions in daily neurosurgical practice in patients with sphenoid wing meningiomas. The work is also characterized by high credibility of the results obtained through the appropriate selection of statistical methods and a thorough analysis of the material in this respect.

As a neurosurgeon who is a representative of a center that also deals with, inter alia, treatment of meningiomas, I rate the work highly presented. I also believe that the dissertation is written in a good and concise language, it proves the author's extensive experience in the field of the discussed subject, his considerable amount of work, as well as the reliability and ability to conduct scientific research.

The correct layout of the work, the legibility of the print and the graphics deserve praise, especially the figures, which are properly selected and of high quality. From among the literature, the author chose the appropriate items, which proves his good orientation in the literature on the subject.

Based on the results of the examination and analysis of the dissertation using the Unicheck program, no signs of academic plagiarism, self-plagiarism, fabrication, or falsification were found.

Conclusion.

The dissertation of Abdalrahman Nassar " Prognostic factors in surgical outcomes of sphenoid wing meningioma" is a qualified, independent, completed, scientific paper. Regarding the relevance of the topic, modern research methods, the scope of

examinations, the practical significance of the results obtained, their novelty and informative conclusions, the paper meets the requirements for theses submitted for obtaining the scientific degree of Doctor of Philosophy in the field of study 22 "Health Care", specialty 222 "Medicine" according to the "Procedure for awarding the degree of Doctor of Philosophy and cancellation of the decision of the one-time specialized academic council of a higher education institution, scientific institution to award the degree of Doctor of Philosophy", approved by Resolution No. 44 of the Cabinet of Ministers of Ukraine dated January 12, 2022, and its author deserves to be awarded the scientific degree of Doctor of Philosophy in the field of study 22 "Health care", specialty 222 „Medicine”.

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