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**Neurocognitive Outcome in Patients with Perioptic Meningioma
Operated by the Pterional Versus the Frontotemporal Epidural
Approach: A Randomized Controlled Double Blinded Clinical Trial**
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Abstract:

Background: Intracranial meningiomas (ICMs) make up 30-40% of all primary central nervous system malignancies.

Aim: The research aimed to evaluate the neurocognitive outcomes within cases with skull base meningiomas, undergoing two surgical approaches

Patients and methods: This randomized controlled double blinded clinical research has been performed on 85 patients diagnosed with perioptic meningiomas after their surgical excision by 2 different approaches. The first group included 42 patients in which intradural tumor excision was done after peeling of the outer layer of the lateral wall of cavernous sinus through the fronto-temporal approach and the second group included 43 patients in which intradural tumor excision was done without peeling of the outer layer of the lateral wall of the cavernous sinus.

Results: Post-operatively, MoCA-B components were statistically comparable within both groups ($p > 0.05$), apart from executive function, abstraction, and naming, which showed higher significantly improvement values in the peeling group. The incidence of cognitive dysfunction demonstrated a significant rise associated with the non-peeling group. In the peeling group, most components of the SCL-90 score demonstrated a significant decline after operation, apart from somatization and anxiety that showed comparable findings at the same time points.

Conclusion: Postoperative quality of life is crucial in neurosurgical care, particularly for managing brain neoplasms. Neurocognitive functions can be affected by anterior and middle cranial fossae meningiomas, especially when frontal and temporal lobe compression occurs. Cavernous wall peeling can improve neurocognitive functions and societal integration.

Keywords: ICMs, cognitive dysfunction, frontotemporal epidural approach

1. Introduction

Intracranial meningiomas (ICMs) account for roughly 30 percent to 40 percent of each 1st central nervous system malignancies (CNS) (1,2).

Over ninety percent of meningiomas are classified as Grade I tumors by the World Health Organization, meaning that they would have a benign clinical history (3).

In general, based on the tumors size and location, in addition to the neurological damage degree, first treatment for these tumors comprises multivariate such as surgical excision, radiation, or the so-called wait-and-scan method (4).

Technological advancements in micro-neurosurgery and radiation have made meningioma treatment more effective in terms of patient survival and morbidity (5).

In the field of brain tumor research, the evaluation of health-associated quality of life (HRQoL) and cognitive function, especially in cases with skull-base meningiomas, has become increasingly prominent as an outcome measure. Cognitive functioning has significant effects on HRQoL and may even serve as an indicator of HRQoL (6).

Approach to the skull base meningioma was a great obstacle in the developing neurosurgical field which later on improved, and new approaches were introduced, the effect of these approaches on cognitive functions of the patients is of great concern to the patients and the surgeons (7).

In previous studies, it was found that most of the patients diagnosed with meningioma will improve after tumor excision from the neurocognitive point of view, but the effect of a particular skull base approach for meningioma excision wasn't assessed (8).

The research aimed to evaluate the neurocognitive result in cases diagnosed with skull base meningiomas of the anterior and middle cranial fossa approached via two different surgical approaches (with, or without peeling of the outer layer of the cavernous sinus).

Patients and methods

This randomized controlled double blinded clinical research has been performed on 85 patients diagnosed with perioptic meningiomas after their surgical excision by 2 different approaches. The first group included 42 patients in which intradural tumor excision was done after peeling of the outer layer of the lateral wall of cavernous sinus through the fronto-temporal approach and the second group included 43 patients in which intradural tumor excision was done without peeling of the outer layer of the lateral wall of the cavernous sinus. Those patients were admitted and operated after diagnosed to have skull base (perioptic) meningiomas using MRI studies.

An ethical acceptance has been gathered from Research Ethics committee in our university under the number (N-71-2016).

Inclusion criteria: Patients with anterior and middle fossa meningiomas, 18 years old or more, fit for surgical intervention and have no history of encephalitis or dementia.

Exclusion criteria: Patients with recurrent meningioma, or meningioma with malignant behavior, patients with severe bilateral visual affection who can't accomplish the neurocognitive test, patients who are not fit for surgical intervention, patients with history of encephalitis or dementia and patients with epilepsy not related to the tumor.

Outcomes:

Primary outcome to be assessed was the cases neurocognitive functions after surgical excision of the tumor in each group. Neurocognitive outcome has been evaluated by Montreal cognitive assessment - Basic (MoCA-B) and the psychological status by the Psychiatric Symptoms and Behavior Checklist-Revised (SCL-90-R). All patients were examined about 3-7 days preoperatively and 7-10 days postoperatively; according to their stay in the ICU. Then we compared postoperative results to preoperative results in each group.

MoCA-B is formed mainly for illiterate persons, in a previous study its results for both educated and illiterate were the same, and Arabic version of MoCA is valid and reliable in Egypt to study cognitive impairment within elderly in Cairo (**9, 10**). The Arabic version of MOCA-B is accessible at ([http:// www.mocatest.org](http://www.mocatest.org)) and may be utilized with authorization. It is a 30-point screening test that is administered in ten minutes and consists of one page. Its purpose is to detect cognitive impairment. The total probable score is 30; a score of 26 or higher is considered normal; and a score below 26 reveals cognitive impairment. The MoCA has a high specificity (87%) and a high sensitivity (90%) for the detection of mild cognitive impairment. MOCA-B assists neurocognitive domains including: Executive functions, Repetition and immediate recall, Orientation, Semantic fluency, Abstraction, Calculation, Visuospatial, Delayed recall, Naming and Attention. At the end of test, we add 2 points for not educated persons and only 1 point for those with education level less than 4 years (**11**). Psychological status of the patients which may have a great effect on their cognitive function was assessed using the revised edition of Psychiatric Symptoms and Behavior Checklist (SCL-90-R) which composed of ninety questions answered by the patient and covers 9 psychological disorders including Obsessive compulsive (OC), Somatization (SOM), Depression (DEP), Interpersonal sensitivity (IS), Hostility (HOS), Anxiety (ANX), Paranoid ideation (PAR), Phobic anxiety (PHOB), and Psychoticism (PSY). The Arabic version of the SCL-90-R was used before and valid among Arabic personnel. It was applied for the patient with MoCA-B at the same session. Score ≥ 20 in any psychological disorder is considered positive for that disorder (**12**). Patients who were positive for any of these psychological disorders received medical care and treatment in the psychiatric department at Cairo university hospital.

Statistical analysis:

The statistical package of social sciences (SPSS 27.0, IBM/SPSS Inc., Chicago, IL) was utilized to analyze the outcomes. Descriptive analysis tools, such as the mean (X), standard deviation (SD), or median (Med), have been utilized. Qualitative data were presented using frequency with percentages (%). We also utilized analytical or inferential tools, like the Pearson Chi-square (χ^2) test, for comparing two or more groups with respect to a single qualitative variable. The Fischer's exact test was utilized instead of the Chi-square (χ^2) test when the assumption that at least eighty percent of the expected frequencies are higher than five was not met. The independent sample t-test (t test) was utilized to evaluate the significance of the variance among two normally distributed groups in continuous data. Shapiro-Wilk and Levine's tests were respectively utilized to verify the assumptions of normality in each group and homogeneity of differences. The Mann-Whitney U-test (Z test) was utilized to evaluate the significance of the variance among two non-normally distributed groups with continuous data. The level of significance (P-value) was established at 0.05, indicating that P-values ≥ 0.05 are statistically non-significant, P-values < 0.05 are significant, and P-values < 0.01 are highly significant.

Results

Table (1): Basic demographic data comparing peeling with non-peeling

Items	Peeling n=42		Non-peeling n=43		Test of significance	P Value
Age (Years)						
Mean ± SE	47.4 ± 1.88		45.05 ± 1.63		t= 0.950	0.354
Sex						
Males	9	21.4%	5	11.6%	$\chi^2= 1.483$	0.223
Females	33	78.6%	38	88.4%		
Duration of education (Years)						
Mean ± SE	8.1 ± 0.94		6.27 ± 0.92		t= 1.381	0.171

P: probability, Quantitative data are shown as mean $\pm$ SE, Categorical data presented as Number (%), χ^2 : Chi-square test, t: Independent sample t-test

There was no statistically significant variance within both groups regarding sex, age and education time (years) (Table 1).

Table (2): Postoperative Psychiatric Symptoms and Behavior Checklist- Revised (SCL-90) results comparing peeling with non-peeling

SCL-90 items	Groups	Number of cases	Mean	Std. Error Mean	Test of significance	P value
Somatization	Peeling	42	6.24	0.49	t= -1.272	0.207
	Non-peeling	43	7.42	0.78		
Obsessive Compulsive	Peeling	42	3.64	0.56	t= -2.637	0.010*
	Non-peeling	43	6.44	0.90		
Interpersonal Sensitivity	Peeling	42	3.57	0.72	t= -1.733	0.087
	Non-peeling	43	5.42	0.78		
Depression	Peeling	42	5.29	0.66	t= -4.271	< 0.001*
	Non-peeling	43	11.09	1.18		
Anxiety	Peeling	42	3.52	0.42	t= -1.300	0.197
	Non-peeling	43	4.53	0.65		
Hostility	Peeling	42	1.98	0.40	t= -0.684	0.519
	Non-peeling	43	2.33	0.36		
Phobic Anxiety	Peeling	42	1.57	0.31	t= -0.464	0.644
	Non-peeling	43	1.79	0.36		
Paranoid Ideation	Peeling	42	0.74	0.23	t= -1.815	0.073
	Non-peeling	43	1.70	0.47		
Psychoticism	Peeling	42	0.79	0.16	t= -2.788	0.007*
	Non-peeling	43	2.47	0.57		

*: significant value < 0.05

Although the severity of obsessive compulsive or interpersonal sensitivity components didn't differ within both groups, the incidence of symptomatic postoperative cases demonstrated a significant rise within the non-peeling group, regarding somatization and depression (Table 2).

Table (3): Postoperative SCL-90 categories results comparing peeling with non-peeling

Items	Peeling n=42	Non-peeling n=43	Test of significance	P Value
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Somatization						
Not symptomatic	40	100%	39	90.7%	FET= 4.100	0.043*
Symptomatic	0	0%	4	9.3%		
Obsessive Compulsive						
Not symptomatic	42	100%	42	97.7%	FET= 0.988	0.320
Symptomatic	0	0%	1	2.3%		
Interpersonal Sensitivity						
Not symptomatic	41	97.6%	43	100%	FET= 1.036	0.309
Symptomatic	1	2.4%	0	0%		
Depression						
Not symptomatic	42	100%	32	74.4%	FET= 12.341	< 0.001*
Symptomatic	0	0%	11	25.6%		

P: probability, Categorical data expressed as Number (%), FET: Fischer's exact test

Post-operatively, MoCA-B components were statistically comparable within both groups ($p > 0.05$), apart from executive function, abstraction, and naming, which showed higher significantly improvement values in the peeling group (Table 3).

Table (4): Postoperative MoCA-B results comparing peeling with non-peeling

MoCA-B items	Groups	Number of cases	Mean	Std. Error Mean	Test of significance	P value
Executive	Peeling	42	0.29	0.07	t= 2.317	0.023*
	Non-peeling	43	0.09	0.04		
Fluency	Peeling	42	1.17	0.11	t= 0.551	0.583

	Non-peeling	43	1.09	0.08		
Orientation	Peeling	42	5.38	0.11	t= 0.923	0.359
	Non-peeling	43	5.21	0.15		
Calculation	Peeling	42	2.02	0.13	t= 0.641	0.523
	Non-peeling	43	1.91	0.13		
Abstraction	Peeling	42	2.00	0.14	t= 2.093	0.039*
	Non-peeling	43	1.56	0.15		
Recall	Peeling	42	3.38	0.20	t= 1.552	0.125
	Non-peeling	43	2.95	0.19		
Visuospatial	Peeling	42	2.14	0.12	t= 1.135	0.260
	Non-peeling	43	1.93	0.15		
Naming	Peeling	42	3.43	0.11	t= 3.759	< 0.001*
	Non-peeling	43	2.74	0.14		
Attention	Peeling	42	2.10	0.17	t= 0.756	0.452
	Non-peeling	43	1.91	0.18		

Total MoCA-B score had significantly greater values in the peeling comparing with the non-peeling group after operation (22.5 vs. 20.28 respectively, $p = 0.028$) (Table 4).

Table (5): Postoperative total MoCA-B score comparing peeling with non-peeling

MoCA-B items	Groups	Number of cases	Mean	Std. Error Mean	Test of significance	P value
Total score	Peeling	42	22.5	0.76	t= 2.240	0.028*
	Non-peeling	43	20.28	0.64		

The incidence of cognitive dysfunction demonstrated a significant rise associated with the non-peeling group (90.77% vs. 59.5% within the peeling group, $p = 0.001$) (Table 5).

Table (6): Postoperative cognitive dysfunction according to total MOCA-B score comparing peeling with non-peeling

Items	Peeling n=42	Non-peeling n=43	Test of significance	P Value
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Cognitive dysfunction	25	59.5%	39	90.7%	$\chi^2 = 11.101$	0.001*
No cognitive dysfunction	17	40.5%	4	9.3%		

In the peeling group, most components of the SCL-90 score demonstrated a significant reduction after operation ($p < 0.05$), apart from somatization and anxiety that showed comparable findings at the same time points (Table 6).

Discussion

There is a scarcity of research on cognition in the context of meningiomas, with a limited number of studies and even fewer centers involved in the publication of such data. This suggests that cognitive disorders may be underestimated and also precludes the extrapolation of the outcomes to a global scale (13). Furthermore, despite the fact that meningiomas are extra-axial lesions, they typically manifest symptoms as a result of a mass effect that affects various cognitive dimensions, contingent upon the tumor's location (2). Few studies had focused on the cognitive finding of meningioma patient, by comparing postoperative scores to preoperative baseline scores of the patients, and in general, each research demonstrated significant developments in cognitive functioning after operation (14).

A statistically insignificant variance has been observed among both groups regarding sex, age and education time (years). Although the severity of obsessive compulsive or interpersonal sensitivity components didn't differ between the two groups, the incidence of symptomatic postoperative cases demonstrated a significant rise within the non-peeling group, regarding somatization and depression. Post-operatively, MoCA-B components were statistically comparable among both groups ($p > 0.05$), apart from executive function, abstraction, and naming, which showed higher significantly improvement values in the peeling group. Total MoCA-B score had significantly greater values in the peeling comparing with the non-peeling group after operation (22.5 vs. 20.28 respectively, $p = 0.028$). The incidence of cognitive dysfunction demonstrated a significant rise related to the non-peeling group (90.77% vs. 59.5% in the peeling group – $p = 0.001$). In the peeling group, most components of the SCL-90 score demonstrated a significant reduction after operation ($p < 0.05$), apart from somatization and anxiety that showed comparable findings at the same time points.

A study by **Rijnen et al.** conducted neuropsychological assessments on 261 cases utilizing CNS Vital Signs one day prior to (T0), three (T3), and twelve (T12) months following meningioma operation. The sociodemographically corrected scores of cases on seven cognitive domains were compared to the performance of a normative sample. The results indicated that cognitive performance was impaired both before and after operations. Despite improvements in group

performance, cognitive scores remained significantly less than those of the normative sample until T12 (15).

Another study by **van der Vossen et al**, in which Cognitive complaints have been evaluated with the Cognitive Failures Questionnaire on patients underwent meningioma surgery, also anxiety and depressive symptoms were assessed. Confirmed that forty percent of cases have cognitive and/or emotional issues. Cognitive complaints were reported by thirty-one cases (23%), anxiety by 39 cases (29%), and depressive symptoms by 31 cases (23%). Therefore, it is recommended that cases undergo screening for these issues in order to promptly provide them with the necessary care (16).

A study by **Zweckberger et al**. conducted neurological investigations and neuropsychological assessments on 58 cases who underwent operation for a skull base meningioma. The investigations were conducted at three time points: one day before operation (T1), 3–5 months following operation (T2), and 9–12 months following operation (T3). The results of the study indicated that 23% of cases shown transient neurological disorders and twelve percent showed permanent new neurological deficiencies with different degrees of manifestation following the operation. However, the quality of life postoperatively maintained stable and showed a slight improvement at the T3 follow-up investigation (60.6 ± 21.5 vs 63.6 ± 24.1 points). No impact was found on anxiety or depression. Within the initial months following operations, long-term verbal memory, working memory, and executive functioning were slightly impacted and seemed to be the most susceptible to impairment by the tumor or the resection. However, almost all cases had stable or improved conditions during long-term follow-up investigations following one year (17).

Our research limitation is lack of long term follow up for cases that was planned to be done. Corona epidemic plays a major role in limiting moving between towns, easy contacting patients.

Conclusion

Consideration of the postoperative quality of life is a cornerstone of the neurosurgical care and practice especially for the management of brain neoplasms. one of the most significant parameters of the life quality is the neurocognitive functions which can be affected by Meningiomas of the anterior and middle cranial fossae that in relation to the optic apparatus (perioptic meningiomas) especially when there is significant compression of the frontal and temporal lobes. The use of a highly demanding cavernous wall peeling approach can significantly improve the neurocognitive functions of the patients who suffer from a benign lesion and in turn improve their intermingling with the society with less affection of their productivity.

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