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Research Article

Quality of Life after Intracranial Tumor Surgery -

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ABSTRACT

Objective: Surgical treatment is always interwoven with risks of complications, and even in uneventful course the decrease in quality of life has to be expected. The primary objective of the study was to assess quality of life after surgical treatment of intracranial tumors.

Material and Methods: The 300 consecutive patients operated on because of intracranial tumors were prospectively evaluated, using quality of life questionnaires: EORTC QLQ-C30 and the EORTC QLQ-BN20 on admission to hospital, on the fifth day and 30 days after surgery.

Results: Medium quality of life before the surgery was 0.706, five days after 0.614, 30 days after treatment 7.707. The differences were significant ($p > 0.05$). The greatest reduction in the quality of life were noted in patients with low grade gliomas (I, II WHO) and the extracerebral tumors (meningiomas and schwannomas). Thirty days after treatment the improvement of the quality of life in all groups was observed, the highest reported in patients after surgery of meningioma and schwannoma, the lowest in metastases.

Conclusions: Intracranial surgical procedures adversely affect the quality of patients only in the early postoperative period independent on the type of tumor, but in the late period meningiomas and schwannomas are correlated with significant improvement.

Keywords: Brain tumor; Surgical treatment; Quality of life

INTRODUCTION

Intracranial tumors are of various origin and they compromise the quality of life in different ways and mechanisms. Intrinsic brain tumors such as astrocytomas alter the brain structure and connectivity. Extrinsic tumors such as meningiomas or schwannomas may disrupt cranial nerves, but also compress the brain tissue. All of these processes may result in raised intracranial pressure in general.

The treatment of intracranial tumors may be operative or non-operative. The decision belongs to the patient after the discussion with a physician concerning all the risks and possible benefits of each treatment.

Surgical treatment is always interwoven with risks of complications, and even in uneventful course some decrease in quality of life has to be expected. The complications rates after particular neurosurgical procedures are published, but the quality of life after the surgical procedures may significantly vary even in uncomplicated course of treatment. Therefore we have decided to make a prospective analysis of the quality of life in all the consecutive patients after intracranial tumor surgery in the first 30 days. We have assumed that significant variations between patients with different kinds of tumors, more or less benefiting from better or less proven efficacy of surgical treatment versus other options could have impact on decisions, patients' consent and even on workers compensation and sick leave planning.

Low-grade gliomas are characteristic of young people and middle-aged people, whereas malignant glial tumors, in particular glioblastoma multiforme tumors occur in older people. A large group of intracranial tumors are meningiomas, which are usually benign. They are often seen in women over 40 years of age. Unfortunately, a common group of brain tumors are metastases, which can represent up to 40% of intracranial tumors. Each of the above proliferative lesions located intracranially may cause many symptoms. These may be general symptoms that are the consequence of increased intracranial pressure, manifested as headache, nausea and vomiting or altered consciousness. Furthermore, the location of the tumor in various structures of the brain results in the appearance of neurological deficits that are characteristic to the particular brain area [1]. It should be emphasized that the quality of life in a holistic approach to the patient, especially in oncology has become a parameter as important

as other in the healing process. Quality of life is like overall survival, the life of the patient free of symptoms and the life expectancy with control of a proliferative process [1,2].

The primary objective of the study was to assess quality of life after surgical treatment of brain tumors, and in particular -

Is the operation of brain tumors of the central nervous system performed today using neuronavigation, intraoperative monitoring potential, intraoperative computed tomography research have a significant impact on patient quality of life change?

Is there a relationship between histological diagnosis of cancer and an increased risk of changes in quality of life after surgery?

Is there a relationship between the location of the tumor and the change in quality of life?

The study was approved by the local Bioethics Committee.

MATERIAL AND METHODS

The consecutive patients qualified for the surgery of the intracranial tumor in one neurosurgical department were included in the study. The study group before surgery consisted of 300 people - 156 women and 144 men aged 16 to 89 years (mean age 46.6 ± 15.2 years). The largest group of patients was aged between 41-60 years - 130 patients (43.3%), the second largest group were patients aged 21 to 40 years - 99 patients (33.0%). The evaluation was conducted three times: on admission to hospital, in the fifth day after brain tumor surgery, and 30 days after the surgery. After analyzing all stages of research full documentation with follow-up was obtained in 236 patients. Therefore, the study 64 people were excluded from the analysis. The patients were grouped in accordance to the histopathological diagnosis and due to the location of the tumor.

Every patient filled the quality of life questionnaires three times (on admission to the Department of Neurosurgery in 5 days after tumor surgery of the brain, in the 30 days after surgery). The questionnaires were the EORTC QLQ-C30 (version 3.0.) (The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - C30), and the module QLQ-BN20 EORTC (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Brain Module). Quality of life

was assessed on a scale from 0 to 1, where 0 meant a very low quality of life, 1 - very good quality of life.

Parametric and nonparametric tests were applied to verify hypotheses at $p < 0.05$.

RESULTS

In assessing the quality of life in questionnaires EORTC QLQ-C30 and EORTC-BN20 before surgery the patients achieved an average of 0.706. In the fifth postoperative day patients mean quality of life decreased and was equal 0.614. Thirty days after surgery before eventual further treatment of cancer the standard of quality of life was 0.707, this value was comparable to the preoperative period (Table 1).

The difference between the preoperative period and the fifth day after the surgery turned out to be a negative value - 0.091, Student's t test showed statistical significance ($p < 0.0001$). Between the fifth and thirtieth day after surgery quality of life increased - the average 0.093 proved to be statistically significant ($p < 0.0001$). Between the first evaluation and the third one the difference was minimal and statistically insignificant ($p = 0.91$) (Table 2).

Analyzing the quality of life after surgery in groups according to different histopathological diagnosis the four groups of patients due to the histopathological diagnosis were defined. These were the patients with tumors of low grade glial (I, II World Health Organization grading, WHO) (group 1), patients with high grade glial tumors (III, IV WHO) (group 2), patients with extracerebral tumors, which included meningiomas and schwannomas (group 3) and patients with metastatic tumors (group 4). In the fifth postoperative day in patients the quality of life in all these groups was decreased. The greatest decrease in quality of life after surgery was observed in patients with glial tumors of low grade (I and II according to the WHO) (-0.140) and in patients with extracerebral tumors such as meningiomas and schwannomas (-0.106). Smaller reduction in quality of life was noted in patients with tumors of glial origin with high malignancy grading and metastatic tumors (Table 3). ANOVA testing suggested that between these means was a significant difference ($p = 0.003$). Shapiro-Wilk test did not reject the hypothesis of normal distribution

of data from a group 4, while using Levene test there were significant differences between the variances ($p = 0.014$). For this reason, a non-parametric Kruskal-Wallis test was applied, which confirmed the above result ($p = 0.0025$). Compared groups significantly differ in terms of deterioration of quality of life (Table 3). In order to clarify the test results the post-hoc test LSD (least significant difference) was used. Using the assay has been shown that the reduction in quality of life in patients with glial tumors and benign extracerebral tumors is significantly higher than in the other groups (Table 4).

Thirty days after the surgery a positive average values change in each group was observed. The results show a general increase in the quality of life one month after brain tumor surgery. Shapiro-Wilk test did not reject the hypothesis of normal distribution of data from a group 4. Levene's test did not detect significant differences between variances in the compared groups ($p = 0.15$). This allowed the use of parametric test, one-way ANOVA, which detected that not all the statistical means are equal ($p = 0.013$), therefore between certain means there is a significant difference (Table 5). Using the post-hoc LSD test there was observed that an increase in quality of life between 5 and 30 days after surgery in patients with benign extracerebral tumors is significantly higher than the groups of patients with malignant glial tumors and brain metastases. There was no difference between the mean levels of quality of life in the other groups (Table 6). Thus, patients with tumors of extracerebral origin (group 3) had a significantly greater increase in the quality of life of between 5 and 30 days after the operation.

The quality of life in patients after surgery of tumors was also analysed according to the localization of the tumor.

The patients were divided into four groups according to the localization. The patients with tumors situated mainly in the temporal lobe (group 1), the frontal lobe (group 2), and in the parietal lobe (group 3), in the ventricle system (group 4) and tumor situated extracerebrally (group 5), similar to the group with meningiomas and schwannomas. In 5 days after surgery the quality of life in all groups decreased, the most significantly in patients with frontal lobe tumors (mean -0.104), and in patients after surgery of tumors located intraventricularly (mean -0.109). ANOVA did not detect any significant difference between mean values ($p = 0.99$). Therefore, in patients with tumors situated within a frontal lobe data distribution differed from the normal distribution and the detected difference between the variances (Levene's test) ($p = 0.0005$), used non-parametric Kruskal-Wallis test, which also did not detect significant the difference between the groups in terms of reduction in quality of life ($p = 0.95$). Hence it can be concluded that lowering the quality of life after operation is not related to the localization of the tumor (Table 7).

The changes in the quality of life in subgroups of varying location of a tumor between 5 and 30 days after the operation were analyzed. Positive changes in the average values of each subgroup meant a general increase in quality of life. Shapiro-Wilk test did not reject the hypothesis of normal distribution of data in the subgroups 2, 3 and 4. Levene's test did not detect significant differences between variances in the compared groups ($p = 0.94$). The parametric test one-way ANOVA did not detect any significant difference between the mean changes in quality of life ($p = 0.62$). Thus it can also be concluded that increasing the quality of life after operation does not depend on the location of the tumor (Table 7).

Table 1: Quality of life in the tumor surgery patients.

Quality of life	before surgery	5th day after	30th day after
min	0.16	0.13	0.17
max	1.00	0.99	1.00
median	0.71	0.63	0.72
mean	0.706	0.614	0.707
SD	0.150	0.169	0.158

Table 2: Change of quality of life.

Change of quality of life (n=236)	Period		
	0-5th day	5-30th day	0-30th day
min	-0.70	-0.41	-0.45
max	0.41	0.57	0.38
median	-0.10	0.10	-0.01
mean	-0.091	0.093	0.001
SD	0.181	0.168	0.140
t Student ($t_{cr}=1.97$)	t	7.72	8.50
	p	<0.0001	<0.0001
			0.91



Table 3: Change of quality of life after surgery in groups of patients according to pathology between first and second evaluation.

	groups				
	1	2	3	4	
Change of quality of life (before surgery versus 5th day after)	n	69	51	61	22
	min	-0.70	-0.45	-0.61	-0.28
	max	0.31	0.41	0.33	0.30
	median	-0.15	-0.05	-0.09	-0.03
	mean	-0.140	-0.036	-0.106	-0.022
	SD	0.153	0.166	0.212	0.151
	W	-	-	-	0.972
Shapiro-Wilk test	W_{kr}	-	-	-	0.911
	normal	-	-	-	yes
	F	<u>3.63</u>			
Levene test ($F_{kr}=2.65$)	p	<u>0.014</u>			
	F	<u>4.70</u>			
ANOVA ($F_{kr}=2.65$)	p	<u>0.003</u>			
	H	<u>14.3</u>			
Kruskale-Wallis test ($H_{kr}=7.81$)	p	<u>0.0025</u>			

Table 4: Quality of life and histologic group in the fifth day.

Group	LSD test indicated are differences $p < 0.05$			
	1	2	3	4
	M=-.1398	M=-.0363	M=-.1060	M=-.0223
1		<u>0.002</u>	0.275	<u>0.007</u>
2	<u>0.002</u>		<u>0.038</u>	0.775
3	0.275	<u>0.038</u>		0.056
4	<u>0.007</u>	0.755	0.056	

Table 5: Change of quality of life after surgery in groups of patients according to pathology between second and third evaluation.

	Groups				
	1	2	3	4	
Change of quality of life between second and third evaluation	n	69	51	61	22
	min	-0.412	-0.289	-0.313	-0.318
	max	0.572	0.300	0.456	0.325
	median	0.073	0.074	0.126	0.064
	mean	0.093	0.052	0.136	0.026
	SD	0.162	0.142	0.169	0.194
	W	-	-	-	0.940
Shapiro-Wilk test	W_{kr}	-	-	-	0.911
	normal	-	-	-	yes
	F	1.80			
Levene test ($F_{kr}=2.65$)	p	0.15			
	F	<u>3.66</u>			
ANOVA ($F_{kr}=2.65$)	p	<u>0.013</u>			

Table 6: Quality of life and histologic group on the fifth day.

Group	LSD test significant differences are underlined $p < 0.05000$			
	1	2	3	4
	M=.09346	M=.05213	M=.13613	M=.02605
1 1		0.172	0.139	0.094
2 2	0.172		<u>0.007</u>	0.532
3 3	0.139	<u>0.007</u>		<u>0.007</u>
4 4	0.094	0.532	<u>0.007</u>	

**Table 7:** Quality of life and tumor localization on the fifth day.

		Group				
		1	2	3	4	5
worsening of the quality of life (5th day)	n	52	45	18	13	76
	min	-0.697	-0.333	-0.288	-0.471	-0.610
	max	0.407	0.174	0.158	0.313	0.333
	median	-0.102	-0.106	-0.097	-0.117	-0.081
	mean	-0.096	-0.104	-0.086	-0.109	-0.096
	SD	0.169	0.134	0.126	0.225	0.218
Shapiro-Wilk test	W	-	0.942	0.979	0.979	-
	W _{kr}	-	0.945	0.897	0.866	-
	normal	-	no	yes	yes	-
Levene test (F _{kr} =2.42)	F	5.23				
	p	0.0005				
ANOVA (F _{kr} =2.42)	F	0.047				
	p	0.99				
Kruskala-Wallis test (H _{kr} =9.49)	H	0.68				
	p	0.95				

DISCUSSION

The methods of treatment of intracranial tumors are evolving rapidly. Surgical treatment has in many cases advantages over other methods, allows to obtain histologic diagnosis, also to reduce tumor mass, which may improve existing neurological symptoms. In some cases, tumors, especially glial cells, macroscopically may be impossible to distinguish from healthy brain tissue, also can be located in the surrounding structures functionally important. Therefore, it is necessary to use supporting tools, such as neuronavigation, intraoperative neurophysiology monitoring, computed tomography, magnetic resonance, or intraoperative ultrasound. These tools seem to improve the safety of operations and allow better volumetric tumor removal.

Quality of life is now often used in clinical trials as an indicator of the severity of the disease or effectiveness of treatment [1-3]. In our study, the method used is a proven and widely used tool to assess quality of life in multidimensional aspect. The average quality of life measured in questionnaire EORTCQLQ-30 and EORTCQLQ-BN20 before the surgery was 0.706, 5 days after treatment 0.614, 30 days after surgery 7.707. After 5 days after surgery there was a significant decrease in quality of life, and after 30 days the level of quality of life significantly increased and reached a level of quality of life prior to treatment.

Many factors may reduce quality of life. Certainly they are all neurological deficits, seizures, as well as the fear and anxiety associated with surgery and the effects of the operation. This is confirmed by research Giovagnoli et al., which showed significant anxiety patients in the preoperative associated with the expectation of diagnosis [2, 4]. In a study Benevicius et al., the quality of life decreasing factors in the preoperative period were insomnia, fatigue, headache and uncertainty about the future [3]. Cheng et al., analyzed patients with glial brain tumors preoperatively [4]. Examining the quality of life questionnaire EORTC QLQ-30, the median for emotional area was 66.7, for the social 75.0 for cognitive 83.3, 86.7 for physical, for functional - 91.7 (assessing quality of life in a linear scale from 0 to 100, the higher the value the better the results). These results suggested that patients had

more difficulty in the areas of social and emotional than cognitive, physical and functional areas [4,5].

In a study of Shin et al., patients with higher functional exercise capacity had significantly better performance and lower symptom scores in all positions of QLQ-C30 and QLQ-BN20 (lower rating - less severe symptom / problem) than patients with lower functional capacity in the Karnofsky scale. In the same study, the authors emphasized that patients who had undergone the same operation of a brain tumor had a better quality of life compared to patients who had been treated non operatively and with adjuvant treatment (worse functioning, lower quality of life, greater uncertainty about the future, larger deficits communications) [5].

Jakola et al. [6] in studies of patients with gliomas EQ-5D index, observed preoperatively mean 0.76, 6 weeks after the operation 0.75. There was no significant difference between the values. In these studies and all the daily activities were significantly changed with a worse outcome following surgery. The dimensions such as: mobility, self-care, pain, discomfort, anxiety and depression were not changed. The authors drew attention to the timing of testing after the operation - 6 weeks after surgery. They stressed that the previous assessment would be substantially influenced by short-term postoperative symptoms, but too late assessment would be inappropriate due to the significant growth of the tumor and adjuvant therapy [6]. This could also explain the decrease in overall quality of life in 5 days after tumor resection in our study.

In our study, the greatest decrease in quality of life was observed in patients with low grade glial tumors (I, II WHO) and in patients with tumors situated extracerebrally such as meningioma and schwannoma, the smallest - in patients with high grade gliomas (III, IV WHO) and metastatic tumors. Thirty days after treatment the quality of life improved in all the groups. The best quality of life was reported in patients after surgery of meningioma and schwannoma, the lowest after surgery of metastatic tumors.

In a study Salo et al., patients with malignant glioma (grade III and IV according to WHO) in the preoperative period had the lowest quality of life [7]. Chiu et al. [8] reviewed the literature on the quality



of patients with primary and metastatic tumors of the brain. After this analysis, the authors concluded that patients with primary brain tumors had better social and functional well-being than patients with a secondary cancer.

Other elements of quality of life were similar [8]. Another report by Chiu et al. compared the differences in the quality of life in patients with primary brain tumors and metastatic tumors according to questionnaires QLQ-BN20 and QLQ-C30 [9]. Performance status of patients in both groups was similar. Patients with primary brain tumors and metastatic brain had the following values: physical function - a weighted average of 79.18 and 74.93, the overall quality of life - 61.88 and 59.44, functioning in the role - 67.37 and 75.00 and emotional functioning - 70.44 and 71.86. The values were not statistically significant. Only cognition (the QLQ-C30) was significantly worse in patients with primary brain tumors (p-value = 0.0199). The patients with metastatic tumors and the primary tumors had very similar profiles of quality of life [9]. In a study of Shin et al., patients with gliomas (39.7%) had a significantly lower physical, cognitive and social functioning and higher uncertainty of the future, movement disorders and disturbances in communication compared with patients with meningiomas brain (P <0.001-0.02) [5]. Tsay et al. in studies in patients with benign tumors of the brain did not show any significant change in quality of life 1 month after surgery [10].

In the present study conducted after surgery (5 day after treatment) there was no effect of the position of the tumor to reduce quality of life. In contrast, 30 days after surgery patients quality of life increased, but the location of the removed tumors also had no influence on it.

Liu et al. [11] demonstrated that the tumor location is correlated with the occurrence of certain symptoms, which may be reflected in the quality of life. Patients with tumors of the left hemisphere may have communication problems even before treatment. In addition, tumor location can affect mood changes that may result from damage to the left hemisphere, whereas anxiety may result from damage to the right hemisphere. Depression can be more common in patients with malignant gliomas situated in the left hemisphere. This is confirmed by studies of patients with tumors of low grade glial situated in the frontal cortex and the ventral change situated in the temporal cortex, which showed statistically significant changes in mood worse after surgery compared to patients with tumors situated in the other structures of the brain. Cognitive disorders may also be associated with the location of the tumor. Tumors of the left hemisphere were associated with decreased performance in tests of verbal, and processes located in the right hemisphere of the brain lead to reduced performance during face recognition. In another study, patients with low-grade gliomas greater cognitive disability found in patients with tumors situated in the dominant hemisphere. Progression of the cancer can affect the severity of cognitive function [7]. According to Salo et al., patients with tumors situated on the right or on the front portion have a worse quality of life as compared to patients with tumors situated on the left side of the brain and posteriorly [7]. In studies of Giovagnoli et al., patients with tumors situated in the right hemisphere and in front of, and in the postoperative period had the best quality of life [12].

Schucht et al. paid attention to the position of low-grade tumors and safety of their operations, especially gliomas located centrally [13]. The authors emphasized that the treatment of these tumors is feasible and safe when used is adequate intraoperative mapping. A comparison group of patients with tumors situated centrally and

patients with tumors front of the frontal lobe. Mild neurologic deficits had similar severity. Relief deficit was observed in 12.1% of patients with tumors situated centrally and 83.9% for patients with tumors in front of the frontal lobe. In patients with tumors situated centrally we gave a poor control of seizures, which may ultimately affect the quality of life of these patients [13].

By Jakola et al., patients with changes in the occipital lobe demonstrated a decrease in quality of life after the procedure. Decreased visual function was associated with the loss of independence and reduced quality of life. It was also reported that patients with major visual impairment had significantly impaired cognitive performance [6]. According to Cheng et al., there was no difference in the evaluation of the quality of life between patients with tumors situated supratentorially and infratentorially between patients with tumors of the left and right hemispheres, and between patients with tumors situated within, the various lobes, as well as in patients with normal and disordered cognitive function [4]. Whittle et al. compared the quality of life of patients with intracranial tumors to spine degenerative disease preoperatively. They found that patients with disease of the spine during this period had worse quality of life in many domains and mood compared to the patients with a brain tumor [14].

Jakola et al. concluded that modern neurosurgical procedures did not affect the quality of life of patients with brain tumors, quality of life was also not a result of treatment. They stress the utmost importance of avoiding new deficits, as they can have a serious adverse effect on the quality of life of patients with brain tumors [6].

CONCLUSIONS

Surgery of intracranial tumors affect the quality of life mainly in the first days after the procedure. One month after the surgery the quality of life reaches the level from the preoperative period.

Tumor pathology has an impact on quality of life. In the first days after surgery the quality of life was lower in the group of low grade glial tumors and benign meningiomas and schwannomas. In contrast, 30 days after the operation the lowest quality of life was observed in patients with metastatic tumors.

There was no correlation between the localization of the tumor and the quality of life.

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