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Predictive factors of complications post intracranial meningioma surgery leading to early unplanned reoperations — a single center study

Borys M. Kwinta[1], Roger M. Krzyżewski[1], Kornelia M. Kliś[2], Marcin R. Dragan[2], Paulina Donicz[2], Małgorzata Gackowska[2], Krzysztof Stachura[1], Marek Moskała[1]

[1]Department of Neurosurgery and Neurotraumatology, Jagiellonian University Medical College, Kraków, Poland
[2]Jagiellonian University Medical College, Kraków, Poland

Corresponding author: Borys M. Kwinta, MD, PhD
Department of Neurosurgery and Neurotraumatology, Jagiellonian University Medical College
ul. Botaniczna 3, 31-503 Kraków, Poland
Phone: +48 12 424 86 62; E-mail: bmkwinta@gmail.com

Abstract: Introduction: Complications occurring after neurosurgical procedures which lead to reoperations are associated with poor treatment outcomes. The aim of our study was to establish predictive factors of unplanned early reoperations after intracranial meningioma removal.
Materials and Methods: We retrospectively analyzed 177 patients who underwent craniotomy due to an intracranial meningioma. Early reoperation was defined as reoperation during the same hospital stay. We used a $\chi 2$ test for proportional values and t-test and Mann-Whitney U tests as appropriate for continuous variables. To determine the potential predictors of early reoperation we used univariate and multivariate logistic regression analyses.
Results: A total of 13 (7.34%) patients underwent unplanned early reoperation. These patients underwent retrosigmoid craniotomies (25.00% vs. 6.40%; $p = 0.047$), suffered from ischemic heart disease (66.67% vs. 6.64%; $p < 0.01$) and atrial fibrillation (60.00% vs. 6.25%; $p < 0.01$), were receiving heparin (50.00% vs. 6.74%; $p < 0.01$) and anticoagulants (66.67% vs. 6.21%; $p < 0.01$) significantly more often than the general study population. In multivariate logistic regression analysis anticoagulant use (OR: 31.463; 95% CI: 1.139–868.604; $p = 0.04$) and retrosigmoid craniotomy (OR: 6.642; 95% CI: 1.139–38.73; $p = 0.034$) remained independently associated with a higher risk of early reoperation.
Conclusions: Patients who underwent retrosigmoid craniotomy, those with a history of ischemic heart disease or atrial fibrillation and those who take heparin or anticoagulants are more likely to require early reoperation. Retrosigmoid craniotomy and anticoagulant use are independent risk factors for early reoperation.

Key words: complications, reoperations, meningioma.

Introduction

Intracranial meningiomas are one of the most frequently diagnosed primary brain tumors [1]. They are typically benign and account for about 33% of all primary brain tumors [2]. Their incidence increases with age and they affect women more commonly than men [3, 4]. One of the most prevalent problems of meningioma surgeries is a high rate of recurrence of the meningioma. Benign meningiomas have a risk of recurrence between 10–32% within 10 years of the primary surgery [5, 6]. One of the strongest predictors of recurrence is incomplete resection [7, 8]. Therefore it is important to achieve total resection of the tumor. However, these surgeries may carry a significant risk of complications such as postoperative bleeding, brain edema, vascular insults (arterial or venous), liquorrhea or increased intracranial pressure. The possible complications of meningioma removal have been analyzed before in terms of postoperative bleeding [9] and venous infarcts [10, 11]. However, after a thorough search of the literature, there are very few studies that analyzed all possible complications which might require reoperation in terms of intracranial meningioma surgery. Therefore we decided to find predictive factors of early reoperation after benign meningioma resection.

Patients and Methods

We retrospectively analyzed 181 patients hospitalized between January 2014 and January 2016 who underwent craniotomy for intracranial meningioma. We included in our study only patients with histologically confirmed benign meningiomas. From their medical records we obtained detailed medical histories including previous diseases, current medications and blood test results taken up to 24 hours before the surgery. We also obtained tumour characteristics, details about the surgery including date, cause, type and side of the craniotomy and whether the doctor who performed the surgery and their assistant were board certified specialists in neurosurgery. Early unplanned reoperation was defined as reoperation that occurred during the same hospitalization. Completeness of tumour resection was assessed using the Simpson Grading scale [12]. All patients in our department are routinely prepared for surgery by cessation of antiplatelets and anticoagulants. Cessation of these drugs is preformed 14 days prior to any surgery and patients are switched to low-molecular weight heparin which is then ceased 24 hours prior to the surgery.

Statistical analysis

For statistical analysis we performed a χ^2 test for proportional values and T-test and Mann-Whitney U tests as appropriate for continuous variables. To determine the potential predictive factors of reoperation after benign meningioma removal we used

univariate and multivariate logistic regression analyses. P-values less than 0.05 were considered to be statistically significant. A threshold p-value of <0.1 was used to qualify data for multivariate logistic regression analysis. Forward logistic regression analysis was followed by backwards logistic regression analysis. To perform all statistical analyses we used RStudio v.10 for Windows (Statsoft, Poland).

Results

Our study group consisted of 181 patients with 132 (72.92%) of them females. The mean age was 60.28 ± 12.61 years and the mean Simpson grade was 1.86 ± 0.76. The meningioma location is shown in Figure 1. The most common complication that required early reoperation was postoperative hemorrhage (46.15%), followed by liquorrhea (38.46%) and brain edema or venous infarction (15.38%). A total of 13 (7.18%) patients required early reoperation. These patients suffered from ischemic heart disease (16.67% vs. 0.59%; p <0.01) and atrial fibrillation (25% vs. 1.18%; p <0.01) significantly more often than the general study population. They also took β-blockers (33.33% vs. 11.83%; p = 0.03) and angiotensin-converting-enzyme (ACE) inhibitors (33.33% vs. 10.06%; p = 0.01) significantly more often (Table 1). The result of the coagulation parameters stayed within normal range (Table 2) Patients who underwent early reoperation were more likely to have undergone a retrosigmoid craniotomy (16.67% vs. 3.55%; p = 0.03). We found no statistically significant difference between meningioma location and Simpson grade (2.00 ± 0.50 vs. 1.85 ± 0.78; p = 0.57) in terms of early reoperative risk (Table 3). In multivariate logistic regression analysis, after adjustment for all possible confounders, anticoagulants (OR: 31.463; 95% CI: 1.139–868.604; p = 0.04) and retrosigmoid craniotomy (OR: 6.642; 95% CI: 1.139–38.73; p = 0.034) remained independently associated with a higher risk of early reoperation (Table 3).

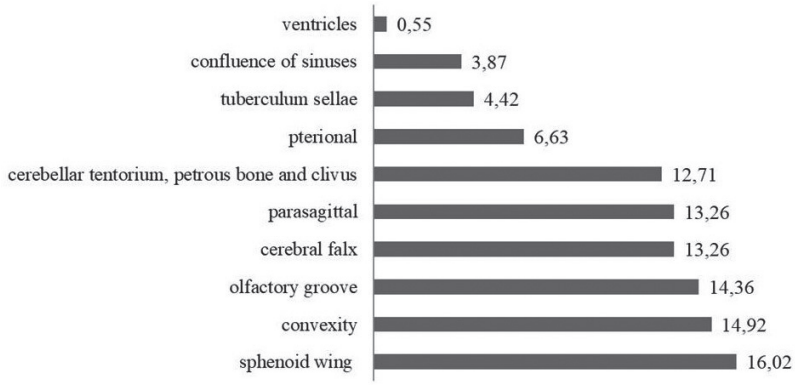

Fig. 1. Intracranial meningioma location.

Table 1. Clinical data of the study group.

	Reoperation (n = 13)	No reoperation (n = 181)	p-value
Age [years] ± SD	61.75 ± 10.44	60.14 ± 12.77	0.67
Female gender [%]	66.67	73.37	0.61
Medical history			
Hypertenstion [%]	50.00	44.38	0.71
Diabetes mellitus [%]	0.00	16.57	0.13
Cigarette smoking [%]	0.00	14.79	0.15
Alcohol abuse [%]	0.00	4.14	0.47
Ischemic heart disease [%]	16.67	0.59	<0.01
History of heart attack [%]	0.00	1.18	0.70
History of ischemic stroke [%]	16.67	4.14	0.053
Atrial fibrillation [%]	25.00	1.18	<0.01
Lungs diseases [%]	0.00	3.55	0.51
Hyperthyroidism [%]	0.00	2.37	0.59
Hypothyroidism [%]	8.33	6.51	0.81
Hypercholesterolemia [%]	8.33	2.96	0.31
Current medications			
Acetylosalicylic acid [%]	0.00	3.55	0.51
Beta-blockers [%]	33.33	11.83	0.03
Angiotensin-converting-enzyme inhibitors [%]	33.33	10.06	0.01
AT_2-blockers [%]	0.00	2.37	0.59
Calcium channel blockers [%]	8.33	8.88	0.95
Diuretics [%]	25.00	14.79	0.34
Steroids [%]	8.33	7.10	0.87
Antidiabetic therapy [%]	0.00	5.92	0.39
Insulin [%]	0.00	3.55	0.51
Heparin [%]	8.33	0.59	0.01
Anticoagulants [%]	8.33	1.18	0.04
Nitrates [%]	0.00	0.59	0.79
Statins [%]	0.00	7.69	0.32

Table 2. Laboratory results of the study group.

	Reoperation (n = 13)	No reoperation (n = 181)	p-value
Blood test results preceding surgery			
White Blood Cell count [10^3/µl] ± SD	9.63 ± 3.06	8.97 ± 6.65	0.75
Red Blood Cell count [10^3/µl] ± SD	4.57 ± 0.51	4.60 ± 0.50	0.85
Mean Corpuscular Hemoglobin [pg] ± SD	89.08 ± 3.95	87.12 ± 4.19	0.13
Hematocrit [%] ± SD	11.61 ± 0.78	11.56 ± 0.79	0.84
Mean Corpuscular Hemoglobin Concentration [g/dl] ± SD	30.21 ± 1.41	29.51 ± 1.64	0.17
Mean Corpuscular Volume [µm^3] ± SD	6.60 ± 2.01	6.17 ± 2.80	0.62
Platelet count [10^3/µl] ± SD	223.09 ± 62.81	249.90 ± 66.32	0.19
Prothrombin Time [s] ± SD	4.21 ± 0.38	4.38 ± 0.46	0.23
International Normalized Ratio ± SD	28.29 ± 4.46	27.67 ± 3.92	0.62
Activated Partial Prothrombin Time [s] ± SD	13.82 ± 1.68	13.58 ± 1.61	0.64
Creatinine [µmol/l] ± SD	1.03 ± 0.07	1,00 ± 0.07	0.26
Glucose [mmol/l] ± SD	66.27 ± 13.43	77.61 ± 50.19	0.46

Table 3. Details of surgeries.

	Reoperation (n = 13)	No reoperation (n = 181)	p-value
Surgery during weekend [%]	16.67	21.30	0.70
"On call" hours of surgery [%]	0.00	1.80	0.72
Bone flap removal [%]	80.00	86.36	0.57
Operator specialized [%]	83.33	89.35	0.52
Assistant specialized [%]	41.67	41.42	0.99
Simpson grade	2.00 ± 0.50	1.85 ± 0.78	0.57
Craniotomy type			
Fronto-temoporo-parietal [%]	0.00	4.73	0.44
Fronto-temporo-occipital [%]	0.00	0.59	0.79
Fronto-parietal [%]	16.67	19.53	0.81
Parieto-temporal [%]	0.00	5.33	0.41

Table 3. Cont.

	Reoperation (n = 13)	No reoperation (n = 181)	p-value
Parieto-occipital [%]	8.33	2.37	0.22
Parietal [%]	16.67	9.47	0.42
Frontal [%]	33.33	21.89	0.36
Pterional [%]	8.33	17.16	0.43
Suboccipital [%]	0.00	12.43	0.19
Retromastoid [%]	16.67	3.55	0.03
Right side [%]	41.67	55.03	0.37
Left side [%]	58.33	53.85	0.76
Meningioma location			
Parasaggital [%]	25.00	12.43	0.21
Cerebral falx [%]	0.00	14.20	0.16
Olfactory groove [%]	16.67	14.20	0.81
Cerebellar tentorium and petrous bone [%]	8.33	13.02	0.64
Pterional [%]	0.00	7.10	0.34
Convexity [%]	25.00	14.20	0.31
Confluence of sinuses [%]	8.33	3.55	0.41
Tuberculum sellae [%]	0.00	4.73	0.44
Sphenoid wing [%]	16.67	15.98	0.95
Intraventricular [%]	0.59	0.00	0.78

Discussion

We found that ischemic heart disease, atrial fibrillation, prior beta-blocker and ACE inhibitor use, and anticoagulant and heparin use are associated with an increased risk of reoperation after intracranial meningioma surgery. After our multivariant regression we found that retrosigmoid craniotomy and a history of anticoagulant use are independently associated with an increased risk of early reoperation after intracranial meningioma surgery.

In the presented study our frequency of reoperation was 7.18%. In terms of all brain tumors, the complication rate was about 17% in the Rolston *et al.* study and

13% in the Sawaya *et al.* study [13, 14]. McLaughlin *et al.* assessed these rates at less than 1% [15].

In our study the rate of unplanned reoperations due to postoperative hemorrhage was about 3%. Nittiby *et al.* established the rate at about 2% [16] for all cranial neurosurgical procedures and Kalfas *et al.* established about 1% [17]. In terms of reoperations on meningiomas due to postoperative hemorrhage, Gerlach *et al.* established the rate at about 7% [9].

An interesting finding of our study was an independent association between retrosigmoid craniotomy and a higher risk of early reoperation. There is limited data presented in other studies concerning type of craniotomy and risk of complications [9, 13–17]. However, the retrosigmoid craniotomy is common surgical approach to challenging tentorial and petroclival meningiomas. An infratentorial location of the tumor was established to be associated with a higher risk of regional complications in the Brell *et al.* study [18].

Another finding of our study was an independent association between heparin or anticoagulant intake and a higher risk of early reoperation. Pre-operative anticoagulant therapy has been proven to be a risk factor for postoperative bleeding in other surgical specialties [19–21]. Also Nittiby *et al.* determined in their study that anticoagulant intake is a risk factor of postoperative bleeding in terms of neurosurgical procedures [16]. However these results were not confirmed by other researchers [15–17]. Similarly Gerlach *et al.* found no significant difference between preoperative coagulation parameters and a higher risk of postoperative bleeding in patients operated on due to a meningioma [9].

In our study we also found that ischemic heart disease and atrial fibrillation were associated with an increased the risk of early reoperation. As both of those diseases can be managed with anticoagulant use, this association might be explained by the above mentioned association. Other researchers focuse limited attention to such factors [9, 13–17]. However, in the Rolston *et al.* study a history of ischemic stroke, which is also correlated with anticoagulant intake, was determined as a predictive factor of complications after neurosurgical procedures [13].

Our study also showed that patients who took β-blockers and ACE inhibitors were at a higher risk of early reoperation. In Rolston *et al.* study, patients who suffered from arterial hypertension and took antihypertensive drugs had a higher risk of complications [16]. Arterial hypertension was also a risk factor for postoperative intracranial bleeding in the Basali *et al.* study [22]. However, we found no association between early reoperation and a history of arterial hypertension. In terms of specific antihypertensive drugs, Smith *et al.* found that ACE inhibitor intake increases the risk of intraoperative hypotensive episodes [23]. Also Cittanova *et al.* discovered that chronic intake of these drugs is associated with a higher risk of postoperative renal impairment [24].

Conclusions

In conclusion, the presence of ischemic heart disease or atrial fibrillation, preoperative anticoagulant therapy, ACE inhibitor or β-blocker intake and retromastoid craniotomy are risk factors of early reoperation after benign meningioma removal and should be taken into consideration before surgery.

Our research was limited by the size of the study group which involved patients from only one neurosurgical facility. Further analysis should be performed on a larger and more varied group of patients. Despite our limitations, this is the first study that analyses the full range of possible risks for neurosurgical complications in terms of benign meningioma removal.

Acknowledgments

None.

Conflict of interest

None declared.

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