



## Risk of seizures before and after neurosurgical treatment of intracranial meningiomas



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### ABSTRACT

**Objective:** To identify variables associated with the development of pre- and postoperative seizures in patients who underwent surgical resection of intracranial meningiomas, in a patient cohort not routinely treated prophylactically with antiepileptic drugs (AED).

**Patients and methods:** Retrospective cohort study of 295 patients that underwent resection of a supratentorial meningioma at Odense University Hospital in between 2007–2015. Multivariate logistic regression was used to identify variables significantly correlating with pre- and postoperative seizures. Retrospective chart review was used to identify the rates of seizure incidence in patients, and the effect of AED on them.

**Results:** The presence of peritumoral edema (OR:18.00, 7.44–43.58) was identified as predictor of preoperative seizure, while headache (OR:0.43, 0.22–0.84) and neurological deficit (OR:0.18, 0.09–0.39) were associated with a reduced incidence of preoperative seizures. The rates of postoperative seizure were increased in meningiomas in the left side (OR:1.91, 1.11–3.29), and reduced for tumor location in the convexity/parasagittal/falx (OR:0.72, 0.59–0.88) as well as in the absence of postoperative complications (OR:0.19, 0.10–0.36). 24.4% of the patients experienced seizures preoperatively, and a complete seizure freedom was achieved in 63.9% of them. 75.6% of the patients did not experience seizures preoperatively, but 15.2% of them then developed seizures postoperatively. A total of 20.3% of the patients experienced seizures after surgery. Time to first seizure in patients that did not experience seizures preoperatively but developed seizures after surgery, was one week (47%). However, first time postoperative seizures were also observed within one month postoperative (21%) and three months after surgery (32%). AED had a treatment success rate of 98.2% in preoperative seizures, and 98.0% in postoperative seizures.

**Conclusion:** Seizures after supratentorial meningioma surgery is common also in patients with no seizures preoperatively and mainly occurs within the first three postoperative months. AED are effective in controlling seizures.

### 1. Introduction

Epilepsy is a frequent symptom accompanying intracranial pathologies, including tumors [1]. Among all benign neoplasms found, meningiomas are the most common, accounting for approximately one third of intracranial neoplasms [2]. A vast majority of meningiomas are benign, and often amenable to surgical resection with good prognosis [3]. Some patients develop seizures resulting from growths in- and outside the brain. Seizures are for some a presenting symptom, while in others the seizures develop after surgical removal of tumor. It is assumed that the pathophysiology behind seizures is a combination of the tumor's mass effect on the epileptogenic cortex, disturbances of

neurotransmitter pathways, and/or acid/base derangements from cerebral edema [4,5]. Antiepileptic drugs (AEDs) can at times fail to completely stop and prevent seizures, and may also have unfavorable neurocognitive side effects [6,7]. Therefore, in Denmark, the administration of AED as prophylactic is not recommended in patients with intracranial tumors. Recurrent seizures negatively impact a patient's quality of life, employment, independence, cognitive functions, and therefore can lead to significant comorbidities, both physical and psychological [2,3].

Nonetheless, seizures in patients with meningiomas and their frequency, predictive factors, and especially their control, have to this day remained relatively understudied. In a recent American systematic

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review and meta-analysis study [2] it was found that only 9 studies in the last 35 years, most of which had a small sample size, had in detail studied the risk factors for seizures associated with meningiomas. Other authors pooled available data from 39 studies reporting seizure rates in supratentorial meningioma. They reported preoperative seizure rates of 29% out of these, seizure freedom was achieved in 69% of the patients. In patients that were seizure-free preoperatively, they reported new seizures occurring among 12% postoperatively. In light of these relatively few prior studies, there is a need for further studies examining both pre- and postoperative variables that could potentially influence the rates of seizures before and after surgery, and additionally if the AED given to the patients indeed have the intended effect. In a recent study regarding AED prophylaxis [8] and its administration among tumor surgeons, it was shown that there is a disagreement as for the indication, duration, and outcome in prescribing AED to their patients.

Since prophylactic AED is not used in Denmark it gives us the unique possibility to perform such studies.

In a patient cohort not routinely treated prophylactically with AED, we examined variables such as clinical characteristics, neuroimaging, and WHO grading of tumor pathology to identify predictors for development of pre- and postoperative seizures in patients surgically treated for a supratentorial meningioma at Odense University Hospital (OUH) from 2007 to 2015.

## 2. Materials and methods

### 2.1. Study design

This study included a retrospective cohort chart review study of 295 adult patients at the Neurosurgical department in Odense University Hospital (OUH), that were treated surgically for intracranial meningiomas (D32.0) in the period of 01.01.2007–31.12.2015. Patients were identified via the ICD code D32.0 in the national patient record database system, and all their medical records and MR scans were reviewed. Inclusion criteria were meningioma diagnosis (D32.0), surgical resection of a meningioma within the requested study period, and sufficient documentation in the medical records with adequate pathology and radiology reports. A total of 313 subjects were identified. However, 18 patients were excluded due to incomplete patient medical records and missing data. The total number of patients was therefore reduced to 295.

The project was approved by The Danish Data Protection Agency and Danish Health Authority. According to Danish legislation individual patient consent was not necessary.

### 2.2. Data collection

All clinical data available for each patient was collected and managed using REDCap electronic data capture tools, a secure web application for building and managing online surveys and databases. The data was divided into 2 main headings (Table 1): preoperative data and postoperative data for an organized and structuralized overview of each patient.

Preoperative data included: gender, tumor size, tumor location including side, headache, peritumoral edema, neurological deficits, tumor size, preoperative epilepsy, AED administration, comorbidities, previous brain radiation therapy, ASA score. Tumor location, size and the presence of peritumoral edema were all taken from admissions and radiology reports. Meningioma locations were categorized as convexity, parasagittal/falx, sphenoid wing, olfactory groove, planum/tuberculum, tentorial, intraventricular, petroclival, and other (including meningioma locations such as cavernous sinus and pituitary fossa that were all grouped together under one variable). The lateralization of the tumor was recorded as right, left, or midline/bilateral. A binary tumor size was evaluated as either  $\leq 4$  cm or  $> 4$  depending on the maximum measured tumor dimension to get an estimation of each tumor and its

**Table 1**  
Patient Characteristics.

Patient characteristic	Number (%)
<b>Gender</b>	
Male	98 (33.2)
Female	197 (66.8)
<b>Side</b>	
Right	112 (38.0)
Left	159 (53.9)
Midline/bilateral	24 (8.1)
<b>Location</b>	
Convexity	111 (37.6)
Parasagittal/falx	76 (25.8)
Sphenoid wing	49 (16.6)
Olfactory groove	10 (3.4)
Planum/tuberculum	16 (5.4)
Tentorial	9 (3.1)
Intraventricular	8 (2.7)
Petroclival	4 (1.4)
Other	12 (4.1)
<b>Headache</b>	
Yes	110 (37.3)
No	185 (62.7)
<b>Peritumoral edema</b>	
Yes	157 (53.2)
No	138 (46.8)
<b>Neurological deficits</b>	
Yes	223 (75.6)
No	72 (24.4)
<b>Size</b>	
$\leq 4$ cm	141 (47.8)
$> 4$ cm	154 (52.2)
<b>Seizure preoperatively</b>	
Yes	72 (24.4)
No	223 (75.6)
<b>Anti-epileptic treatment preoperatively</b>	
Yes	72 (24.4)
No	223 (75.6)
<b>Comorbidity</b>	
Ischemic heart condition	24 (8.1)
Hypertension	95 (32.2)
Diabetes mellitus	27 (9.2)
Other	151 (51.2)
None	105 (35.6)
<b>Previous radiation</b>	
Yes	18 (6.1)
No	227 (93.9)
<b>ASA score</b>	
1	11 (3.7)
2	122 (41.4)
3	35 (11.9)
4	1 (0.3)
5	0 (0.0)
6	0 (0.0)
Unknown	126 (42.7)
<b>Seizures postoperatively</b>	
Yes	60 (20.3)
No	235 (79.7)
<b>Anti-epileptic treatment postoperatively</b>	
Yes	95 (32.2)
No	200 (67.8)
<b>Simpson grade</b>	
1	62 (21.0)
2	157 (53.2)
3	68 (23.1)
4	8 (2.7)
<b>Complications</b>	
Hematoma requiring surgery	11 (3.7)
CSF leakage requiring surgery	2 (0.7)
Pulmonary embolism	3 (1.0)

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