

## Review

## Focused review on seizures caused by meningiomas



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## ABSTRACT

**Background:** Meningiomas belong to the most common intracranial neoplasms in adults. One of the most common symptoms patients with meningioma experience is seizures. However, it remains unclear whether prophylactic preoperative anticonvulsant treatment is worthwhile. Furthermore, it is not clear which patients are likely to experience seizures in the course of the disease. In recent years, many studies and meta-analyses addressed this question with particular contradictory results. Therefore, we aimed to identify the most important risk factors for seizures in patients with meningiomas.

**Methods:** For the search terms “meningioma and seizure”, “meningioma and epilepsy”, and “Simpson and seizure” Medline query identified 865 articles. After applying inclusion and exclusion criteria, 20 papers were chosen for further study. The papers were analyzed for all risk factors for pre- and postoperative risk factors for seizures.

**Results:** Preoperative seizures were mostly associated with extensive brain edema, localization, and bigger tumor size. Even though data were sometimes very contradictory, higher postoperative seizure rate in patients with meningioma was associated with distinct localizations, preoperative seizures, tumor size, brain edema, extent of resection, tumor recurrence, and new neurological deficits. There were no randomized trials showing a prophylactic effect of anticonvulsant drugs.

**Conclusions:** There are relevant risk factors for seizures in patients with meningioma. There is the need for a double blind randomized trial for the prophylactic use of antiepileptic drugs (AEDs).

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## 1. Introduction

Meningiomas account for 25%–30% of intracranial neoplasms. They mostly occur in the adult population with a peak in the sixth and seventh decades [1]. Meningiomas in children are a rarity. One of the most frequent symptoms caused by meningiomas are seizures in about one-quarter of the patients, shown in a major epidemiological study examining 13,038 patients between 2006 and 2010 [2]. Headache was the most frequent symptom in about one-third of the patients, followed by motor-sensory deficits in 29%, seizures in 25%, and mental status disorders in 19% of the patients. Interestingly, patients with meningioma experience seizures even more frequently than patients with primary glioblastoma or brain metastasis. This is in particular a high rate taken into account that meningiomas are extraaxial tumors [3]. For a long time, the high seizure rate in patients with meningioma has been a matter of debate with regard to antiepileptic medication. In

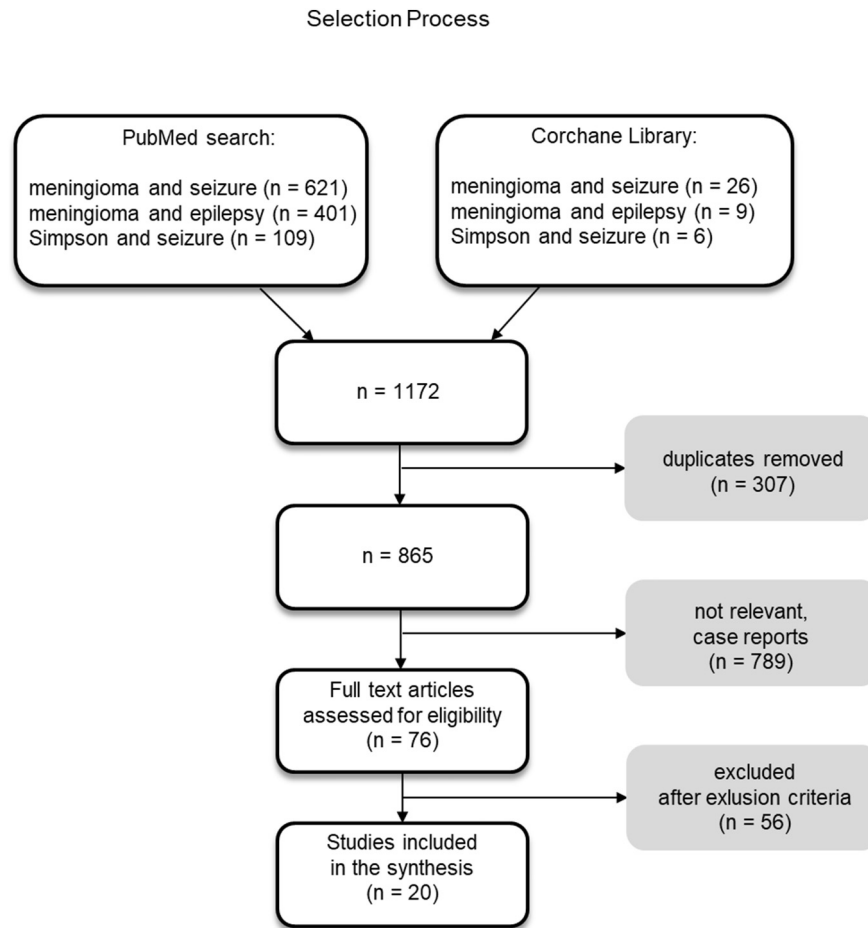
this context, very recent studies aimed to identify the risk factors for pre- and postoperative seizures. The following review summarizes the most important identified risk factors and spotlights the evidence for antiepileptic treatment in either prophylactic or therapeutic indication.

## 2. Methods

Medline query July 2018 in the PUBMED database and in the Cochrane Library identified 865 articles using the terms “meningioma and seizure”, “meningioma and epilepsy”, and “Simpson and seizure”. We set the following inclusion criteria: minimal patient number greater than 20, focus on meningioma, English language, and articles not older than 1995. Seventy-six papers or meta-analyses were left over for substantial investigation and final exclusion process under the criteria of not focussing on seizures, missing statistical analysis, review papers, and no identified risk factors; 20 papers were chosen for further study (Fig. 1). We have analyzed the articles and summarized all risk factors investigated, subdivided into risk factors for pre- and postoperative seizures. Results are summarized in Table 1 for pre- and in Table 2 for postoperative risk factors.

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**Fig. 1.** Flowchart showing the selection process for the focused review.

### 3. Results

#### 3.1. Preoperative seizure rate

Preoperative seizure rates for meningiomas often showed a great variance. Since the included studies varied extensively in the number of patients, we performed our own meta-analysis. We evaluated 8250 patients from 13 studies [2,4–18]. A total of 1939 patients with preoperative seizures were described, leading to a calculated seizure rate of 23% in preoperative patients. Six studies of our final analysis needed to be excluded because of preselection of patients [19–23]. The very large epidemiological study by Zouaoui et al. [2] examined 13,038 patients with meningioma in France and identified a mean seizure rate of 25%.

#### 3.2. Preoperative seizure frequency correlated with epidemiological and clinical data and tumor-specific characteristics

Higher age as risk factor for preoperative seizures could only be shown by one study [24] while seven studies did not find significance [4,5,8,10,14–16]. The gender “female” as risk factor was identified by one [4], the gender “male” by two more recent studies [6,8]. The majority, with seven of the studies investigating the influence of gender on preoperative seizures in contrast did not show any significant influence [5,10,11,14–16,24]. Only two studies investigated the influence of the Karnofsky Performance Score (KPS) on preoperative seizures: Chaichana et al. [4] showed that a KPS of lower than 80 was associated with higher seizure rate, Islim et al. [10] could not find significance. The factor “headache” was positively associated with more preoperative seizures in three studies [4,6,7]. There is an association between preoperative seizures and new postoperative

neurological deficits, shown by three groups [6,10,15]. However, this could not be shown by Chaichana et al. [4]. Four studies could show positive correlation between tumor size and preoperative seizure rate [6–8,16]. Three other studies could not show this before mentioned influence [4,10,24]. Extended edema was shown to be associated with preoperative seizures in all studies investigating it [4–6,9,10,14,16,24]. There is a significant association of higher preoperative seizure rate and tumor localization according to most studies addressing this question [4,6–10,14,15,25] with just one study lacking significance for preoperative seizures [5]. Das et al. and Lieu et al. [14,26] identified temporal, Chaichana et al. [4] tuberculum sellae, and Lieu et al. and Islim et al. [10,14] identified parietal meningiomas to be significantly associated with preoperative seizures. Skardelly et al. [8] further identified parafalcine meningiomas to be significantly associated with preoperative seizures. Tumor side and number of lesions had no significant influence on preoperative seizure rate [10,11]. Skardelly et al. demonstrated an increase of preoperative seizures from World Health Organization (WHO) grade II to III [8]. In all other studies, histological subtype and WHO grade if investigated did not have significant influence on pre- or postoperative seizure rate [11,24,27].

#### 3.3. Postoperative seizures

Reviewing the literature, postoperative seizures were described less frequently than preoperative seizures. In our meta-analysis, 13 papers published a preoperative seizure rate, however, only six studies without preselection of patients reported about the postoperative seizure rate [7,9,12,13,15,17]. We further separated into early and late postoperative seizures. Early postoperative seizures are timely defined as to appear within seven days after surgery. Four studies with 1216 patients

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