



# Predictors of postoperative epileptic seizures after microsurgical treatment in supratentorial single cerebral cavernous malformations: a retrospective study

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## Abstract

**Purpose** Seizures are the most common symptom of supratentorial cerebral cavernous malformations (CCMs). This study aimed to investigate the predictors of seizure freedom in patients with single supratentorial CCMs after microsurgical treatment.

**Methods** Clinical data were retrospectively obtained from 164 patients with CCM (including 98 patients with preoperative seizures, and 66 patients without preoperative seizures) who underwent microsurgical treatment between January 2016 and December 2023 at the First Affiliated Hospital of Sun Yat-sen University.

**Results** After microsurgical treatment, early postoperative seizures ( $\leq 1$  week) occurred in 2 of 98 (2.04%) and 2 of 66 (3.03%) CCM patients with and without preoperative seizures, respectively. The mean length of follow-up for all the patients was  $44.70 \pm 2.04$  months (range: 1–98 months). Sixty-four of the 66 (96.97%) patients without preoperative seizures were seizure free during the follow-up period. Among the patients with preoperative seizures, 77 of 98 (78.57%) patients achieved followed-up seizure remission, including 18 of 28 (64.29%) patients with drug-resistant epilepsy and 59 of 70 (84.29%) patients with drug-controlled epilepsy. Univariate analysis indicated that preoperative seizure duration, drug-resistant epilepsy, tailored resection and the application of intraoperative electrocorticography (ECoG) were important risk factors that affected followed-up seizure remission among patients with preoperative seizures. However, according to multivariate regression, only the use of intraoperative ECoG was an independent predictor related to the followed-up seizure remission.

**Conclusion** For CCM patients with preoperative seizures, intraoperative ECoG was an independent predictor of followed-up seizure remission. The application of intraoperative ECoG is beneficial for improving seizure outcome among CCM patients after microsurgical treatment, especially among patients with preoperative drug-resistant epilepsy.

**Keywords** Cerebral cavernous malformations · Epilepsy · Microsurgery · Electrocorticography · Seizure

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## Introduction

Cerebral cavernous malformations (CCMs) are a unique type of vascular malformation, and they are characterized by clusters of dilated capillaries, which can lead to significant neurological complications, including recurrent seizures and hemorrhagic events [1]. Seizures are the most common symptom of supratentorial CCMs, occurring in 30–40% of patients, and many patients progress to drug-resistant epilepsy (DRE) [2, 3]. The pathophysiology underlying seizures in CCM patients is complex and may involve several factors, including the anatomical location of the malformations, the presence of hemosiderin deposition, and

acute or subacute hemorrhaging [4, 5]. The iron presented in the hemosiderin deposits is a well-known epileptogenic substance. In addition, seizures are also correlated with the number and size of CCMs [1, 5, 6]. Microsurgical resection is considered the most effective treatment for symptomatic CCMs, especially for those with intractable seizures. Achieving gross-total resection (GTR) of the lesion and hemosiderotic rim is traditionally associated with better outcomes. Recent studies suggest that the application of intraoperative electrocorticography (ECoG) may improve the control of postoperative seizures by identifying epileptogenic tissue (including the hemosiderotic rim and adjacent cortex) beyond the visible lesion [7, 8]. Although the extent of resection is critical, the roles of factors such as lesion size, lesion location, and preoperative seizure duration in predicting postoperative seizure outcomes remain controversial [9–11].

This study aimed to investigate the predictors of postoperative seizure outcomes among patients with supratentorial CCMs, focusing on the application of intraoperative ECoG and its impact on long-term seizure freedom. Identifying the factors that influence successful surgical outcomes will provide valuable insights for improving surgical strategies and patient management of patients with CCM-related epilepsy.

## Materials and methods

### Study population

A consecutive series of 164 CCM patients who underwent microsurgical treatment between January 2016 and December 2023 at the First Affiliated Hospital of Sun Yat-sen University were retrospectively enrolled. Among these enrolled patients, 98 had preoperative seizures and 66 did not have preoperative seizures. A total of 76 female and 88 male patients (aged 4–66 years, mean  $33.73 \pm 1.03$  years) were included in the study. Clinical data including age, sex, clinical symptoms, size and location of the CCM, history of hypertension and diabetes, history of antiepileptic drug (AED), postoperative results and complications, were retrospectively analyzed. Drug-resistant epilepsy (DRE) was defined as seizures that occurred for more than 2 years despite antiepileptic treatment with at least 2 adequate and different AEDs. Patients with drug-controlled epilepsy in this study included patients with a single epileptic seizure and patients who had more than two epileptic seizures before surgery and were seizure free after antiepileptic treatment. Patients with multiple CCMs, patients with infratentorial CCMs, and patients with CCMs as well as other brain tumors (e.g., glioma, meningioma, and metastatic tumors) were excluded from the study. Patients with a history of

craniocerebral trauma, craniotomy or other cerebral hemorrhage caused by hypertension, arteriovenous malformation (AVM), moyamoya disease or ruptured aneurysms were also excluded.

### Preoperative imaging examination

All the enrolled patients underwent magnetic resonance imaging (MRI) preoperatively to evaluate peritumoral edema and the location and size of the CCM. The largest diameter of the CCM was the largest axial diameter of the CCM in 2 planes. Susceptibility weighted imaging (SWI) images were used to exclude multiple CCMs. Patients with acute cerebral hemorrhage underwent computed tomography angiography (CTA) to exclude AVM, moyamoya disease and aneurysms. If necessary, digital subtraction angiography (DSA) were performed to further confirm the diagnosis. Long-range video electroencephalogram (VEEG) monitoring was applied for patients with frequent epileptic seizures preoperatively.

### Surgical procedures and intraoperative ECoG

On the day of surgery, intraoperative ECoG was performed on patients with preoperative seizures. The scalp ECoG was recorded at 5 min before and 1 min after anesthesia drug administration. The electrodes on the craniotomy side were then removed. After endotracheal anesthesia, neuronavigation was used to locate the tumor and design surgical incisions. An operating microscope (OPMI PENTERO 800, Carl Zeiss AG) was used to open the dura. When the dura was incised and the cortex was exposed, disinfected cortical electrodes were sequentially placed on the cortex, with an inter-electrode distance of 1 cm, to record the cortical ECoG. The lesion was subsequently removed with the aid of intraoperative neuronavigation. After resection of the CCM, the electrodes were replaced on the resected surface and the cortical margins to record the cortical ECoG. The recording duration was 5 min. If the spiked waves disappeared or were significantly suppressed, the surgery and monitoring could be finished. However, if spiked waves persisted in certain areas, further resection was performed in this part of the glial hyperplasia zone until the spiked waves disappeared or were significantly suppressed. Residual spiked waves located in functional regions that could not be resected were instead managed through postoperative medication. Intraoperative ECoG was introduced into our hospital in April 2019. Since then, intraoperative ECoG has been performed by the same electrophysiologist during elective surgery.

## Follow-up and remission criteria

Early postoperative seizures were defined as epileptic seizures that occurred within one week after microsurgery,

**Table 1** Clinical features of 164 CCM patients with and without preoperative seizures

Characteristics	With pre-operative seizures ( <i>n</i> = 98)	Without preoperative seizures ( <i>n</i> = 66)	<i>P</i> values
Age (years)	31.65 ± 1.26	36.80 ± 1.68	0.013*
Sex (%)			
Female	45 (45.82%)	31 (46.97)	0.895**
Male	53 (54.08)	35 (53.03)	
Clinical symptoms			
Headache (%)	15 (15.31%)	32 (48.48%)	< 0.001**
Dizziness (%)	6 (6.12%)	23 (34.85%)	< 0.001**
Vomit (%)	2 (2.04%)	4 (6.06%)	0.223†
Motor disturbance (%)	2 (2.04%)	8 (12.12%)	0.015†
Neurological deficits (%)	0	2 (3.03%)	0.16†
Sensation disturbance (%)	3 (3.06%)	9 (13.64%)	0.011**
Maximum diameter (mm)	19.32 ± 0.87	24.51 ± 1.63	0.003*
Hemisphere (%)			
Left	40 (40.82%)	35 (53.03%)	0.075**
Right	57 (58.16%)	28 (42.42%)	
Midline	1 (1.02%)	3 (4.55%)	
Localization of CCM (%)			
Frontal lobe	36 (36.73%)	22 (33.33%)	0.179**
Temporal lobe	39 (39.80)	16 (24.24%)	
Parietal lobe	11 (11.22%)	12 (18.18%)	
Occipital lobe	5 (5.10%)	3 (4.55%)	
Insula	2 (2.04%)	1 (1.52%)	
Corpus callosum	1 (1.02%)	3 (4.55%)	
Basal ganglia	2 (2.04%)	5 (7.58%)	
Thalamus	2 (2.04%)	3 (4.55%)	
Preoperative hemorrhage (%)	22 (22.44%)	15 (22.73%)	0.967**
Peritumoral edema (%)	10 (10.20%)	8 (12.12%)	0.7**
Hypertension (%)	3 (3.06%)	3 (4.55%)	0.62**
Diabetes (%)	1 (1.02%)	2 (3.03%)	0.565†
Resection degree (%)			
Residue	3 (3.06%)	3 (4.55%)	< 0.001†
Gross-total resection	77 (78.57%)	63 (95.45%)	
Tailored resection	18 (18.37%)	0	
Postoperative neurological deficits (%)	7 (7.14%)	5 (7.58%)	0.931**
Postoperative Hemorrhage (%)	2 (2.04%)	2 (3.03%)	1.0†
Early postoperative seizure (%)	2 (2.04%)	2 (3.03%)	1.0†
Followed-up seizure freedom (%)	77 (78.57%)	64 (96.97%)	0.001†

CCM cerebral cavernous malformations; \*One way Anova; †Fisher's exact; \*\*Chi-square test;

and late postoperative seizures were defined as seizure that occurred one week after microsurgery. Follow-up seizure remission was defined as being completely seizure-free without AEDs or completely seizure-free with AEDs at the last follow-up before May 2024. Patients who experienced seizures after microsurgery during the period of AED withdrawal were not considered to experience seizure recurrence. The mean length of follow-up for all the patients was 44.70 ± 2.04 months (range: 1–98 months). The degree of resection was divided into residue (lesion or hemosiderin deposition was not completely removed), gross-total resection (lesion and hemosiderin deposition were completely removed) and tailored resection (the lesion, hemosiderin deposition and adjacent cortex were removed). The degree of resection was analyzed by surgical records and postoperative MRI, which was routinely performed 3 months after surgery. AEDs were administered after surgery under the guidance of epilepsy specialists and VEGG.

## Statistical analysis

SPSS version 25.0 software (IBM, Somers, New York) was used to perform the data collection and analyses. The data are presented as the mean ± standard deviation (SD). Student's *t* test was used for the analyses of numerical data, and for categorical data, the chi-square test or Fisher's exact test was performed. A follow-up seizure remission curve was constructed through the Kaplan–Meier method. Stepwise logistic regression was used to detect the predictors of seizure remission during follow-up after microsurgical resection in CCM patients with preoperative seizures. The candidate variables in the model included age, sex, CCM size (> 15 mm) [12], preoperative seizure duration, seizure type, number of seizures, localization of the CCM, preoperative hemorrhage, intraoperative ECoG, drug-resistant epilepsy and resection degree. Significant variables in the univariate logistic regression analysis (*p* < 0.05) were then further analyzed by multivariate stepwise logistic regression. *P* < 0.05 was considered to indicate a statistically significant difference.

## Results

### Clinical characteristics of CCM patients

The clinical characteristics of 164 CCM patients are listed in Table 1. Among these patients, 98 patients experienced preoperative seizures, and 66 patients did not experience preoperative seizures. Patients with preoperative seizures were significantly younger than those without preoperative seizures (*p* = 0.013). The proportions of patients without

preoperative seizures who experienced headache and dizziness were significantly higher than those of patients with preoperative seizures (both  $p < 0.001$ ). In addition, patients without preoperative seizures had a higher risk of motor disturbance and sensation disturbance than patients without preoperative seizures ( $p = 0.015$ ,  $p = 0.011$ , respectively). The differences of sex ratio as well as the proportions of patients who experienced vomiting and neurological deficits were not significant between these two groups. The mean maximum diameter of CCMs in patients without preoperative seizures was significantly larger than in patients with preoperative seizures ( $24.51 \pm 1.63$  vs.  $19.32 \pm 0.87$  mm,  $p = 0.003$ ). There was no significant association between location (including side and brain lobes) and preoperative seizures ( $p = 0.075$ ,  $p = 0.179$ , respectively). The associations among preoperative hemorrhage, peritumoral edema, hypertension, diabetes and preoperative seizures were not significant. The residue rates in patients with and without preoperative seizures were 3.06% and 4.55% ( $p = 0.62$ ), respectively. After surgery, 7 of 98 (7.14%) and 5 of 66 (7.58%) patients with and without preoperative seizures experienced neurological deficits ( $p = 0.931$ ), respectively. Postoperative hemorrhage occurred in 2 of 98 (2.04%) and 2 of 66 (3.03%) patients with and without preoperative seizures, respectively ( $p = 1.0$ ). Two of 98 (2.04%) patients with preoperative seizures experienced early postoperative seizures, and early postoperative seizures occurred in 2 of 66 (3.03%) patients without preoperative seizures. The difference in early postoperative seizure rates between these two groups was not significant ( $p = 1.0$ ). Of the 98 patients with preoperative seizures, 77 (78.57%) were seizure free throughout follow-up ( $49.96 \pm 24.11$  months, range: 8–92 months), while 21 (21.43%) patients continued to experience frequent seizures. A total of 64 of 66 (96.97%) patients without preoperative seizures were seizure free during the follow-up period. Thus, patients without preoperative seizures had a higher rate of followed-up seizure freedom compared with patients with preoperative seizures ( $p = 0.001$ ).

### Characteristics of patients with drug-resistant epilepsy (DRE) vs. Those with drug-controlled epilepsy

The clinical characteristics of 98 CCM patients with preoperative seizures are listed in Table 2, including 28 (28.57%) patients with DRE and 70 (71.43%) patients with drug-controlled epilepsy. There was no significant difference in age or gender between these two groups. The mean maximum diameters of the CCMs in patients with drug-resistant epilepsy and drug-controlled epilepsy were  $17.27 \pm 1.78$  mm and  $20.14 \pm 0.98$  mm, respectively ( $p = 0.136$ ). The mean preoperative seizure duration in patients with DRE was

$90.86 \pm 13.89$  months, which was significantly longer than that in patients with drug-controlled epilepsy ( $20.14 \pm 0.98$  months,  $p < 0.001$ ). In addition, patients with DRE had a greater risk of generalized tonic-clonic or mixed epileptic seizures than patients with drug-controlled epilepsy preoperatively ( $p = 0.038$ ). Twenty-nine of the 70 (41.43%) patients with drug-controlled epilepsy had only one seizure attack before surgery, whereas all the patients with DRE experienced multiple seizures before surgery ( $p < 0.001$ ). In addition, AEDs were administered preoperatively to 55 of 70 (78.57%) patients with drug-controlled epilepsy, while all the patients with drug-resistant epilepsy received AED treatment ( $p = 0.005$ ). The CCMs in patients with DRE were more likely to be located in the temporal lobe (17/28, 60.71%), whereas those in patients with drug-controlled epilepsy were more likely to be located in the frontal lobe (32/70, 45.71%). Between these two groups the difference in the involved lobe was statistically significant ( $p = 0.039$ ), but the difference in the hemisphere of the CCM location was not significant ( $p = 0.247$ ). Hemorrhage caused by CCM was found in 28.57% of patients with drug-controlled epilepsy, which was significantly greater than that in patients with DRE (7.14%,  $p = 0.03$ ).

Intraoperative ECoG was performed in 47 of 98 (47.96%) patients with preoperative seizures, including 29/70 (41.43%) patients with drug-controlled epilepsy and 18 of 28 (64.29%) patients with DRE ( $p = 0.041$ ). Among 70 patients with drug-controlled epilepsy, gross-total resection and tailored resection were achieved in 66 (94.28%) and 2 (2.86%) patients, respectively. Among 28 patients with DRE, 11 (39.29%) patients achieved gross-total resection and 16 (57.14%) patients achieved tailored resection. Patients with DRE had a higher tailored resection rate than patients with drug-controlled epilepsy ( $p < 0.001$ ). Early postoperative seizure occurred in one patient in both these two groups ( $p = 0.492$ ). Followed-up seizure remission was achieved in 18 of 28 (64.29%) patients with DRE, and the remaining 10 patients (35.71%) experienced late postoperative seizures with a mean recurrence time of  $13.50 \pm 3.97$  months. Fifty-nine of 70 (84.29%) patients with drug-controlled epilepsy achieved followed-up seizure remission and 11 (15.71%) patients experienced late postoperative seizure with a mean recurrence time of  $12.82 \pm 3.56$  months. Therefore, patients with drug-controlled epilepsy had a higher rate of followed-up seizure freedom than patients with DRE ( $p = 0.029$ ).

**Table 2** Clinical features of 98 CCM patients with preoperative seizures

Characteristics	Drug-resistant epilepsy ( <i>n</i> = 28)	Drug-controlled epilepsy ( <i>n</i> = 70)	<i>P</i> values
Age (years)	34.75 ± 2.17	30.41 ± 1.51	0.12*
Sex (%)			
Female	11 (39.29%)	34 (48.57%)	0.405**
Male	17 (60.71%)	36 (51.43%)	
Maximum diameter (mm)	17.27 ± 1.78	20.14 ± 0.98	0.136*
Seizure as the first manifestation (%)	25 (89.29%)	60 (85.71%)	0.638**
Preoperative seizure duration (month)	90.86 ± 13.89	4.37 ± 0.67	< 0.001*
Seizure type (%)			
Simple partial only	0	10 (14.29%)	0.038**
Complex partial only	3 (10.71%)	14 (20%)	
Generalized tonic-clonic or mixed	25 (89.29%)	46 (65.71%)	
Number of seizures (%)			
1	0	29 (41.43%)	< 0.001†
>1	28 (100%)	41 (58.57%)	
Preoperative AED (%)	28 (100%)	55 (78.57%)	0.005**
Type of first AED (%)			
Valproic acid	18 (64.29%)	57 (81.43%)	0.215**
Levetiracetam	7 (25%)	9 (12.86%)	
Carbamazepine/Oxcarbazepine	3 (10.71%)	2 (2.86%)	
Lamotrigine	0	1 (1.43%)	
Phenytoin	0	1 (1.43%)	
Hemisphere (%)			
Left	10 (35.71%)	30 (42.86%)	0.247**
Right	17 (60.71%)	40 (57.14%)	
Midline	1 (3.57%)	0	
Localization of CCM (%)			
Frontal lobe	4 (14.29%)	32 (45.71%)	0.039**
Temporal lobe	17 (60.71%)	22 (31.43%)	
Parietal lobe	2 (7.14%)	9 (12.86%)	
Occipital lobe	2 (7.14%)	3 (4.29%)	
Insula	1 (3.57%)	1 (1.43%)	
Corpus callosum	1 (3.57%)	0	
Basal ganglia	0	2 (2.86%)	
Thalamus	1 (3.57%)	1 (1.43%)	
Resection degree (%)			
Residue	1 (3.57%)	2 (2.86%)	< 0.001†
Gross-total resection	11 (39.29%)	66 (94.28%)	
Tailored resection	16 (57.14%)	2 (2.86%)	
Preoperative hemorrhage (%)	2 (7.14%)	20 (28.57%)	0.03†
Peritumoral edema (%)	2 (7.14%)	8 (11.43%)	0.72†
Intraoperative ECoG	18 (64.29%)	29 (41.43%)	0.041**
Postoperative neurological deficits (%)	1 (3.57%)	6 (8.57%)	0.669†
Postoperative Hemorrhage (%)	2 (7.14%)	0	0.08†
Early postoperative seizure (%)	1 (3.57%)	1 (1.43%)	0.492†
Followed-up seizure remission (%)	18 (64.29%)	59 (84.29%)	0.029**
Average recurrence time of late postoperative seizure (month)	13.50 ± 3.97	12.82 ± 3.56	0.899*

CCM cerebral cavernous malformations; ECoG electrocorticography; \*One way Anova; †Fisher's exact; \*\*Chi-square test

### Clinical factors affecting followed-up seizure remission after microsurgical treatment in CCM patients with preoperative seizures

Among 98 CCM patients who experienced seizures preoperatively, 77 (78.57%) patients (including 18 patients with

DRE and 59 patients with drug-controlled epilepsy) were seizure free after microsurgical treatment. The present study revealed that patients with preoperative seizures lasting longer than 2 years had a greater risk of late postoperative seizures than patients with preoperative seizures lasting less than 2 years according to univariate logistic regression



(OR: 3, 95%CI: 1.122–8.024,  $p = 0.029$ ; Table 3). In addition, patients who did not undergo intraoperative ECoG had a higher rate of late postoperative seizures (OR: 0.125, 95%CI: 0.034–0.460,  $p = 0.002$ ). Compared with patients with drug-controlled epilepsy, patients with DRE had a greater rate of late postoperative seizures (OR: 2.98, 95%CI: 1.09–8.148,  $p = 0.033$ ). Tailored resection is one of the important risk factors that affects the rate of followed-up seizure remission in patients with preoperative seizures (OR: 0.174, 95%CI: 0.036–0.836,  $p = 0.029$ ). Age, gender, CCM size, seizure type, number of seizure attacks, CCM location and preoperative hemorrhage were not related to the occurrence of late postoperative seizures after surgery. Furthermore, multivariate stepwise logistic regression revealed that the application of intraoperative ECoG was an independent predictor associated with late postoperative seizures (OR: 0.122, 95%CI: 0.018–0.810,  $p = 0.029$ ). Preoperative seizure duration, DRE and tailored resection were not independent predictors related to late postoperative seizures ( $p = 0.226$ ,  $p = 0.75$ ,  $p = 0.324$ , respectively).

Among 98 patients who experienced preoperative seizures, 47 (47.96%) patients underwent intraoperative ECoG (including 18 patients with DRE and 29 patients with drug-controlled epilepsy). Among these 47 patients, 44 (93.62%)

patients achieved follow-up seizure remission (including 16 of 18 (88.89%) patients with DRE and 28 of 29 (96.56%) patients with drug-controlled epilepsy). In contrast, 18 of the 51 (35.29%) patients who did not receive intraoperative ECoG experienced late postoperative seizures (including 8 of the 10 (80%) patients with DRE and 10 of the 41 (24.39%) patients with drug-controlled epilepsy). Among the 18 DRE patients who underwent intraoperative ECoG, 2 experienced late postoperative seizures, and 8 of the 10 patients who did not undergo intraoperative ECoG experienced late postoperative seizures (Fig. 1A). Among 29 patients with drug-controlled epilepsy who underwent intraoperative ECoG, only one person experienced late postoperative seizures. However, 10 of the 41 patients who had drug-controlled epilepsy and did not receive intraoperative ECoG experienced late postoperative seizures (Fig. 1B). These results indicate that the application of intraoperative ECoG can reduce the risk of late postoperative seizures in patients with drug-resistant epilepsy or drug-controlled epilepsy ( $p = 0.001$ , and  $p = 0.021$ , respectively; Fig. 1). Furthermore, the present study constructed a curve of follow-up seizure remission and compared the follow-up periods for CCM patients with preoperative DRE and drug-controlled epilepsy according to the application of intraoperative ECoG via Kaplan–Meier analysis. The Kaplan–Meier analysis confirmed that intraoperative ECoG was a significant predictor of followed-up seizure remission in patients with preoperative drug-resistant epilepsy or drug-controlled epilepsy ( $p < 0.001$ , and  $p < 0.05$ , respectively; Fig. 2).

Therefore, preoperative seizure duration, DRE and tailored resection were important risk factors that affected the followed-up seizure remission. The application of intraoperative ECoG was an independent predictor related to the followed-up seizure remission.

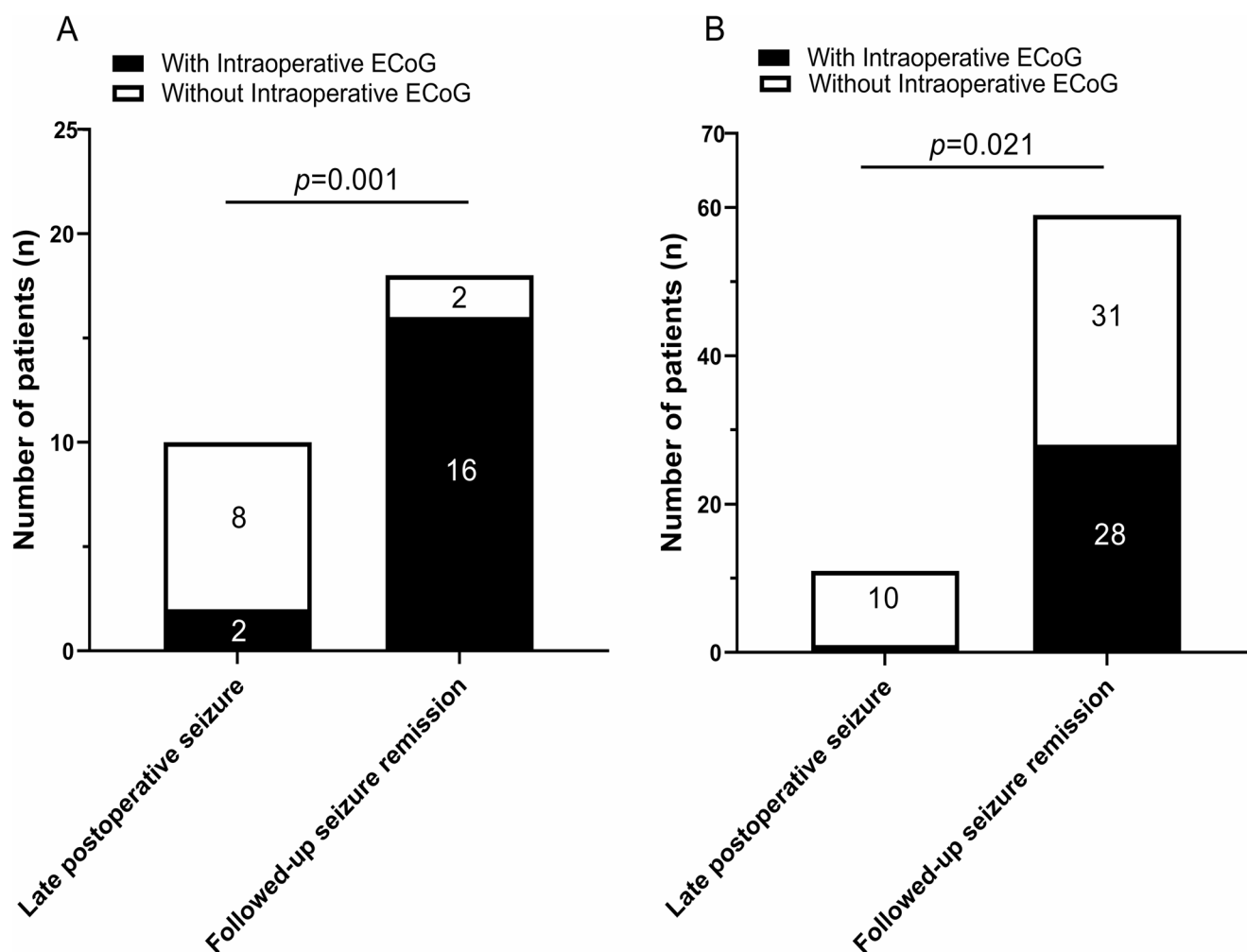
## Discussion

This study identified intraoperative ECoG as an independent predictor of postoperative seizure remission among patients with supratentorial CCMs following microsurgical resection. Our results reinforced previous findings about the importance of real-time neurophysiological monitoring during surgery to optimize seizure outcomes [10, 13–16]. The application of intraoperative ECoG was found to significantly enhance postoperative seizure remission, particularly among patients with drug-resistant epilepsy (DRE). This was consistent with previous studies that demonstrated the effect of intraoperative ECoG in detecting epileptogenic zones beyond the visible lesion, allowing for a higher rate of tailored resections [17–20]. Previous studies have shown

**Table 3** Predictors of late postoperative seizure after microsurgery in 98 CCM patients with preoperative seizures

Predictor	Univariate logistic regression		Multivariate stepwise logistic regression	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Age $\geq 18$ years	0.762 (0.216–2.679)	0.671	-	-
Sex	1.66 (0.624–4.416)	0.31	-	-
CCM size $\geq 15$ mm	1.645 (0.578–4.684)	0.351	-	-
Preoperative seizure duration $\geq 2$ years	3 (1.122–8.024)	0.029	7.577 (0.285–201.64)	0.226
Seizure type	2.095 (0.803–5.467)	0.131	-	-
Number of seizures $> 1$	2.206 (0.675–7.210)	0.190	-	-
Localization of CCM	0.979 (0.708–1.352)	0.895	-	-
Preoperative hemorrhage	0.716 (0.214–2.391)	0.587	-	-
Intraoperative ECoG	0.125 (0.034–0.460)	0.002	0.122 (0.018–0.810)	0.029
Drug-resistant epilepsy	2.98 (1.09–8.148)	0.033	1.703 (0.064–45.274)	0.75
Tailored resection	0.174 (0.036–0.836)	0.029	0.3 (0.027–3.284)	0.324

CCM cerebral cavernous malformations; ECoG electrocorticography

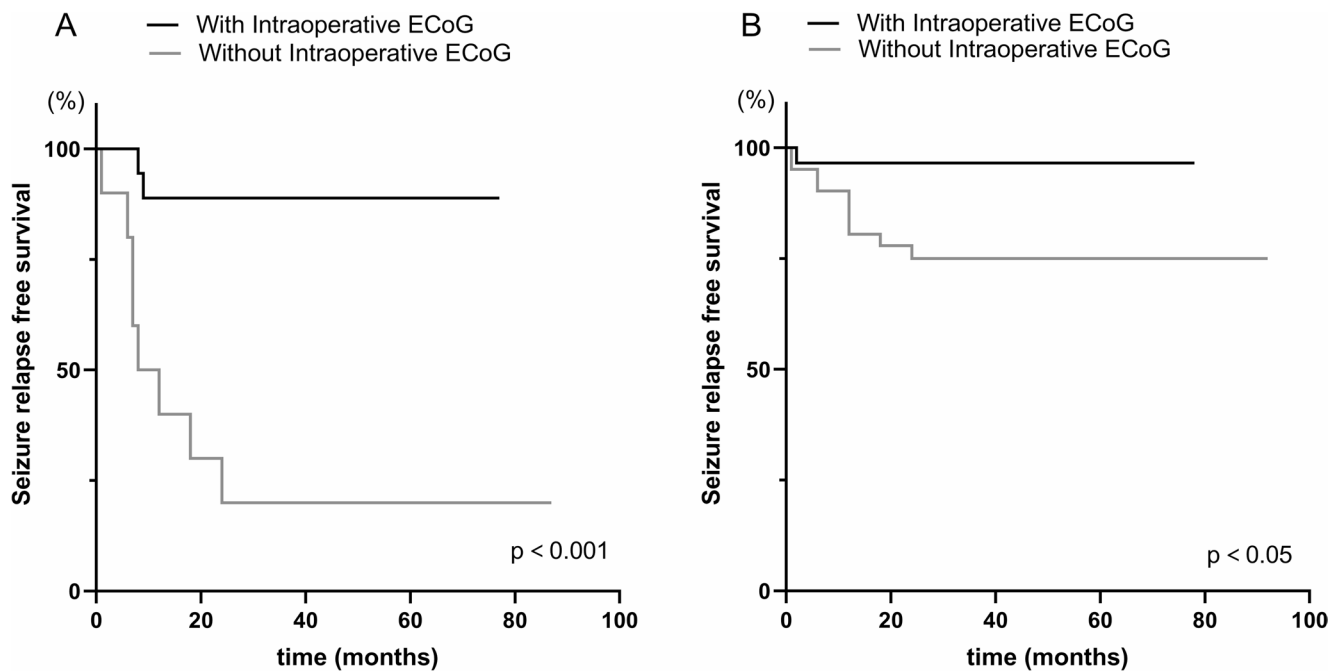


**Fig. 1** Follow-up seizure remission in CCM patients with preoperative drug-resistant epilepsy (A) and drug-controlled epilepsy (B) according to the application of intraoperative electrocorticography (ECoG)

that CCM patients who undergo ECoG-guided resection have a lower rate of seizure recurrence than those who do not undergo this type of intraoperative monitoring [7, 21]. In the present study, followed-up seizure remission was achieved in 18 of 28 (64.29%) patients with DRE and in 59 of 70 (84.29%) patients with drug-controlled epilepsy. With the application of intraoperative ECoG, 44 of 47 (93.62%) patients achieved follow-up seizure remission (including 16 of 18 (88.89%) patients with DRE and 28 of 29 (96.56%) patients with drug-controlled epilepsy). In contrast, 35.29% of patients who did not undergo intraoperative ECoG experienced late postoperative seizures. Multivariate analysis revealed that preoperative factors such as lesion size and location were not independent predictors of seizure outcomes, highlighting the greater predictive value of functional mapping through ECoG over anatomical characteristics [2, 13]. This finding suggested that while surgical planning was informed by lesion characteristics, real-time

intraoperative information was crucial for achieving optimal seizure control [22, 23].

Previous studies have highlighted the importance of achieving GTR to optimize seizure outcomes, particularly in CCM patients who experienced preoperative seizures. Repeated bleeding is a pathological characteristic of CCMs. CCM lesions do not contain neural tissue and therefore do not directly induce seizures; rather, the adjacent tissue is the reason for the seizure. Hemosiderin deposition and its toxic effects on adjacent brain tissue are considered the main causes of seizures; therefore, removing the hemosiderotic rim is a key surgical principle. Intraoperative ECoG can be applied to assess whether epileptic discharges are present in the tumor-adjacent areas or even in distant cortical regions after tumor resection. If epileptic activity is detected in these areas, which are distant from functional regions, further resection is needed. In tumors near functional regions, intraoperative ECoG plays a crucial role in determining whether the adjacent area needs to be removed.



**Fig. 2** Kaplan–Meier analysis of follow-up seizure remission in CCM patients with preoperative drug-resistant epilepsy (A) and drug-controlled epilepsy (B) according to the application of intraoperative electrocorticography (ECoG)

The monitoring of cortical ECoG during surgery is essential to limit the extent of lesion resection to the actual epileptic focus while preserving as much normal brain tissue as possible, thereby reducing unnecessary damage. This is very important because the surgical operation itself may induce additional seizures [7, 23, 24]. In the present study, univariate logistic regression revealed that preoperative seizure duration, DRE, tailored resection and intraoperative ECoG were important risk factors that influence followed-up seizure remission. However, according to multivariate regression, only the use of intraoperative ECoG was an independent predictor of followed-up seizure remission. All the senior neurosurgeons in our unit performed surgery strictly according to the principles of CCMs (removing the hemosiderotic rim unless it involved eloquent areas); therefore, gross-total resection was achieved for most CCMs. However, without the application of intraoperative ECoG, 35.29% of patients (including 80% DRE patients and 24.39% drug-controlled epilepsy patients) experienced late postoperative seizures. After intraoperative ECoG, 93.62% of patients achieved follow-up seizure remission (including 88.89% of patients with DRE and 96.56% of patients with drug-controlled epilepsy). Therefore, our study adds to increasing evidence that intraoperative ECoG plays a critical role, particularly in patients with DRE and when GTR is limited by lesion location near eloquent brain regions. These findings are consistent with the epileptogenic zone (EZ) theory, which posits that seizures may originate from areas beyond the primary lesion. ECoG enables the intraoperative identification of

these epileptogenic zones, which may not be detectable via imaging alone [25]. This enhances the precision of resection, reducing the likelihood of residual epileptic activity.

The incorporation of ECoG into the standard surgical protocol for CCMs offers significant clinical benefits. Our results suggest that ECoG-guided resection should be a routine practice, particularly for patients with DRE, patients with long preoperative seizure duration or patients for whom complete resection is not possible. The application of ECoG minimized the risk of postoperative seizures while avoiding the extensive resection of eloquent brain areas. These findings support the broader application of ECoG in improving surgical outcomes and quality of life for patients with CCM-related epilepsy [18, 19, 26].

## Strengths and limitations

While this study provides important insights, several limitations should be acknowledged. First, as a single-center retrospective analysis, the generalizability of our findings may be limited. Further multicenter studies with larger cohorts are needed to confirm these results. Additionally, future research should explore the combined use of advanced neuroimaging techniques, such as magnetoencephalography (MEG) and functional MRI, with ECoG to enhance intraoperative mapping of epileptogenic networks. Finally, the long-term impact on cognitive outcomes in patients



undergoing resection near eloquent brain regions warrants further investigation.

## Conclusion

Intraoperative ECoG is an important tool for optimizing seizure outcomes among patients undergoing microsurgical resection of supratentorial CCMs. By providing real-time functional data, ECoG enhances surgical precision and significantly reduces postoperative seizure recurrence, particularly in patients with drug-resistant epilepsy. These findings emphasize the need for routine implementation of ECoG during epilepsy surgery and its incorporation into clinical guidelines to improve long-term patient outcomes.

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**Author contributions** QZ, YZ and RH conceived the design of the study, analyzed the clinical information and drafted the manuscript. JX, JY, HT and YY performed the followed-up. XL and WS supervised the study and revised the manuscript. All authors read and approved the final manuscript.

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## Declarations

**Competing interests** The authors declare no competing interests.

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