Surgical Neurology International

OPEN ACCESS

For entire Editorial Board visit : http://www.surgicalneurologyint.com

Editor: **James I. Ausman,** MD, PhD University of California, Los Angeles, CA, USA

Original Article

Microsurgical treatment of patients with refractory epilepsy and mesial temporal cavernous malformations: Clinical experience of a tertiary epilepsy center

Lucas Crociati Meguins, Rodrigo Antônio Rocha da Cruz Adry, Sebastião Carlos da Silva Júnior, Carlos Umberto Pereira[1], Jean Gonçalves de Oliveira[2,3], Dionei Freitas de Morais, Gerardo Maria de Araújo Filho[4], Lúcia Helena Neves Marques[5]

Department of Neurologic Sciences, Division of Neurosurgery, Hospital de Base, Faculdade de Medicina de São José do Rio Preto, [2]Department of Medical Sciences, Division of Neurosurgery, School of Medicine, University Nove de Julho, [3]Department of Cerebrovascular and Skull Base Surgery, Center of Neurology and Neurosurgery Associates, Hospital Beneficência Portuguesa de São Paulo, [4]Department of Psychiatry and Medical Psychology, Faculdade de Medicina de São José do Rio Preto, [5]Department of Neurologic Sciences, Division of Neurology, Hospital de Base, Faculdade de Medicina de São José do Rio Preto, São Paulo, [1]Department of Medicine, Universidade Federal de Sergipe, Aracaju, SE, Brazil

E-mail: *Lucas Crociati Meguins - lucascrociati@hotmail.com; Rodrigo Antônio Rocha da Cruz Adry - rodrigoadry@hotmail.com; Sebastião Carlos da Silva Júnior - sebastiaosilvajr@hotmail.com; Carlos Umberto Pereira - umberto@infonet.com.br; Jean Gonçalves de Oliveira - jeangol@uol.com.br; Dionei Freitas de Morais - dionei.fm@terra.com.br; Gerardo Maria de Araújo Filho - gerardofilho@hotmail.com; Lúcia Helena Neves Marques - lucianevesm@hotmail.com
*Corresponding author

Received: 08 April 15 Accepted: 03 September 15 Published: 16 November 15

Abstract

Background: Mesiotemporal cavernous malformation can occur in 10–20% of patients with cerebral cavernomas and are frequently associated with refractory.

Methods: A retrospective investigation was performed in the epilepsy clinic of a Brazilian tertiary referral epilepsy center, from January 2000 to March 2012.

Results: A total of 21 patients were included in the study. Thirteen patients (62%) evolved to Engel I; 5 (24%) to Engel II, 2 (10%) to Engel III, and 1 (5%) to Engel IV. We observed that 10 (48%) patients with 12 years or less of epilepsy duration evolved to Engel I and 1 (5%) to Engel II; whereas from a total of 10 patients with epilepsy duration of more than 12 years, 3 (30%) evolved to Engel I and 7 (70%) to Engel II, III, or IV ($P < 0.001$ [bilateral]; $P1 \neq P2$).

Conclusion: Postsurgical seizure outcome for temporal lobe epilepsy associated with mesiotemporal cavernomas is very satisfactory.

Key Words: Cavernous malformations, mesiotemporal cavernous malformation, temporal lobe epilepsy

Access this article online

Website: www.surgicalneurologyint.com

DOI: 10.4103/2152-7806.169552

Quick Response Code:

INTRODUCTION

Cerebral cavernous malformations are known to be highly epileptogenic lesions, but the underlying epileptogenic mechanisms are not fully understood. Asymptomatic microhemorrhages into the surrounding brain, with subsequent perifocal hemosiderosis and gliosis, are considered the major cause of seizure activity.[6] Mesiotemporal cavernomas (MTC) can occur in 10–20% of patients with cerebral cavernomas[13,20] and

How to cite this article: Meguins LC, Adry RA, Silva Júnior SC, Pereira CU, de Oliveira JG, de Morais DF, *et al*. Microsurgical treatment of patients with refractory epilepsy and mesial temporal cavernous malformations: Clinical experience of a tertiary epilepsy center. Surg Neurol Int 2015;6:169.

http://surgicalneurologyint.com/Microsurgical-treatment-of-patients-with-refractory-epilepsy-and-mesial-temporal-cavernous-malformations:-Clinical-experience-of-a-tertiary-epilepsy-center/

are frequently associated with refractory.[21,22] Surgical removal of safely achievable symptomatic lesions has been frequently consistent with good long-term seizure outcomes.[8,9,21,22] The aim of the present study is to analyze retrospective data on consecutive patients with temporal lobe epilepsy associated with MTC (TLE-MTC), surgically treated in a Brazilian tertiary epilepsy referral center, in order to assess the effect of microsurgical resection on seizure activity and general outcome.

METHODS

Study delineation

A retrospective observational investigation was conducted with data collection from all inpatients and outpatients treated in the epilepsy clinic of Faculdade de Medicina de Sao Jose do Rio Preto, a Brazilian tertiary referral epilepsy center, diagnosed with TLE-MTC from January 2000 to March 2012. Clinical data were obtained retrospectively from the patient records and files. For all patients with the diagnosis of MTC on magnetic resonance images (MRIs), the following data were collected: Gender, age at the surgery, handedness, type and number of antiepileptic drugs (AEDs) used, and results of formal neuropsychological evaluations. In addition, noninvasive video-electroencephalography (EEG) data and side of surgery were registered.

Presurgical evaluation

Patients were submitted to video-EEG monitoring using the Neuro Workbench software (Nihon Kohden Corporation) and Nihon Kohden hardware (Nihon Kohden Corporation) to record and later evaluated all the epileptic events. Every patient was analyzed by an experienced epileptologist as an integral part of inpatient assessment.

All patients were submitted to a neuropsychological assessment pre- and post-surgically (at 12 months). Verbal memory was assessed by a list of learning design, and figural memory by a design learning test using independent items. Memory deficits were defined as performance one standard deviation (SD) below of the normal performance of age-matched controls.

Brain MRI was obtained accordingly with specific epilepsy protocol using a 1.5 tesla scanner, Philips, at the Department of Neuroradiology in our institution. All MRIs were analyzed by an experienced neuroradiologist that confirmed the visual radiological diagnosis of mesial temporal lobe (parahippocampal gyrus, hippocampus, amigdalum, and uncus) cavernomas. Displaying the sagittal three-dimensional T1-weighted gradient-echo sequences, the next sequences were an axial and coronal fluid-attenuated inversion recovery fast spin-echo (section thickness, 3 mm), axial and coronal T2-weighted fast spin-echo (section thickness, 2 mm) and T1-weighted inversion recovery sequences (section thickness, 5 mm) [Figure 1].

Biopsy specimens were obtained from all patients with chronic drug-resistant and radiological evidence of MTC, who underwent surgical treatment. Surgical removal of the hippocampus was clinically indicated in every case, and all the patients were submitted to complete lobectomy. The standardized neuropathological analysis was performed in all the patients under this study. Surgical specimens submitted for neuropathological evaluation were microscopically analyzed by using hematoxylin and eosin staining. The pathologist reported their findings without the clinical or imaging data.

Outcome assessments and follow-up

Follow-up investigations were carried out in operated patients. At the 12 months follow-up, all the patients received a neurological examination including observation of behavior disorders, exploration of seizure outcome, and a cerebral 1.5 tesla MRI. Seizure outcome was classified as completely seizure-free since surgery, that is, Engel I, or not seizure-free (Engel II–IV).

Ethical statement

The Ethical Committee of our institution analyzed the project of the present study and approved the performance of our investigations. The study complies with the Declaration of Helsinki. Informed consent was taken from all patients and/or genitors.

Statistical analysis

Data collected from all the patients were organized in tables. Averages are expressed as the mean ± SD for parametric data and as median values for nonparametric data. Statistical analysis was performed utilizing the Fisher's exact test. A $P < 0.01$ was considered statistically significant.

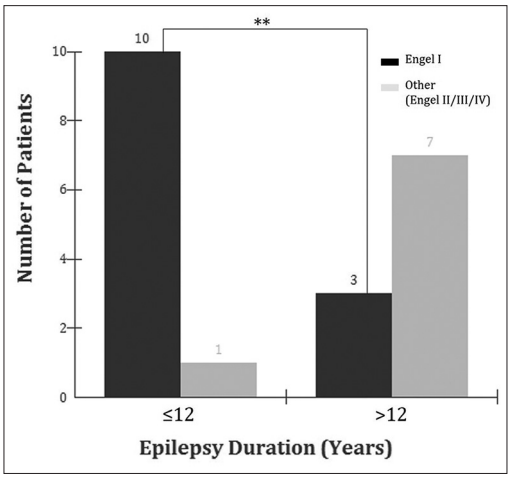

Figure 1: Comparison of surgical outcome between the patients with ≤ 12 years or > 12 years of epilepsy duration ($P < 0.01$, Fisher's exact test)**

RESULTS

Presurgical demographic and clinical characteristics

At the moment of the study, 533 patients underwent multidisciplinary investigation for epilepsy, and 21 (3.9%) patients fulfilled the inclusion criteria of radiological and pathological diagnosis of MTC. Table 1 summarizes the demographic and clinical data of all patients. The presurgical mean age was of 34.38 ± 8.82 years, with 13 male (61.9%) and 8 female (38.1%). The mean epilepsy duration at surgery was of 11.95 ± 4.25 years. Thirteen patients (61.9%) had complex partial seizures (CPSs) and 8 (38.1%) had generalized tonic-clonic seizures. Nineteen (90.5%) patients were right-handed and 2 (9.5%) left-handed. Nine (42.8%) patients presented a previous history of febrile seizure during infancy. Six patients (28.6%) were taking a single AED, and 15 (71.4%) were taking two or more AEDs. Neuropsychological assessment revealed that 5 (23.8%) presented cognitive impairment before surgery. In addition, 19 patients (90.5%) presented unilateral epileptic discharge on ictal EEG and two bilateral (9.5%); 16 subjects (76.2%) had unilateral and 5 (23.8%) had bilateral epileptic discharges on interictal EEG, respectively. Two patients (9.5%) presented with multiple (2 or more) lesions and 19 (90.5%) with only one lesion on the temporal lobe. The location of the lesion was found as follow: 16 (76.2%) on the lateral temporal neocortex and 5 (23.8%) affecting mesiotemporal structures, that is, two in the head of the hippocampus and three in the parahippocampal gyrus. Radiological investigation also showed some degree of sclerosis of the lateral temporal lobe neocortex and/or the mesial structures in 19 (90.5%).

Seizure control and follow-up

All the patients were followed during a minimum period of 1 year and a maximum of 7 years. The mean follow-up duration was of 3.14 ± 1.68 years. Three patients (14%) were followed during 1 year; 6 (29%) during 2 years; 5 (24%) during 3 years; 2 (10%) during 4 years; 2 (10%) during 5 years; 1 (5%) during 6 years; and 1 (5%) during 7 years. Seven patients (33%) stopped their AED; 6 (29%) reduced, and 8 (38%) maintained the AED use.

Seizure outcome following surgery revealed that 13 patients (62%) became Engel I, 5 (24%) to Engel II, 2 (10%) Engel III, and 1 (5%) Engel IV. We observed that 10 (48%) patients with 12 years or less of epilepsy duration evolved to Engel I and 1 (5%) to Engel II, whereas from a total of 10 patients with epilepsy duration of more than 12 years, 3 (30%) evolved to Engel I and 7 (70%) to Engel II, III, or IV ($P < 0.001$ [bilateral]; $P_1 \neq P_2$) [Figure 1].

Postoperative neuropsychological assessment showed deterioration in 4 patients with the previous cognitive deficits. One patient recovered to its baseline. No

Table 1: Clinical data of patients with mesiotemporal cavernomas

Subject number	Gender	Age	Epilepsy duration	Seizure semiology	AED	Cognitive deficit	Affected hemisphere	Surgical technique	Seizure outcome	Follow-up (years)
1	Male	21	10	CPS	Stopped	No	Right	SAH	Ia	2
2	Female	29	11	GTCS	Stopped	No	Right	ATL	Ia	3
3	Male	33	16	CPS	Maintained	Yes	Left	ATL	Ic	2
4	Female	28	11	CPS	Stopped	No	Right	ATL	Ia	3
5	Male	46	17	CPS	Maintained	Yes	Left	ATL	III	5
6	Male	51	19	GTCS	Maintained	Yes	Left	ATL	IV	7
7	Female	34	14	CPS	Reduced	No	Right	ATL	II	2
8	Male	27	12	CPS	Reduced	No	Left	ATL	Ia	4
9	Female	39	16	GTCS	Maintained	Yes	Left	ATL	II	1
10	Male	37	14	CPS	Reduced	No	Right	SAH	Ia	6
11	Male	42	13	GTCS	Maintained	No	Right	ATL	Ic	5
12	Male	24	7	GTCS	Stopped	No	Left	ATL	Ia	1
13	Female	36	9	CPS	Reduced	No	Right	ATL	Ic	3
14	Female	22	4	CPS	Stopped	No	Left	SAH	Ia	2
15	Male	25	6	GTCS	Stopped	No	Right	ATL	Ia	3
16	Female	37	12	CPS	Reduced	No	Right	ATL	Ib	4
17	Male	41	14	CPS	Maintained	No	Right	ATL	II	2
18	Male	46	18	CPS	Maintained	Yes	Left	ATL	III	5
19	Female	38	13	GTCS	Reduced	No	Right	ATL	II	1
20	Male	23	4	CPS	Stopped	No	Right	ATL	Ia	2
21	Male	43	11	GTCS	Maintained	No	Right	ATL	II	3

CPS: Complex partial seizure, GTCS: Generalized tonic-clonic seizure, AED: Antiepileptic drug, ATL: Anterior temporal lobectomy, SAH: Selective amygdalo-hippocampectomy

patients with normal cognition preoperatively evolved memory deficits. No patients reported visual field defect after the surgery.

Complications

No operative death (30 days after surgery) was recorded. In the present investigation, 2 (9%) of patients evolved with infection of the surgical wound and were treated exclusively with oral antibiotics. No additional clinical complications where noted.

DISCUSSION

Cavernous brain malformations are vascular lesions with an estimated prevalence between 0.4% and 0.9%,[12] appearing mainly as singular supratentorial lesions[16] frequently associated with refractory seizures.[21,22] In addition, 35–80% of all patients with supratentorial cavernomas are affected by 1st time seizures, of which up to 40% are resistant to AED treatment.[2,10,11,14,17]

In the present study, we presented our surgical series of 21 patients with refractory TLE-MTC. We found an average incidence of 1.61 case/year, affecting mainly man with age ranging from 30 to 40 years old. It was also noted that CPSs was the most common semiological feature, present in 62% of patients. Kivelev *et al.*,[13] in 2011, and Sommer *et al.*,[19] in 2013, although showing different results regarding gender prevalence, presented similar results median age. Elsharkawy *et al.*[10] and Cohen-Gadol *et al.*[9] showed that other degenerative lesions, such as mesial temporal sclerosis, presented a better surgical and seizure outcome in comparison with tumors and gliosis. Rydenhag *et al.*[18] reported the surgical treatment of patients with refractory TLE-MTC, with a good seizure control. In the present investigation, 13 patients (62%) evolved to Engel I and 5 (24%) to Engel II, which is consistent with the previous studies.[3,5,18] We decide to perform anterior temporal lobectomy associated with amigdalo-hippocampectomy and not only a tailored resection of the lesion for some reasons:[1] Some authors report that hemosiderin may also be epileptogenic[11,12] and, in our cases, sometimes it was difficult to differentiate precisely the tissue and how far should we go to include all the epileptogenic zone;[2] most patients also had some degree of temporal lobe and mesial structures sclerosis, and[3] the preoperatory electrophysiological features also suggested an epileptogenic zone usually wider the cavernous malformation size.

The present study also observed that patients suffering from epilepsy for a longer period might present a worse seizure outcome. In our analysis, 10 (48%) patients with 12 years or less of epilepsy duration evolved to Engel I and 1 (5%) to Engel II; whereas from the 8 patients with epilepsy duration of more than 12 years, 1 (5%) evolved to Engel I and 7 (33%) to Engel II, III, or IV ($P = 0.0075$ [bilateral]; $P_1 \neq P_2$) [Figure 1]. Our results are in agreement with investigators who reported that seizure outcome can be improved if epilepsy surgery is considered earlier in patients with epileptogenic lesions.[1,4,7,14,15,18]

There are several methodological aspects in the present findings, which should be interpreted in the context of a number of limitations. First, this study is a nonrandomized, retrospective investigation performed in a highly selected population of a tertiary epilepsy center. Second, these findings cannot be generalized for all types of TLE since the patients with dual pathology, or single disease other than MTC were excluded. On the other hand, the present study described the surgical outcomes of a relatively large number of patients that underwent surgery due to this uncommon pathology for a relatively extended follow-up duration.

CONCLUSION

The present study highlights that seizure outcome after respective epilepsy surgery for epileptogenic lesions, especially MTC, in adults is very satisfactory. However, surgical treatment should be considered early in the course of the disease to improve seizure control and to reduce suffering.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Arita K, Kurisu K, Iida K, Hanaya R, Sugiyama K, Akimitsu T, *et al.* Surgical treatment for intractable epilepsy caused by cavernous angioma in the temporal lobe of the dominant hemisphere – Three case reports. Neurol Med Chir (Tokyo) 2000;40:439-45.
2. Aronica E, Leenstra S, van Veelen CW, van Rijen PC, Hulsebos TJ, Tersmette AC, *et al.* Glioneuronal tumors and medically intractable epilepsy: A clinical study with long-term follow-up of seizure outcome after surgery. Epilepsy Res 2001;43:179-91.
3. Attar A, Ugur HC, Savas A, Yüceer N, Egemen N. Surgical treatment of intracranial cavernous angiomas. J Clin Neurosci 2001;8:235-9.
4. Bertalanffy H, Benes L, Miyazawa T, Alberti O, Siegel AM, Sure U. Cerebral cavernomas in the adult. Review of the literature and analysis of 72 surgically treated patients. Neurosurg Rev 2002;25:1-53.
5. Boesebeck F, Janszky J, Kellinghaus C, May T, Ebner A. Presurgical seizure frequency and tumoral etiology predict the outcome after extratemporal epilepsy surgery. J Neurol 2007;254:996-9.
6. Bourgeois M, Di Rocco F, Sainte-Rose C. Lesionectomy in the pediatric age. Childs Nerv Syst 2006;22:931-5.
7. Cappabianca P, Alfieri A, Maiuri F, Mariniello G, Cirillo S, de Divitiis E. Supratentorial cavernous malformations and epilepsy: Seizure outcome after lesionectomy on a series of 35 patients. Clin Neurol Neurosurg 1997;99:179-83.
8. Chang EF, Gabriel RA, Potts MB, Garcia PA, Barbaro NM, Lawton MT. Seizure characteristics and control after microsurgical resection of supratentorial cerebral cavernous malformations. Neurosurgery 2009;65:31-7.
9. Cohen-Gadol AA, Wilhelmi BG, Collignon F, White JB, Britton JW, Cambier DM, *et al.* Long-term outcome of epilepsy surgery among 399

patients with nonlesional seizure foci including mesial temporal lobe sclerosis. J Neurosurg 2006;104:513-24.
10. Elsharkawy AE, Alabbasi AH, Pannek H, Oppel F, Schulz R, Hoppe M, *et al.* Long-term outcome after temporal lobe epilepsy surgery in 434 consecutive adult patients. J Neurosurg 2009;110:1135-46.
11. Englot DJ, Han SJ, Lawton MT, Chang EF. Predictors of seizure freedom in the surgical treatment of supratentorial cavernous malformations. J Neurosurg 2011;115:1169-74.
12. Hammen T, Romstöck J, Dörfler A, Kerling F, Buchfelder M, Stefan H. Prediction of postoperative outcome with special respect to removal of hemosiderin fringe: A study in patients with cavernous haemangiomas associated with symptomatic epilepsy. Seizure 2007;16:248-53.
13. Kivelev J, Niemelä M, Blomstedt G, Roivainen R, Lehecka M, Hernesniemi J. Microsurgical treatment of temporal lobe cavernomas. Acta Neurochir (Wien) 2011;153:261-70.
14. Kivelev J, Niemelä M, Hernesniemi J. Characteristics of cavernomas of the brain and spine. J Clin Neurosci 2012;19:643-8.
15. Luyken C, Blümcke I, Fimmers R, Urbach H, Elger CE, Wiestler OD, *et al.* The spectrum of long-term epilepsy-associated tumors: Long-term seizure and tumor outcome and neurosurgical aspects. Epilepsia 2003;44:822-30.
16. Menzler K, Thiel P, Hermsen A, Chen X, Benes L, Miller D, *et al.* The role of underlying structural cause for epilepsy classification: Clinical features and prognosis in mesial temporal lobe epilepsy caused by hippocampal sclerosis versus cavernoma. Epilepsia 2011;52:707-11.
17. Moran NF, Fish DR, Kitchen N, Shorvon S, Kendall BE, Stevens JM. Supratentorial cavernous haemangiomas and epilepsy: A review of the literature and case series. J Neurol Neurosurg Psychiatry 1999;66:561-8.
18. Rydenhag B, Flink R, Malmgren K. Surgical outcomes in patients with epileptogenic tumours and cavernomas in Sweden: Good seizure control but late referrals. J Neurol Neurosurg Psychiatry 2013;84:49-53.
19. Sommer B, Kasper BS, Coras R, Blumcke I, Hamer HM, Buchfelder M, *et al.* Surgical management of epilepsy due to cerebral cavernomas using neuronavigation and intraoperative MR imaging. Neurol Res 2013;35:1076-83.
20. Steiger HJ, Markwalder TM, Reulen HJ. Clinicopathological relations of cerebral cavernous angiomas: Observations in eleven cases. Neurosurgery 1987;21:879-84.
21. von der Brelie C, Malter MP, Niehusmann P, Elger CE, von Lehe M, Schramm J. Surgical management and long-term seizure outcome after epilepsy surgery for different types of epilepsy associated with cerebral cavernous malformations. Epilepsia 2013;54:1699-706.
22. von der Brelie C, Schramm J. Cerebral cavernous malformations and intractable epilepsy: The limited usefulness of current literature. Acta Neurochir (Wien) 2011;153:249-59.