

Case Report

Presurgical evaluation of temporal lobe epilepsy: Is an outpatient prolonged ambulatory EEG study sufficient to recommend a surgical resection?



Ada Chicharro^{a,b,c,*}, Alejandro de Marinis^{a,b,c}, Anna Milán^c, Daniel Mansilla^c, Alberto Prat^b, Alvaro Velásquez^a, Mónica González^{a,b}, Hernán Acevedo^d, Andrés M. Kanner^e

^a Clínica Alemana de Santiago, Santiago, Chile

^b Facultad de Medicina Clínica Alemana-Universidad del Desarrollo, Santiago, Chile

^c Liga Chilena contra la Epilepsia, Santiago, Chile

^d Clínica Davila, Santiago, Chile

^e University of Miami, Miller School of Medicine, Epilepsy Center, 1120 NW 14th Street, Room 1324, Miami, FL 33136, USA

ARTICLE INFO

Article history:

Received 4 August 2020

Revised 9 September 2020

Accepted 22 September 2020

Available online 17 October 2020

Keywords:

Epilepsy surgery

Refractory temporal lobe epilepsy

ABSTRACT

Purpose: Inpatient Video EEG Monitoring (VEM) is the typical study performed in presurgical evaluations. It is expensive and not widely available in developing countries. Recent studies suggested that in selected patients with mesial temporal lobe epilepsy secondary to unilateral mesial temporal sclerosis (MTS), the recording of unilateral interictal epileptiform activity ipsilateral to the MTS may yield sufficient presurgical EEG data. Outpatient prolonged ambulatory EEG (AEEG) could be an alternative in these cases. The purpose of this study was to compare the post-surgical seizure outcome and costs between patients evaluated with AEEG versus VEM.

Methods: Thirty patients with TLE were included: 21 evaluated with VEM and 9 with AmbBEEG and underwent surgery between 2011 and 2017. The minimum, post-surgical follow-up period was 1 year.

Results: Seven of nine patients who underwent AEEG had seizures ipsilateral to MTS. In two patients only unilateral interictal activity ipsilateral to the lesion was recorded. All patients were free of disabling seizures (Engel Class I) at last follow-up. The mean cost per patient of AEEG was \$980 and was \$4680 for VEM.

Conclusion: AEEG may be used to identify candidates for temporal lobectomy in selected patients with unilateral lesional mesial TLE. This approach to EEG monitoring could make epilepsy surgery more affordable to some patients in developing countries.

© 2020 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Anterior temporal lobectomy (ATL) is the most frequently performed surgical procedure in Latin America in adults with drug-resistant focal epilepsy as it is cost-effective, particularly in patients with mesial temporal sclerosis (MTS) and/or lesional TLE. In these patients non-invasive presurgical evaluation can often yield reliable localization of the epileptogenic area when there is concordance among ictal clinical semiology, brain MRI, neuropsychological findings, and interictal and ictal epileptiform activity [1–3].

* Corresponding author at: Vitacura 5951, Laboratorio neurofisiología piso 10, Santiago de Chile, Chile.

E-mail address: achicharro@alemana.cl (A. Chicharro).

Several studies have suggested that in selected patients with mesial temporal lobe epilepsy (MTLE) secondary to unilateral MTS, the presence of unilateral ipsilateral interictal epileptiform activity may not require the recording of ictal activity in order to proceed to an ATL [4,5]. This would result in significant cost savings caused by long inpatient hospitalizations, which are often an obstacle to access to epilepsy surgery in many developing countries. Yet, this strategy has yet to be accepted in all centers and has generated some controversy regarding its validity.

The use of prolonged AEEG studies could be an alternative option in these cases. It is a diagnostic tool that has been available for the last three decades and with which interictal and ictal epileptiform activity can be recorded with an ambulatory EEG system at home. Compared with VEM, the costs of AEEG are significantly lower. In addition, the exposure to the daily environmental stressors can facilitate the occurrence of seizures

at home, without having to lower the dose of antiseizure medications (ASM). Some of the new AEEG systems have the capability for video recording as well [6]. The principal aim of this study was to compare the postsurgical seizure outcome between patients with MTL secondary to MTS or a mesial lesion who were evaluated with AEEG and VEM. In addition, we compared the time to the first seizure between the two monitoring studies and their respective costs.

2. Methods

This was a retrospective study of 30 consecutive patients who underwent an ATL at Clínica Alemana de Santiago de Chile between 2011 and 2017. All patients had drug-resistant focal epilepsy of temporal lobe origin, defined as persistent seizures after two different ASMs used in monotherapy or in combination at optimal doses. The first 24 patients underwent a VEM study. Three did not experience any seizures during the monitoring study and therefore underwent a prolonged AEEG (without video), during which all three experienced their typical seizures. Six additional patients with unilateral MTS underwent an AEEG as their initial study.

Eligibility for epilepsy surgery was based on seizure semiology, neuroimaging data based on high-resolution brain MRI, interictal and/or ictal activity obtained with VEM or AEEG and neuropsychological data. All patients underwent a high-resolution brain MRI that included fine-cut sequences through the temporal lobes. Hippocampal sclerosis was defined by qualitative analysis based on hippocampal T2/FLAIR hyperintensity, loss of its internal architecture and quantitative volumetric measurements.

VEM was done with scalp electrodes positioned according to the 10–20 international system of electrode placement in addition to basal and anterotemporal electrodes. In AEEG studies, anterotemporal and basal electrodes were used in seven of the nine patients. Electrodes were attached to the scalp with Ten 20 conductive paste. Head was wrapped with a sticky bandage attached with Fixomull to decrease artifacts and ensure optimal contact of the electrodes with the scalp. A test recording was performed in every patient at the beginning of the study to ensure the proper operational state of the ambulatory system. Each system had an event button which the patients and family members were instructed to press in case of seizures or auras. Patients and family members documented each event in a diary, detailing the specific time, clinical phenomena, and duration of each event. The duration of the studies were tailored to each patient, based on the timing for the recording of the first typical seizure.

The maximal duration of VEM was 10 days. The mean duration of VEM was 3,7 days (range 1–10 days). The average seizure frequency prior to the study was 1,6 seizures per week and patients were taking an average of 2,4 ASM each. The dose of ASMs was lowered after the first 24 hours and thereafter according to seizure occurrence.

The duration of the AEEG was 2,9 days (range: 1–5 days). The average seizure frequency prior to the study was 1,4 seizures per week and patients were taking an average of 2,6 ASM each. During AEEG, ASMs were maintained at usual doses. Patients returned to the EEG laboratory every day to get electrodes impedance checked and optimized, download the EEG data and check the integrity of the ambulatory system. If a patient reported a seizure in the previous 24 h, the EEG data were immediately reviewed by an experienced epileptologist. The AEEG study was stopped after the recording of a focal seizure of temporal lobe origin ipsilateral to the MTS, in the setting of frequent unilateral interictal epileptiform activity also ipsilateral to the MTS. In the case of bilateral independent interictal epileptiform activity, the patient was referred for

VEM; however, this was not necessary in any of the nine patients who underwent the AEEG.

The post-surgical seizure outcome was evaluated using the Engel classification system and was updated at the last visit. Given the small number of patients, no statistical analyses were used to compare postsurgical seizure outcomes between patients evaluated with AEEG and VEM.

Kaplan-Meier method was used to analyze time to first seizure occurrence, and the log-rank test was used to assess for differences between the VEM and AEEG subgroups. A 5% significance was used and data analysis was performed using STATA version 14.0.

3. Results

Clinical and demographic data as well as post-surgical seizure outcome of the 30 patients are presented in [Tables 1 And 2](#). Among the nine patients who underwent an AEEG, eight had MTS and one a cavernous angioma in the mesial temporal region. Among the 21 patients who were studied with VEM, 14 had MTS, five had a focal lesion in mesial temporal structures and two in extra-mesial temporal region. Post-surgical follow-up period was comparable between the two groups: 3.67 ± 1.7 (range 1–6 years) years in patients who underwent an AEEG and 3.66 ± 2.24 (range 1–6 years) in those evaluated with VEM.

3.1. Duration of EEG recordings

The mean duration of VEM among the 21 patients was $3,7 \pm 2,2$ days (range: 1–10 days). On the other hand, among the nine patients who underwent an AEEG, the mean duration of recordings was $2,9 \pm 2$ days (range 1–5 days). Furthermore, time to the first seizure did not differ between VEM [2,3 days (range 1–4 days)] and AEEG [2,5 days (range:1–4 days)]. See [Fig. 1](#).

3.2. AEEG recordings

In seven patients with MTS, focal seizures with loss of awareness were recorded. Unilateral ictal and interictal epileptiform activity of temporal lobe origin and ipsilateral to the MTS were recorded in all patients. This included the three patients who had been previously studied with VEM and were discharged home on a prolonged AEEG. In the other two patients ([Table 2](#): patient 4 and 9) one with MTS and the other with the cavernous angioma only unilateral interictal epileptiform activity of anterior-temporal origin ipsilateral to the lesion was recorded.

3.3. Postsurgical seizure outcome

All nine patients evaluated with AEEG were free of disabling seizures (Engel Class I) following the ATL. Example of one patient is shown in [Fig. 2](#). As seen in [Tables 1 and 2](#), the post-surgical seizure outcome is very similar in patients with unilateral MTS studied either with VEM or AEEG.

3.4. Costs

In Clínica Alemana, the cost of the AEEG is around \$350.00 (US dollars) per day, while the cost of VEM is \$1300.00 (US) per day. Considering the number of days of EEG monitoring required, the mean cost/patient was \$ 980 vs \$ 4680 for patients who underwent an AEEG and a VEM, respectively. In other Latin American countries the cost of 24 h VEM is highly variable, ranging from \$600 (US) and \$1500 (US) per day.

Table 1

Patients studied with VEM as part of their presurgical evaluation. F, female; M, Male; MTS, mesial temporal sclerosis; LT, Left temporal; RT, Right temporal; sz, Seizure.

Case	Age/ Sex	MRI Findings/Biopsy findings	Video-EEG interictal discharges	Duration Video-EEG/ictal recordings	Interictal MRI concordance	Ictal EEG MRI concordance	Outcome/ Follow up
1	38/F	Right MTS/Right MTS	RT 90%, LT 10 %	5 days, 3 RT sz (Sz on day 3)	Yes	Yes	IIA, 6 years
2	37/M	Left MTS/Left MTS	LT	5 days, 4 LT sz (Sz on day 4)	Yes	Yes	IA, 6 years
3	45/M	Right MTS/Right MTS	RT	4 days, 1 RT sz (Sz on day 3)	Yes	Yes	ID, 6 years
4	40/F	Right MTS/Right MTS	RT 80%, LT 20%	4 days, 2 RT sz (Sz on day 3)	Yes	Yes	IB, 6 years
5	37/M	Right MTS/Right MTS	RT	1 day, 4 RT sz	Yes	Yes	IA, 5 years
6	44/M	Right MTS/Right cysticercosis	RT	4 days, 1 RT sz (Sz on day 3)	Yes	Yes	IA, 3 years
7	10/F	DNET LT/DNET LT	LT	10 days, 3 LT sz (Sz on day 1)	Yes	Yes	IA, 6 years
8	42/M	Right MTS/Right MTS	RT (TIRDA)	5 days, No sz	Yes	—	IA, 4 years
9	23/M	LT Dysplasia/LT Dysplasia	LT	5 days, 1 LT sz (Sz on day 4)	Yes	Yes	IA, 2 years
10	24/F	Left MTS/Left MTS	LT	4 days, 2 LT sz (Sz on day 3)	Yes	Yes	IB, 4 years
11	27/M	Left MTS/Left MTS	LT	5 days, 1 LT sz (Sz on day 3)	Yes	Yes	IC, 3 years
12	33/M	Right MTS/Right MTS	RT	4 days, 1 RT sz (Sz on day 3)	Yes	Yes	ID, 4 years
13	29/F	Left MTS/Left MTS	LT	3 days, 2 LT sz (Sz on day 2)	Yes	Yes	IA, 2 year
14	58/F	Left MTS/Left MTS	LT	1 day, 1 LT Sz	Yes	Yes	IA, 1 year
15	29/M	RT Dysplasia/RT Dysplasia	RT	1 day, 1 RT sz	Yes	Yes	IIIA, 1 year
16	37/M	RT cavernoma/RT cavernoma	No	1 day, 5 electrographic sz	No interictal activity	Yes	IA, 7 years
17	35/F	LT cavernoma/LT cavernoma	No	5 days, 1 LT Sz (Sz on day 3)	No interictal activity	Yes	IA, 7 years
18	43/M	Right MTS/Right MTS	RT	5 days, 2 RT sz (Sz on day 4)	Yes	Yes	IA, 1 year
19	24/F	Left MTS/LT Dysplasia	LT	1 day, 1 LT Sz	Yes	Yes	IA, 1 year
20	23/F	Left T Hamartoma/Left T Hamartoma	LT	1 day, 1 LT	Yes	Yes	IA, 1 year
21	5/F	Left T Tuber/Left T tuber	LT	3 days, 3 LT sz (SZ on day 2)	Yes	Yes	IA, 1 year

Table 2

Patients studied with AEEG as part of their presurgical evaluation. F, female; M, Male; MTS, mesial temporal sclerosis; LT, Left temporal; RT, Right temporal; sz, Seizure.

Case	Age/ Sex	MRI Findings/Biopsy findings	AEEG interictal discharges	Duration AEEG/ictal recordings	Duration VEM/ictal recordings	Interictal MRI concordance	Ictal EEG MRI concordance	Outcome/ Follow up
1	44/F	Left MTS/Left MTS	L T	1 day, 1 LT sz	No	Yes	Yes	ID, 5 years
2	49/F	Right MTS/Right MTS	RT	5 days, 4 RT sz (Sz on day 4)	10 days, no sz	Yes	Yes	IB, 5 years
3	21/M	Left MTS/Left MTS	LT	1 day, 1 LT sz	2 days, no sz	Yes	Yes	IA, 6 years
4	58/M	RT cavernoma/RT cavernoma	RT	1 day, No Sz	No	Yes	No Sz	IC, 5 years
5	35/F	Right MTS/Right MTS	RT	1 day, 1 RT sz	No	yes	yes	IC 3 years
6	32/M	Left MTS/Left MTS	LT	5 days, 1 LT sz (Sz on day 4)	5 days, no sz	Yes	yes	IA 2 years
7	28/F	Right MTS/Right MTS	RT	5 days, 2 RT sz (Sz on day 3)	No	yes	yes	IA, 3 years
8	50/M	Right MTS/Right MTS	RT	5 days, 5 RT sz (Sz on day 4)	No	yes	yes	IA, 2 year
9	63/M	Right MTS/Dysplasia IA	RT	2 days, No Sz	No	Yes	No Sz	IA, 1 year

4. Discussion

Anterior temporal lobectomy has been associated with very good post-surgical seizure outcome in patients with drug-resistant focal epilepsy of unilateral mesial temporal origin secondary to MTS or a structural lesion [1–3]. The high costs of presurgical evaluations, in particular those of VEM continue to be an obstacle for epilepsy surgery particularly in developing countries. The findings of this study suggest that in this selected

group of patients, reliable interictal and ictal data can be obtained with AEEG studies, which could potentially be used in a presurgical evaluation. The following conditions need to be met if AEEG is to replace a VEM: (i) clinical semiology of seizures has to be typical of seizures of mesial temporal origin. (ii) The EEG data must include recording of unilateral interictal (with a relatively high frequency) and ideally ictal epileptiform activity ipsilateral to the MTS or lesion. (iii) The EEG data and neuropsychological data have to be concordant. (iv) The presurgical evaluation must be performed by epileptologists with expertise in epilepsy surgery.

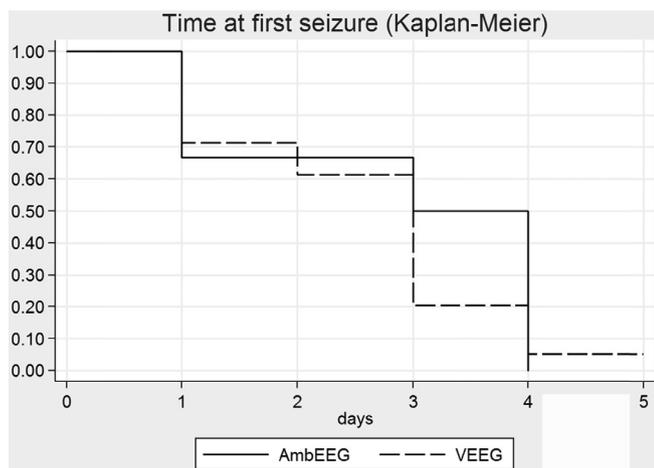


Fig. 1. Kaplan-Meier analysis of time to first seizure. Dashed line represents AEEG subgroup and continuous line the VEM group.

These data are encouraging as the use of AEEG can increase access to presurgical evaluations in centers and countries with limited resources and can save costs in the evaluation of this selected type of patients. Moreover, other studies have investigated the usefulness of AEEG in presurgical evaluations of drug-resistant TLE and have also shown that in selected patients successful resective surgeries can be performed after outpatient presurgical EEG monitoring studies [7–9].

A recently published prospective study carried out in a tertiary epilepsy center compared the post-surgical outcomes between patients with unilateral TLE secondary to MTS evaluated with and without VEM. The authors concluded that VEM is not imperative in this type of patients if their interictal recordings clearly reveal ipsilateral epileptiform discharges in 6–10 routine EEGs in the setting of compatible clinical ictal semiology [4,5]. Our data supports these findings as the recording of only unilateral interictal epileptiform activity ipsilateral to the mesial temporal lesion without ictal data during AEEG was considered to be acceptable EEG data in two of our nine patients, both of whom achieved seizure freedom. Furthermore, a prolonged AEEG is a more effective

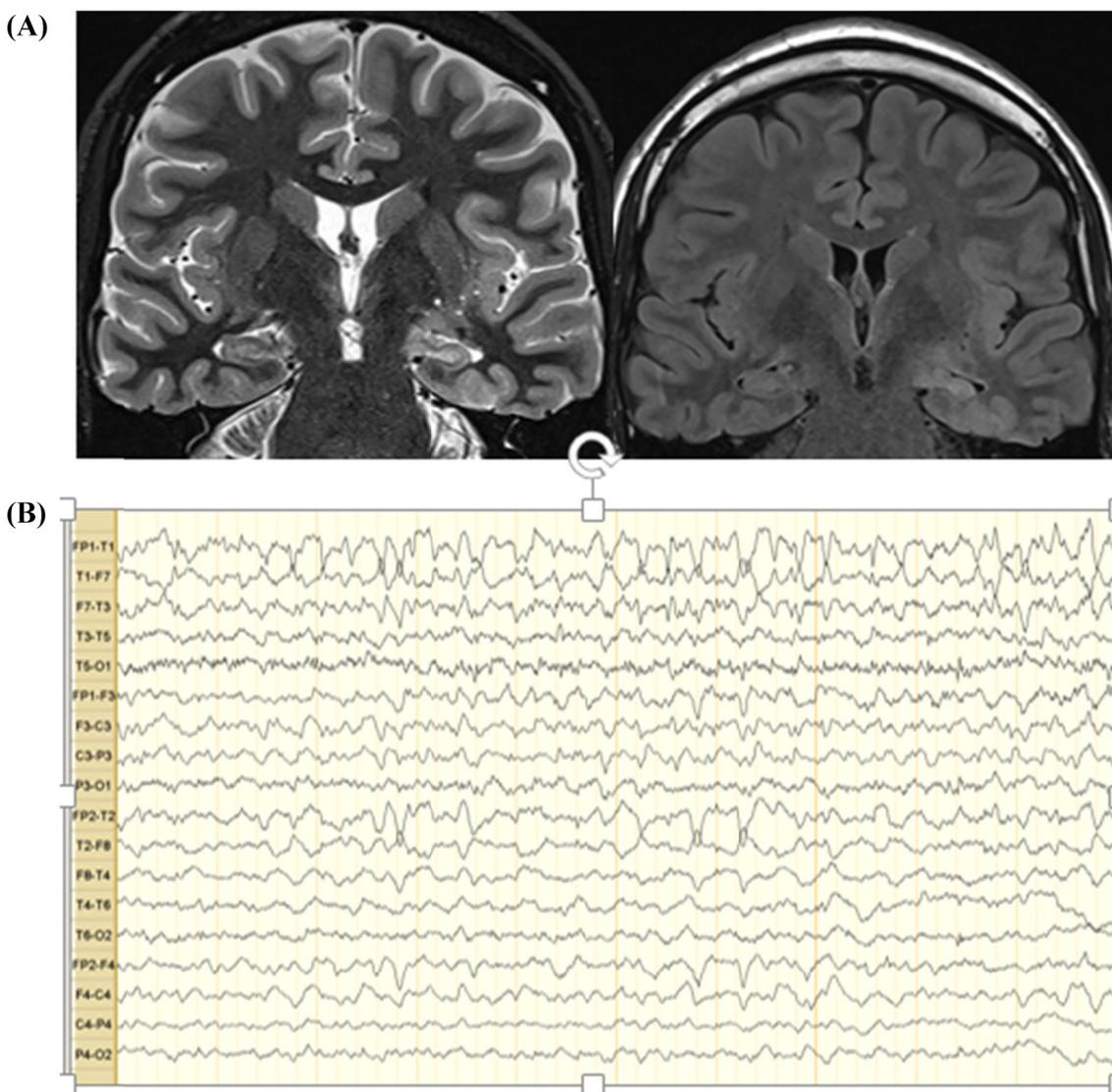


Fig. 2. Illustrative case (Table 2, case 6). Fig. 1A: MRI: Left Hippocampal Sclerosis. Fig. 1B: Left anterior temporal lobe seizure registered on AEEG. This is a 32-year-old right-handed male who started having seizures at the age of 12. His seizures consist of a rising epigastric sensation followed by speech arrest and then loss of awareness of his surroundings and automatic left-hand movements and dystonic posture of his right upper limb.

alternative than repeated EEG studies as it is performed in one step, provides prolonged sleep recordings and allows for the recording of seizures without change in doses of ASM. Finally, as suggested by other authors, patients on stable doses of ASMs are more likely to experience their typical seizures when the study is performed in their usual environment [9]. It should be emphasized, however, that when interictal epileptiform activity is the only EEG data used in the presurgical evaluation, a higher threshold must be met before accepting it as reliable EEG data. First, 100% of the interictal epileptiform discharges must be unilateral and ipsilateral to the side of the MTS; second, the activity must be frequent in awake and sleep states and recordings must include antero-temporal and/or basal temporal electrodes to demonstrate an antero-temporal source.

In our study, the mean duration of VEM was one day longer than that of AEEG (3,7 days vs 2,9 days). The post-surgical seizure outcome of patients with MTS was comparable between those evaluated with VEM and AEEG.

4.1. Availability and cost

Epilepsy surgery in Chile has become one of the therapeutic options offered to patients with drug-resistant focal epilepsy. Yet, among all the hospitals in this country, only 5% have a VEM monitoring unit, and some of these units only operate during daytime hours. Furthermore, most patients don't have private insurance and cannot afford this type of evaluation.

At our institution, the mean daily cost of an AEEG is around \$350 US vs \$1300 US for VEM. In other Latin American countries, the total daily cost can range between \$600 and \$1500 USD (unpublished personal data by AC). Thus, given the lower costs by 50%–65%, AEEG can be an alternative to VEM in selected patients provided that the caveats listed above are met.

Several studies in different countries had attributed these cost limitations as the principal reason for the under-utilization of epilepsy surgery [11,12]. Other authors have recommended the shortening of the VEM duration to 48 h [12]. To facilitate the occurrence of seizures, ASMs were rapidly withdrawn. While in most patients the evaluation was uneventful, three developed complications, including status epilepticus requiring transfer to an ICU and intubation. In fact, some authors have suggested that AEEG and VEM yield comparable presurgical data in patients with TLE and frequent seizures.

Yet, compared to VEM, AEEG has some limitations, which include: (i) technical problems, which cannot be corrected as soon as they arise and can result in significant artifacts masking the underlying EEG activity. Fortunately, in none of the patients included in our study artifacts limited the interpretation of the recordings. (ii) The lack of video recordings and the need to rely on descriptions of the ictal semiology by family members. Yet, with the widespread availability of cell phones, family members can be asked to take a video of seizures, which was done in three of our patients. (iii) Ictal recordings may not yield a focal or regional ictal onset in temporal regions. Clearly, when basing the EEG evaluation on recordings obtained with AEEG, the interictal and ictal data must provide an unquestionable localization of the epileptogenic area before considering it acceptable in any recommendation to proceed to surgery is made.

Our study has several limitations: All surgeries were performed by a single surgeon at a single institution over a 4-year period, limiting generalizability. The study was based on retrospective analysis of the data and the number of subjects included was small, particularly in the AEEG arm. The post-surgical follow-up period was of one or two years in several cases. Accordingly, our results should be considered preliminary.

5. Conclusion

Drug-resistant TLE secondary to MTS is an epileptic syndrome considered as “surgically curable”. AEEG can be potentially considered as an alternative to VEM for presurgical evaluations in very carefully selected patients as outlined above. These evaluations must be performed in a center with expertise in epilepsy surgery.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Neither of the authors has any conflict of interest to disclose.

Conflict of interest

Neither of the authors has any conflict of interest to disclose.

Ethical Statement

Ada Chicharro testifies on behalf of all co-authors that our article submitted to Epilepsy Behavior Reports

- 1) Has not been published in whole or in part elsewhere;
- 2) the manuscript is not currently being considered for publication in another journal;
- 3) all authors have been personally and actively involved in substantive work leading to the manuscript, and will hold themselves jointly and individually responsible for its;
- 4) all patients have inform consent.

Acknowledgements

We thank Gabriel Cavada, Program of Epidemiology, School of Public Health, Universidad de Chile for helping us perform statistical analysis.

References

- [1] Guerreiro C, Montenegro M, Kobayashi E, Noronha A, Cendes F. Daytime outpatient versus inpatient video-EEG monitoring for presurgical evaluation in temporal lobe epilepsy. *J Clin Neurophysiol* 2002;19(3):204–8.
- [2] Wiebe S, Blume W, Girvin J, Eliasziw M. A randomized, controlled trial of surgery for temporal-lobe epilepsy. *NEJM* 2001;345:311–8.
- [3] Wiebe S, Jetté N. Epilepsy surgery utilization: who, when, where and why?. *Curr Opin Neurol* 2012;25:187–93.
- [4] Alvim M, Morita M, Yasuda C, Damasceno B, Lopes T, Coan A, et al. Is inpatient ictal video-electroencephalographic monitoring mandatory in mesial temporal lobe epilepsy with unilateral hippocampal sclerosis? A prospective study. *Epilepsia* 2017;1–10.
- [5] Vollmar C, Stredl I, Heinig M, Noachtar S, Rémi J. Unilateral temporal interictal epileptiform discharges correctly predict the epileptogenic zone in lesional temporal lobe epilepsy. *Epilepsia* 2018;59(8):1577–82.
- [6] Chang B, Ives J, Schomer D, Drislane F. Outpatient EEG monitoring in the presurgical evaluation of patients with refractory temporal lobe epilepsy. *J Clin Neurophysiol* 2002;19(2):152–6.
- [7] Rizvi S, Téllez J, Crawford S, Wu A. Outpatient ambulatory EEG as an option for epilepsy surgery evaluation instead of inpatient EEG telemetry. *Epilepsy Behav Case Rep* 2013;1:39–41.
- [8] Dash D, Hernandez-Ronquillo L, Moien-Afshari F, Tellez-Zenteno J. Ambulatory EEG: a cost-effective alternative to inpatient video-EEG in adult patients. *Epileptic Disord* 2012;14(3):290–7.
- [9] Morris G. The clinical utility of computer-assisted ambulatory 16-channel EEG. *J Med Eng Technol* 1997;21:47–52.
- [10] Unnwongse Pimprapa Kitwittee Kanjana, Srikijvilaiikul Teeradej, et al. Cost-utility of video-electroencephalography monitoring followed by surgery in adults with drug-resistant focal epilepsy in Thailand. *World Neurosurg* 2017;98:750–60.
- [11] Lima Kheng-Seang, Fonga Si-Lei, Lea Minh-An Thuy, et al. 48-hour video-EEG monitoring for epilepsy presurgical evaluation is cost-effective and safe in resource-limited setting. *Epilepsy Res* 2020;162:106298.