

Research Article

Surgical treatment of Temporal Lobe Epilepsy: comparative results of selective amygdalohippocampectomy versus anterior temporal lobectomy from a referral center in Brazil

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Introduction

Temporal Lobe Epilepsy (TLE) is a high prevalence neurological disorder and tends to drug refractoriness. Surgery has emerged as a promising treatment for managing seizures and a better quality of life for these patients. The objective of this work is to compare the surgical results in terms of seizure control concerning the surgical technique performed (Anterior temporal lobectomy (ATL) vs. Selective amygdalohippocampectomy (SAH)) in a cohort of 132 patients operated in an epilepsy reference center.

Materials and methods

We performed a retrospective study based on the review of medical records of 146 patients operated for TLE from 2008 to 2019 at the Santa Casa de Misericórdia in Belo Horizonte, Brazil. Initially, 13 patients were excluded from the study due to insufficient medical record data or follow-up loss. One patient was excluded from the analysis of the results due to death in the first postoperative week. We used the ILAE scale to classify seizure control after surgery. In patients with left hippocampal sclerosis, the most selective approach was performed (SAH), and in right temporal lobe epilepsy, ATL was the approach of choice. We compared the surgical groups using the survival and Kaplan-Meier curves.

Results

A total of 132 patients were evaluated in this study, with a mean follow-up time after surgery of 57.2 months (12-137). In our data analysis, we found that the group of patients undergoing ATL had a higher prevalence of being completely seizure-free (ILAE I) (57.1% vs. 31%) and a higher rate of satisfactory seizure control (88.6% vs. 69.3%) $p = 0.006$, when compared to patients undergoing SAH.

Conclusion

The literature is still controversial about seizure control results concerning the surgical technique used due to the lack of studies with a robust methodology for an adequate comparison. Our data analysis identified the superiority of ATL over SAH in seizure outcomes. ATL may be the best option for adequately controlling seizures with minimal additional morbidity in countries with a cost limitation for extended propaedeutics.

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Introduction

Temporal lobe epilepsy (TLE) is the most common human epileptic syndrome^[1], being a disabling and progressive entity^[2]. In addition to seizures, which already represent clinical management difficulties, they may also be associated with cognitive, language, or psychiatric disorders^{[3][4]}. A tendency to drug refractoriness characterizes it, and up to a third of patients are drug-resistant^[5]. In recent years, surgery has proven to be a therapeutic option with good results, with a controlled clinical trial demonstrating its superiority to drug treatment alone^[6].

The hippocampal sclerosis etiology is multifactorial, typically caused by inflammatory, infectious insults, trauma, or febrile

seizures^{[7][8]}.

There are technical variations in TLE surgery, and there is no consensus on the best surgical approach. The most common techniques are Anterior temporal lobectomy (ATL) and selective amygdalohippocampectomy (SAH). Foerster pioneered subtotal temporal lobectomy in 1925^[9]. Falconer developed en bloc resection of the temporal lobe and mesial structures in 1953^[10]. Morris, in 1956 used the term standard temporal lobectomy for a 6.5 cm resection of the temporal lobe^[11]. Spencer refined this technique with 4.5 cm in the non-dominant cortex and 3 cm in the dominant cortex^[12]. Niemeyer, in 1958, described selective access to mesial temporal structures through an incision in the medial temporal lobe^[13]. Wieser and Yasargil proposed a transsylvian approach to the amygdala and hippocampus^[14].

There is still controversy about the best surgical approach for mesial temporal epilepsy^[15]. Elseways, selective resections of mesial structures could have less cognitive effects, whereas an anterior temporal lobectomy has better seizure control.

In a review in 2008, Schramm^[16] cites eight studies that compared selective surgery against temporal lobectomy concerning seizure control. In six of these studies, the authors found no difference in seizure control despite the surgical approach. ATL was more effective in two papers, one in children^{[17][18]}.

Josephson^[19] compared ATL and SAH in a meta-analysis of 13 articles and 1203 patients, showing better control of seizures in ATL.

Materials and methods

A retrospective study was carried out based on the medical records of 146 patients operated on for temporal lobe epilepsy from 2008 to 2019. The ILAE classification (Table 1) was used to determine the degree of seizure control, and we compared the descriptive results according to the technique used.

The preoperative evaluation of these patients included neuropsychological testing, video-EEG, and high-resolution MRI. In cases where the video-EEG with scalp electrodes failed to define the temporal lobe as an epileptogenic source, a foramen ovale electrode was implanted as a complementary method. We included only patients with unilateral hippocampal sclerosis on MRI and concordant epileptic onset on video-EEG. Non-invasive options such as functional MRI would add additional costs and time, being a method not exempt from clinical differences^[20].

The same surgeon performed all surgeries. In right-sided hippocampal sclerosis, a temporal lobectomy was performed using the Spencer technique^[12], resecting 3.5 cm of the anterior border of the temporal lobe. In left hippocampal sclerosis, a selective amygdalohippocampectomy was used as described by Niemeyer^[13].

The rationale for the choice of surgical access

The choice between ATL and SAH based on the sclerosis side followed the following rationale:

1. All patients have typical temporal lobe seizures
2. The Video-EEG showed seizures with semiology and a typical electrographic pattern.
3. Volumetric MRI showed no lesions other than unilateral hippocampal sclerosis.

In Brazil and several developing countries, the cost is a limiting factor in performing surgeries. Invasive research so that we can individualize each access based on details of electrophysiology brings an increase in the expenses that would make it impossible to perform the procedures.

The amount paid by the public health system for the evaluation with video EEG and the surgical procedure for temporal lobe epilepsy is equivalent to 1200 US dollars. This total includes medical fees and hospital costs.

Adding an extended workup with invasive monitoring is impossible within this scenario.

On the other hand, we have a constant lack of drugs for epilepsy in the public health system, making clinical treatment uncertain.

All this favors the idea of a safe surgical treatment that brings good results. Even if within a reality of limited resources.

The literature shows that both accesses have excellent results in seizure control and neuropsychological outcome^[16]. Despite overall good results, some studies show a worse language performance in patients operated with left ATL. Similarly, SAH would have a worse outcome in epilepsy control^{[17][21]}.

We compared the two groups using contingency tables. We used analysis of variance (ANOVA) to compare the results with the kind of surgery (ATL or SAH) and also performed a Kaplan–Meier survival analysis until the "seizure" event, ILAE 1 status, and a good result (ILAE 1 to 3). The data were analyzed with the IBM SPSS Statistics Software. A p– value of less than 0.05 was considered significant.

Results

Our database computed 146 patients operated for temporal lobe epilepsy, secondary to hippocampal sclerosis, between 2008 and 2019. 13 were excluded from the study in our initial analysis due to incomplete medical records or follow-up loss. One patient died in the immediate postoperative period from pulmonary thromboembolism (mortality of 0.06%) and was excluded from the analysis. The remaining 132 patients were evaluated. Seventy-two patients were female (53%) and 60 male (47%). The mean age at the time of surgery was 37.85 years (9–65 years).

In 70 (53%) patients, hippocampal sclerosis was on the right side and 62 (47%) on the left. All the operated cases were submitted to anatomopathological and immunohistochemical analysis of the resected tissues. The results showed absence of abnormalities or a neuronal depopulation suggestive of hippocampal sclerosis.

We found no statistical difference between age, sex and follow-up time in the two groups (ATL and SAH), as summarized in table 2.

The mean follow-up time after surgery was 57.2 months (12–137). Sixty-six (50%) patients had at least one seizure in the follow-up period (events in the first 30 days after surgery were not considered). At the end of the follow-up period, 105 (79.5%) patients were on ILAE 1 to 3 (good result). Of the patients submitted to ATL, 62 (88.6%) obtained a good result against 43 (69.3%) of the patients in the SAH group (p = 0.006).

In our series, only 58 (43.9%) patients were on ILAE 1 at the end of the follow-up period, 40 (57.1%) in the ATL group and 18 (31.0%) in the SAH group (p = 0.001). These results are summarized in (Table 2).

The average interval until an epileptic event was 22.8 months (ranging from 1 to 86.1 months). Patients undergoing ATL had a mean time to the first seizure of 23.04 months against 21.86 in those undergoing SAH, with no statistical difference (p = 0.82). (Chart 1). The Kaplan Meyer mortality curves (Chart 2), using the Log Rank (Mantel–Cox) statistical analysis, with seizure as the event, showed a significant difference between the ATL and SAH (p= 0.024).

Our surgical morbidity rate was 11.8% (17/143), and mortality was 0.6% (1/143), consistent with the results described in the literature. The death occurred in the first postoperative week and was caused by Pulmonary Thromboembolism (PTE), and this patient was excluded from the analysis of results regarding epilepsy control. The other complications are simplified in Table 3.

Discussion

The primary purpose of surgery is to control seizures. Maintaining a good functional status of patients is also mandatory. The search for a more selective resection is based on not worsening memory and language deficits, especially in the dominant hemisphere. It has been shown in several articles that the selective resection of mesial structures has a benefit, even if marginal, in the cognitive assessment of patients^{[22][23][24]}. Other authors do not show differences between ATL and SAH regarding neuropsychological prognosis^{[25][26]}. Helmstaedter^[21] postulates that the cognitive deficit after eloquent temporal resection could be more linked to perioperative cortical injury, visible in post-surgical MRI, than to the type of resection.

The only multicenter randomized study showing the outcome of surgery in terms of seizure control was performed by Wiebe et al. in 2001. In the group of patients operated on, always by ATL, 38% were completely free of seizures (Engel 1).

Concerning the control of epilepsy, there are variable results in the literature when comparing SAH and ATL. Several authors show equality in seizure control^{[27][28][29]}, while others show better results in ATL^{[17][18]}.

Clusmann^[18], in a series of 89 children and adolescents, found a worse result in seizure control in SAH when compared to ATL. Also, patients with left hippocampal sclerosis had a worse result despite the surgical technique. In a meta-analysis including 13 studies and 1203 patients, Josephson^[19] found better control of seizures in ATL than in SAH.

Our evaluation sought to compare the two types of surgery, not only in terms of good surgical outcomes but also in the occurrence of seizures and the complete control of seizures (ILAE 1).

The ANOVA statistical analysis show a better outcome in occurrence of seizures ($p = 0.005$), ILAE 1 final result ($p = 0.001$) and good result ($p = 0.006$) in favour of ATL.

We performed Kaplan Meyer's survival analysis having a seizure as the target event. The curves showed better results in ATL over SAH. The Log Rank statistical analysis significantly favors the ATL group ($p = 0.029$).

The Kaplan Meier graphs show a downward curve with a progressive worsening of the results over time, consistent with the findings described in the literature. The results are consistent with a better surgical prognosis in resections that include the temporal neocortex over more selective resections.

Interestingly, the interval until the first epileptic event was similar when comparing the two groups. However, patients in the SAH group had seizures more often after this initial event (Chart 1). This finding could be related to the maintenance of an altered neuronal network in patients with more selective resection, which quickly resumes the pattern of seizures after a first ictal event^[30].

The same difficulty of resources that makes it difficult to carry out a more individualized approach to cases makes the surgery attractive from a cost-benefit point of view.

As the procedure is safe with very low morbidity and mortality, surgery proves to be an effective procedure for our reality. Clinical treatment has a significant cost and, in most cases, it is paid for by the state, which cannot maintain this treatment without interruptions due to lack of funds.

Limitations of the study

We did not assess neuropsychological, speech, and language differences between groups, as all surgeries in the left hemisphere were SAH.

In our series, preoperative tests to determine hemispheric dominance for language were not performed. By convention, all cases on the left (predominantly dominant hemisphere in humans^{[31][32]}) were submitted to SAH, and those on the right to ATL, the interpretation of our results is limited. It is essential to mention that Clusmann^[18], in 2004, observed that surgeries in the dominant hemisphere had worse results despite the technique used. It is a possible bias in our work. Despite these limitations, we believe that the data obtained adds relevance to the discussion about the difference in results regarding the technique used.

We excluded all patients who had MRI lesions other than HS to avoid a worse result in selective surgeries for patients who had lesions in the temporal neocortex. However, MRI is not always able to clearly show small dysplastic lesions.

The postoperative evaluation time was long enough to show the differences between the two techniques. As there is a tendency for the results to progressively worsen over time, as demonstrated in our survival curves, a longer follow-up perhaps showed that the two techniques tend to match up with a longer follow-up.

Conclusion

There is still controversy about the influence of more selective procedures in surgery for ATL epilepsy. Our work has shown better results concerning the control of epilepsy when we use ATL compared to SAH. Despite the varied results of articles on the subject, our data show that performing ATL may be more effective in controlling epilepsy, emphasizing the importance of assessing language and

memory before and after surgery to define the standard of comparison between the two surgical techniques. Whenever possible, the choice of access route should be made individually for each patient, based on neurophysiological and imaging findings. In countries with a cost limitation for extended propaedeutics, ATL may be the best option for the proper control of seizures with minimal additional morbidity.

Appendices

Outcome classification	Definition
1	Completely seizure free; no auras
2	Only auras; no other seizures
3	One to three seizure days per year; \pm auras
4	Four seizure days per year to 50% reduction of baseline seizure days; \pm auras
5	Less than 50% reduction of baseline seizure days to 100% increase of baseline seizure days; \pm auras
6	More than 100% increase of baseline seizure days; \pm auras

Table 1. ILAE outcome classification (from Wieser HG, Blume WT, Fish D, Goldensohn E, Hufnagel A, King D, et al. ILAE Commission Report. Proposal for a new classification of outcome with respect to epileptic seizures following epilepsy surgery. 2001. pp. 282–6).

		Total	ATL Right HS	SAH Left HS	p
n		132	70 (53.0%)	62 (47.0%)	
Gender	M	60 (47.0%)	30 (42.9%)	30 (48.4%)	
	F	72 (53.0%)	40 (57.1%)	32 (51.6%)	
Mean age in years		37,85	36,94	38,87	
Mean Follow up in months		57.2	55,7	58,8	
ILAE	1	58 (43.9%)	40 (57.1%)	18 (31.0%)	P=0.001
	2	2 (1,5%)	0 (0.0%)	2 (3.2%)	
	3	45 (34.1%)	22 (31.4%)	23 (37.1%)	
	1 to 3	105 (79.5%)	62 (88.6%)	43 (69.3%)	P=0.006
	4	16 (12.1%)	5 (7.1%)	11 (17.7%)	
	5	11 (8.3%)	3 (4.3%)	8 (12.9%)	
	6	0 (0.0%)	0 (0.0%)	0 (0.0%)	

Table 2. Frequencies comparing anterior temporal lobectomy (ATL) and selective amygdalo hippocampectomy (SAH) groups for the treatment of hippocampal sclerosis (HS). ILAE 1 to 3 are considered as good result.

Age, sex	Complication
29, Male	Cardiorespiratory arrest in anesthetic induction
41, Male	Wound infection, cranioplasty, chronic headache
25, Female	Wound infection
43, Female	Wound infection
20, Female	Wound infection
20, Female	Wound infection
40, Female	Memory impairment
41, Female	Memory impairment
30, Female	Memory impairment
48, Male	CSF leak submitted to external lumbar shunt, acute subdural hematoma, decompressive craniectomy, wound infection, debridement, cranioplasty.
46, Female	Postoperative hemiparesis with subsequent recovery
48, Female	Visual field disorder
41, Female	Visual field disorder
51, Female	Visual field disorder
27, Male	Visual field disorder
65, Male	Intraparenchymal hematoma
39, Female	Deep Vein Thrombosis

Table 3. Complications reported in our case series

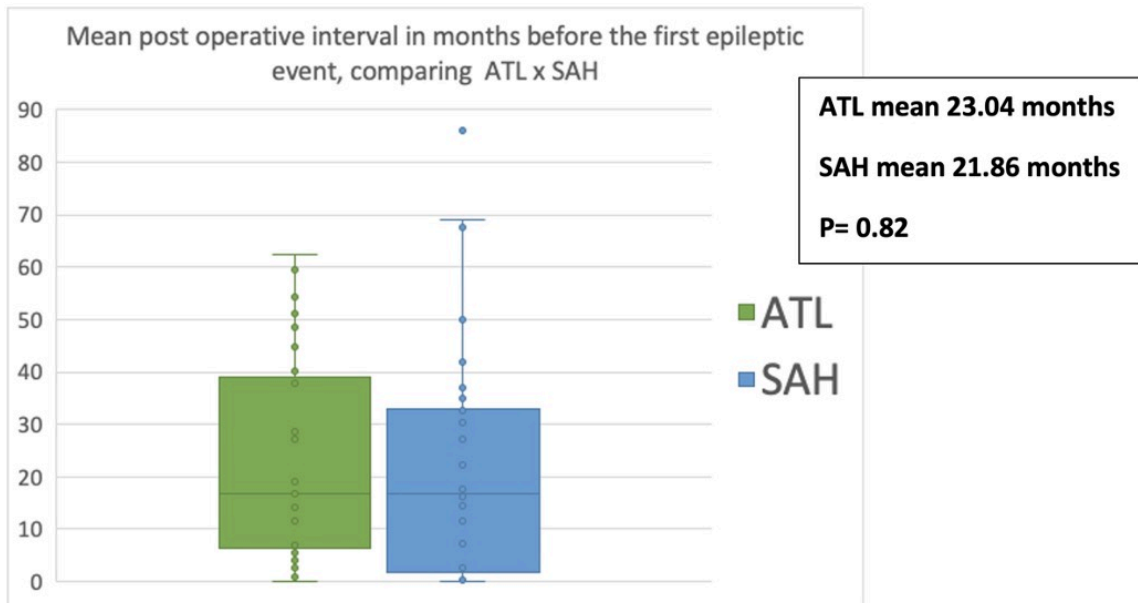


Chart 1. Event free interval comparing the ATL and SAH groups. ATL: anterior temporal lobectomy SAH: selective amygdalo hippocampectomy Student T test between surgerygroups: $p=0.82$.

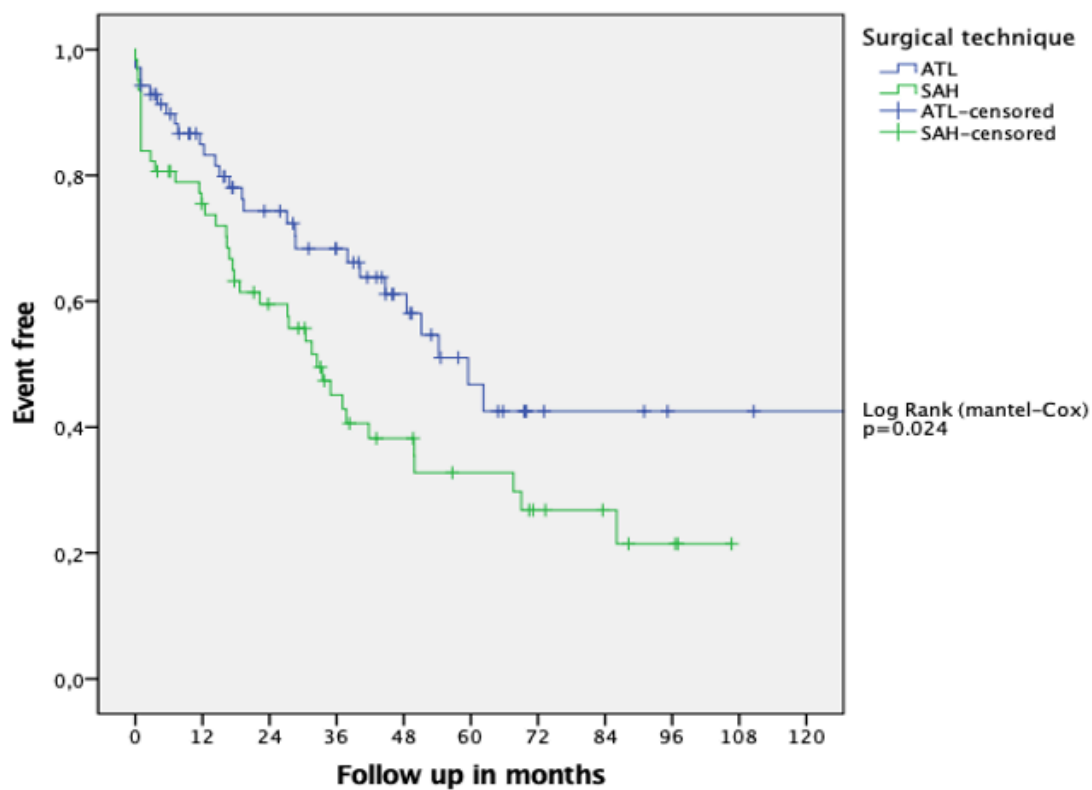


Chart 2. Kaplan-Meier survival analysis with seizure as event, comparing ATL and SAH. ATL: anterior temporal lobectomy. SAH: selective amygdalohippocampectomy Statistical analysis using Mantel-Cox Log Rank. $P=0.024$.

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