Faculdade de Medicina de São José do Rio Preto
Programa de Pós-graduação em Ciências da Saúde

LUCAS CROCIATI MEGUINS

CORTICOAMIGDALOHIPOCAMPECTOMIA PARA O TRATAMENTO DA EPILEPSIA REFRATÁRIA ASSOCIADA À ESCLEROSE MESIAL TEMPORAL

São José do Rio Preto
2014

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Dissertação apresentada à Faculdade de Medicina de São José do Rio Preto para obtenção do título de Mestre no Curso de Pós-Graduação em Ciências da Saúde.

Eixo Temático: Medicina Interna.

Orientador: Prof. Dr. Gerardo Maria de Araújo Filho

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Corticoamigdalohipocampectomia para o tratamento da epilepsia refratária associada à esclerose mesial temporal / Lucas Crociati Meguins

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SUMÁRIO

DEDICATÓRIA

A Deus, fonte de energia.

À minha família que tanto me incentiva.

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Ao meu orientador e amigo, Prof. Dr. Gerardo Maria de Araújo Filho, pela confiança e infinito apoio, sem o qual certamente esta caminhada haveria de ser mais árdua.

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À minha noiva, Nadine Siqueira, por renovar minha alegria e força diariamente.

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AED	Anti-epileptic drugs
ATL-AH	Standard anterior temporal lobectomy with amygdalohippocampectomy
BMC	BioMed Central
CAH	Corticoamigdalohipocampectomia
CI	Confidential interval
CNS	Central nervous system
DAE	Drogas anti-epilépticas
EEG	Eletroencephalogram
ELT	Epilepsia do lobo temporal
EMT	Esclerose mesial temporal
FAMERP	Faculdade de Medicina de São José do Rio Preto
FLAIR	Fluid-attenuated inversion recovery
MRI	Magnetic resonance image
MTS	Mesial temporal sclerosis
OMS	Organização Mundial da Saúde
QOL	Quality of life
RCT	Randomized controlled trial
SD	Standard deviation
SelAH	Selective amygdalohippocampectomy
TCE	Traumatismo cranioencefalico
TLE	Temporal lobe epilepsy

RESUMO

INTRODUÇÃO: A esclerose mesial temporal (EMT) representa a doença cirúrgica mais comumente associada à epilepsia do lobo temporal (ELT) atingindo uma porcentagem de 28% a 62% nas séries de ressecção do lobo temporal. **OBJETIVOS:** O objetivo do presente estudo é descrever as características sócio-demográficas e clínicas de pacientes com ELT-EMT submetidos à corticoamigdalohipocampectomia (CAH) e investigar a influência da idade do paciente no momento da cirurgia e a duração da doença antes do tratamento cirúrgico no resultado clínico da ELT em um centro terciário para tratamento da epilepsia. **MÉTODOS:** Uma investigação observacional retrospectiva com coleta de dados de uma coorte de pacientes consecutivos, tratados cirurgicamente no Hospital de Base da Faculdade de Medicina de São José do Rio Preto (FAMERP), um centro terciário brasileiro para o tratamento de epilepsia, a partir de janeiro de 2000 a março de 2012. Os pacientes foram divididos de acordo com sua idade no momento da cirurgia (<ou ≥50 anos) e duração da epilepsia antes do tratamento cirúrgico (<ou> 10 anos). **RESULTADOS:** Duzentos e vinte e nove pacientes foram incluídos no presente estudo. A idade média no momento da cirurgia foi de 39,9 ± 11,57 anos, com 105 (45,8%) do sexo masculino e 124 (54,2%) do sexo feminino. Duzentos e vinte e um (96,5%) pacientes eram destros e oito (3,5%) canhotos. Trinta (13,1%) pacientes apresentavam história prévia de convulsão febril na infância e 27 (11,7%) relataram traumatismo craniano antes do início das crises refratárias. Trinta e seis (16%) usavam um único drogas anti-epiléptico (DAE) e 193 (84%) estavam tomando dois ou mais DAE. No acompanhamento pós-operatório dos pacientes observou-se que 144 (62,8%) foram classificados como Engel I e 200 (87,5%) foram classificados como Engel I ou II. Onze pacientes (4,7%) foram Engel III e 18 (7,8%) foram

Engel IV. Aos seis, doze e vinte quatro meses de seguimento, 144, 137 e 132 pacientes, respectivamente, foram classificados como Engel I. Cento e onze de 179 pacientes (62%) foram classificados como Engel I no grupo com <50 anos de idade, ao passo que 33 de 50 (66%) como Engel I no grupo com ≥50 anos grupo de idade (p = 0,82). Do total de pacientes livres de crises (Engel I), 88 (61%) relataram a duração da epilepsia inferior a 10 anos e 56 (39%) superiores a 10 anos (p <0,01). Do total de pacientes não livres de crises (Engel II, III e IV), 36 (42%) relataram a duração da epilepsia inferior a 10 anos e 49 (58%) superiores a 10 anos (p <0,01). Não houve deficit neurológico significativos relacionadas à cirurgia ou mortes. **CONCLUSÕES:** No presente estudo, demonstramos que CAH é uma modalidade cirúrgica segura e viável para tratar eficazmente pacientes com ELT-EMT. Além disso, observou-se que a menor duração da epilepsia no momento da cirurgia é um importante fator de risco que deve ser considerado antes de tratamento cirúrgico. O reconhecimento precoce e tratamento adequado de pacientes com ELT-EMT podem melhorar o resultado do controle das crises.

Palavras-chave: Esclerose mesial temporal; epilepsia do lobo temporal; corticoamigdalo-hipocampectomia

ABSTRACT

INTRODUCTION: Mesial temporal sclerosis (MTS) is the commonest surgical pathology associated with refractory temporal lobe epilepsy (TLE) with a percentage in series of temporal lobe resection ranging from 28% to 62%. **OBJECTIVE:** The aim of the present study is to describe the clinical and sociodemographic characteristics of patients with TLE-MTS submitted to cortico-amygdalohippocampectomy (CAH) and to investigate the influence of patient's age at surgery and seizure onset on surgical outcome of TLE in a Brazilian tertiary epilepsy center. **METHODS:** A retrospective observational investigation was performed with data collection from a cohort of consecutive patients surgically treated in the epilepsy clinic of Faculdade de Medicina de Sao Jose do Rio Preto (FAMERP), a Brazilian tertiary referral epilepsy center, from January 2000 to March 2012. Patients were divided accordingly to their age at surgery (< or ≥50 years) and to epilepsy duration at surgery (< or > 10 years). **RESULTS:** Two hundred and twenty-nine patients were included. The mean age at surgery was of 39.9±11.57 years, with 105 (45.8%) male and 124 (54.2%) female. Two hundred and twenty-one (96.5%) patients were right-handed and eight (3.5%) left-handed. Thirty (13.1%) patients presented a previous history of febrile seizure during infancy and 27 (11.7%) reported head trauma before the beginning of refractory seizures. Thirty-six (16%) were taking a single anti-epileptic drug (AED) and 193 (84%) were taking two or more AEDs. Patients' follow-up observed that 144 (62.8%) were classified as Engel I and 200 (87.5%) were classified as Engel I or II. Eleven patients (4.7%) were Engel III and 18 (7.8%) were Engel IV. At six, twelve and twenty-four months of follow-up, 144, 137 and 132 patients, respectively, were classified as Engel I. One-hundred and eleven of 179 patients (62%) were classified as Engel I in the group with <50 years old, whereas 33 of

50 (66%) as Engel I in the group with ≥50 years old group (p=0.82). From the total of patients seizure free (Engel I), 88 (61%) reported epilepsy duration inferior to 10 years and 56 (39%) superior to 10 years (p<0.01). From the total of patients not seizure free (Engel II, III and IV), 36 (42%) reported epilepsy duration inferior to 10 years and 49 (58%) superior to 10 years (p<0.01). There were no surgery-related significant neurological deficits or deaths. **CONCLUSION:** In the present study, we demonstrated that CAH is a safe and feasible surgical modality to effectively treat patients with refractory TLE-MTS. Additionally, it was observed that a shorter epilepsy duration at surgery is an important risk factor that must be considered before surgical management of MTS. Early recognition and surgical treatment of patients with refractory TLE-MTS may improve seizure outcome.

Key-words: Mesial temporal sclerosis; temporal lobe epilepsy; cortico-amygdalohippocampectomy

1. INTRODUÇÃO

INTRODUÇÃO

A epilepsia é a doença neurológica mais comumente encontrada no mundo, atingindo cerca de 50 milhões de pessoas em todo o planeta, e destas, aproximadamente 40 milhões apenas em países em desenvolvimento. Indivíduos de todas as raças, gêneros, condições socioeconômicas e regiões são atingidos.[1, 2] No Brasil, segundo estimativa do Ministério da Saúde, cerca de 157.070 casos novos são diagnosticados a cada ano (100/100.000) com uma prevalência de 11,9/1.000 a 16,5/1.000 de formas ativas da doença.[3, 4]

Embora diversas investigações epidemiológicas tenham revelado a sua importância clínica e social, os dados de prevalência das epilepsias são muito variáveis. Essas variações são explicadas tanto pelas dificuldades metodológicas, que vão desde as definições adotadas para a doença até a fonte de obtenção dos dados, quanto pelas características individuais dos pacientes estudados.[5]

A maioria dos pacientes acometidos por epilepsia tem um bom prognóstico a longo prazo.[4] Segundo dados da OMS (2006),[5] 70% dos casos recém diagnosticados podem alcançar a remissão com o uso das drogas antiepilépticas e após dois a cinco anos de tratamentos sem crises, esses medicamentos podem ser retirados em 70% das crianças e 60% dos adultos. Esse prognóstico, contudo, depende de inúmeros fatores, tais como idade, etiologia da epilepsia, componentes estruturais encefálicos, tipos de crises convulsivas e padrões eletroencefalográficos.[4]

Dessa forma, investigações epidemiológicas que visam a revelar essas variáveis são fundamentais não apenas para o reconhecimento prognóstico, mas também, para fornecer dados que permitam ao médico esclarecer ao paciente e à família sobre sua condição crônica, mas não

intratável, pois isso favorece a adesão ao tratamento e contribui para eliminar os aspectos do preconceito existentes com relação às epilepsias.

Epidemiologia Internacional da Epilepsia

A incidência anual de epilepsia na maioria dos pesquisas varia entre 40 e 70/100.000,[6] atingindo 122 a 190/100.000 nos países em desenvolvimento.[7] Estas elevadas taxas nos países em desenvolvimento são atribuíveis a causas parasitárias (principalmente neurocisticercose), infecções intracranianas virais ou bacterianas, traumatismo cranio encefálico (TCE) e doenças cerebrovasculares.[1,8-12] Na maioria das investigações internacionais, as taxas de prevalência pontual de epilepsia ativa na população geral ficam entre 0,4% e 1% e as de prevalência de vida entre 1,5% e 5%.[6] Aspectos genéticos, fatores de risco relacionados ao meio ambiente e metodologia de pesquisa influenciam a prevalência. Estudos em pequena escala, ou envolvendo populações isoladas ou selecionadas em países em desenvolvimento, acharam altas taxas de prevalência.[13, 14] Mas estudos em larga escala em países em desenvolvimento apontaram taxas de prevalência semelhantes às de países desenvolvidos.

Epidemiologia Brasileira da Epilepsia

Há poucos investigações epidemiológicas avaliando a prevalência e incidência da epilepsia no Brasil. Ainda existe um outra dificuldade referente às dimensões geográficas do Brasil que delimitam regiões e povoados com características próprias de vida e trabalho, determinando grandes diferenças epidemiológicas. Almeida Filho estudou habitantes do bairro de Amaralina de Salvador/BA, que na época contava com 27 mil habitantes, e encontrou prevalência de epilepsia ativa de 0,1%, surpreendentemente baixa para os padrões latino-

americanos.[15] Em outro estudo populacional em Porto Alegre/RS, Da Costa et al., estimaram que 0,2 a 2% dos habitantes da região devem apresentar uma ou mais crises durante a vida.[16] Marino Jr. et al. encontraram uma prevalência de epilepsia de 1,19% na cidade de São Paulo/SP.[17] Fernandes et al. encontraram uma taxa de prevalência de 1,65% de epilepsia ativa e 2,03% de epilepsia inativa em Porto Alegre/RS.[3] Borges et al. avaliaram a comunidade dos índios Bakairi residentes às margens do rio Paranatinga, afluente do rio Xingu. A prevalência foi de 1,2% para epilepsia ativa e de 0,6% para inativa.[18]

Baseados nos estudos internacionais, poderíamos então inferir aproximadamente 340 mil casos novos ao ano (estimativa de incidência anual de 190/100.000), 1,8 milhões de pessoas com epilepsia ativa (estimativa de 1% de prevalência pontual) e 9 milhões de pessoas que já apresentaram crises epilépticas alguma vez nas suas vidas (estimativa de 5% de prevalência de vida).

Impacto econômico da epilepsia

O impacto econômico da epilepsia se tornou um assunto importante em anos recentes. Várias das novas drogas antiepilépticas (DAE) têm um custo mais de 100 vezes superior ao do fenobarbital e 10 a 20 vezes superior ao da fenitoína e carbamazepina.[19]

O custo do tratamento pelas DAE é, entretanto, apenas uma pequena parte da "conta" global. Custos indiretos (custos de morbidade, benefícios, mortalidade excessiva, pensões, desemprego, dias de trabalho perdidos e outros custos sociais), assim como custos relacionados ao tratamento, particularmente hospitalização, são muito mais significativos. A Organização Mundial de Saúde (OMS) calculou o impacto global das doenças: epilepsia foi estimada como responsável por 1% dos dias perdidos com doenças em todo o mundo.[20]

Prognóstico

Aproximadamente três quartos das pessoas que desenvolvem epilepsia podem se tornar livres de crises através do uso de DAE.[21] Muitas podem, eventualmente, ter a sua medicação retirada após algum tempo, mas outras precisarão dar continuidade ao tratamento por tempo indefinido. Estudos baseados em comunidades e em populações mais selecionadas consistentemente revelam que as pessoas com epilepsia têm uma mortalidade duas a três vezes superior da população geral.

2. OBJETIVO

OBJETIVOS

Objetivo Geral

Avaliar clínica e epidemiologicamente os pacientes submetidos ao procedimento de corticoamigdalohipocampectomia para o tratamento da epilepsia refratária associada à esclerose mesial temporal.

Objetivos Específicos

1. Identificar o perfil clínico, epidemiológico e sociodemográfico dos pacientes submetidos à cirurgia de epilepsia do lobo temporal.
2. Avaliar a influência da idade do paciente no momento da cirurgia na evolução clínica pós-operatória da frequência das crises convulsivas.
3. Avaliar a influência da duração da epilepsia antes do procedimento cirúrgico na evolução clínica pós-operatória da frequência das crises convulsivas.

3. ARTIGOS CIENTÍFICOS

ARTIGOS CIENTÍFICOS

Os resultados referentes aos objetivos dessa dissertação estão apresentados na forma de artigos científicos conforme a descrição abaixo:

Artigo 1

Título: Cortico-amygdalohippocampectomy for refractory temporal lobe epilepsy with mesial temporal sclerosis: surgical series of a tertiary epilepsy center.

Periódico: BMC Neurology (ISSN: 1471-2377), submetido em 15/07/2014.

Status: Artigo sob revisão do comitê editorial.

Artigo 2

Título: Shorter epilepsy duration is associated with better seizure outcome in temporal lobe epilepsy surgery.

Periódico: Arquivos de Neuro-Psiquiatria (ISSN: 1678-4227), submetido em 14/09/2014.

Status: Artigo sob revisão do comitê editorial.

A. ARTIGO CIENTÍFICO 1

ARTIGO CIENTÍFICO 1

Título: Cortico-amygdalohippocampectomy for refractory temporal lobe epilepsy with mesial temporal sclerosis: surgical series of a tertiary epilepsy center.

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ABSTRACT

Introduction: Mesial temporal sclerosis (MTS) is the commonest surgical pathology associated with refractory temporal lobe epilepsy (TLE).

Objective: The aim of the present study is to describe the clinical and sociodemographic characteristics of patients with (TLE-MTS) submitted to cortico-amygdalohippocampectomy (CAH) in a tertiary Brazilian epilepsy center.

Mehods: A retrospective investigation was performed with data collection from a cohort of consecutive patients from the epilepsy clinic of Faculdade de Medicina de Sao Jose do Rio Preto (FAMERP), a Brazilian tertiary referral epilepsy center, from January 2000 to March 2012.

Results: Two hundred and twenty-nine patients were included. The mean age at surgery was of 39.9±11.57 years, with 105 (45.8%) male and 124 (54.2%) female. Two hundred and twenty-one (96.5%) patients were right-handed and eight (3.5%) left-handed. Thirty (13.1%) patients presented a previous history of febrile seizure during infancy and 27 (11.7%) reported head trauma before the beginning of refractory seizures. Thirty-six (16%) were taking a single anti-epileptic drug (AED) and 193 (84%) were taking two or more AEDs. Patients' follow-up observed that 144 (62.8%) were classified as Engel I and 200 (87.5%) were classified as Engel I or II. Eleven patients (4.7%) were Engel III and 18 (7.8%) were Engel IV. At six, twelve and twenty-four months of follow-up, 144, 137 and 132 patients, respectively, were classified as Engel I. There were no surgery-related significant neurological deficits or deaths.

Conclusion: In the present study, we demonstrated that CAH is a safe and feasible surgical modality to effectively treat patients with refractory TLE-MTS.

Key-words: Mesial temporal sclerosis; cortico-amygdalohippocampectomy; seizure outcome.

INTRODUCTION

Mesial temporal sclerosis (MTS) is the commonest surgical pathology associated with refractory temporal lobe epilepsy (TLE) with a percentage in series of temporal lobe resection ranging from 28% to 62%.[1-3] Falconer and colleagues were the first to describe the favorable outcome for seizure remission if this lesion was confirmed at pathology.[4, 5] In 2001, a randomized, controlled trial demonstrated the superior efficacy of surgery over prolonged pharmacological therapy for TLE-MTS.[6] Epilepsy surgery has become an important treatment option for 30 to 40% of patients with refractory TLE-MTS. Current evidence suggests a 60-to-70% remission rate for long-term epileptic symptoms and significant improvements in quality of life (QOL).[6-8] Data from previous studies have demonstrated that cortico-amygdalohippocampectomy (CAH) is a safe, efficient surgical procedure for patients with refractory TLE-MTS. The latter condition compromises the primary structures of the limbic system, particularly the hippocampus and amygdala.

However, there remains significant variation among centers in patient selection criteria and surgical technique for management of MTS.[7, 8] Moreover, many studies reporting on MTS use disparate definitions of seizure freedom, assess seizure freedom at different times of follow-up, and use different statistical methods.[9, 10] Such discrepancies may explain the wide variations in clinical and surgical results. The aim of the present study is to describe the clinical and sociodemographic characteristics of patients with (TLE-MTS) submitted to cortico-amygdalohippocampectomy (CAH) in a tertiary Brazilian epilepsy center, as well as their surgical outcome and the incidence and types of surgical complications.

METHOD

Study Delineation

A retrospective observational investigation was conducted with data collection of consecutive patients from the epilepsy clinic of the Faculdade de Medicina de Sao Jose do Rio Preto (FAMERP), a Brazilian tertiary referral epilepsy center, from January 2000 to March 2012. Patients with neuroradiological evidence and neuropathological confirmation of other diseases than MTS, as well as additional potential epileptogenic MRI-lesions, were excluded.

Clinical data were obtained retrospectively from the patient records and files. For all patients with the diagnosis of MTS on MRI, the following data were collected: gender, age at operation, handedness, type and number of AEDs used and results of neuropsychological evaluation. In addition, non-invasive video-EEG data and side of surgery were registered.

Pre-surgical Evaluation

All patients were submitted to non-invasive video-EEG monitoring using the Stella system, Neuro Workbench software and a Nihon Kohden hardware 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 below one standard deviation of normal, age-matched control persons.

Brain MRI were obtained accordingly with a specific epilepsy protocol using a 1.5 Tesla Scanner, Philips, at the Department of Neuroradiology in our institution. Displaying the sagittal 3D T1-weighted gradient-echo sequences, the next sequences were an axial and coronal fluid-attenuated inversion recovery (FLAIR) 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).

All MRIs were analyzed by an experienced neuroradiologist who confirmed the visual radiological diagnosis of MTS, which was determined to be present if atrophy, an increased T2-weighted signal, a decreased T1-weighted signal and a disrupted internal structure of the hippocampus were present, accompanied by atrophy of the amygdala and/or temporal pole signal alteration on visual inspection of the MRI pictures.

Biopsy specimens were obtained from all patients who underwent surgical treatment and standardized neuropathological analyses were performed. Surgical specimens were microscopically analyzed using hematoxylin-eosin staining. MTS was diagnosed via pathological findings: cell loss in the CA3 and CA1 pyramidal cells and dentate hilar neurons with relative sparing of the dentate granular cells and CA2 pyramidal cells. The pathologist reported their findings independently of clinical or imaging data. Patients with dual pathology (MTS plus another epileptogenic lesion) were excluded.

Surgical Technique

The surgical approach was similar for all patients, and only one neurosurgeon experienced in surgery for epilepsy (SCS Jr.) performed all patients' surgeries. Patient positioning includes placing a shoulder roll to elevate the trunk and then turning the head 15-20

degrees from the midline so that the operative side is up. The head is slightly extended to bring the sylvian fissure to a perpendicular plane to the operating approach. Finally, dropping the vertex down toward the floor improves surgeon access to mesial structures and allows less retraction on the temporal lobe. A reverse question mark incision was made from just above the zigoma extending back in the temporal region. An anterior temporal craniotomy was performed respecting the anatomical landmarks of the temporal lobe from the root of the zygoma to the anatomic keyhole. The anterior and lateral remaining bone was removed by drilling down to the limits of the medial fossa floor. At the end of the craniotomy, all bone edges were waxed as necessary, any exposed air cells sealed and take-up sutures were performed before opening the dura-mater to prevent epidural bleeding. A maximum of 4.0 to 5.0 cm of the anterior lateral temporal lobe was resected. The mesial resection included amygdala removal and the anterior 2.0 to 3.0 cm of the hippocampus.

Post-surgical Follow-Up

Follow up investigation were carried out in six, 12 and 24 months after surgery. At the 12 months follow up, all 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 (including auras), i.e. Engel IA, or not seizure-free (Engel IB-IV). Operative mortality was defined as death within 30 days of surgery.

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

The software used to perform statistical analysis were Microsoft Excel 2013, R 3.0.3 and SPSS. Data collected from all patients were organized in tables and compared with previous studies. Averages were expressed as the means ±SD for parametric data and as median values for nonparametric data. Seizure-free survival rate was assessed using Kaplan-Meier curves. A p-value<0.05 was considered statistically significant.

RESULTS

Pre-surgical Demographic and Clinical Characteristics

At the moment of the study, 533 patients underwent multidisciplinary investigation of epilepsy, and 229 (42.9%) fulfilled the inclusion criteria. Table 1 summarizes the demographic and clinical data of all patients. The preoperative mean age was of 39.9±11.57 years, with 105 (45.8%) male and 124 (54.2%) female. Two hundred and twenty-one (96.5%) patients were right-handed and eight (3.5%) left-handed. Thirty (13.1%) patients presented a previous history of febrile seizure during infancy and 27 (11.8%) reported head trauma before the beginning of refractory seizures. Thirty-six (15.7%) were taking a single anti-epileptic drug (AED) and 193 (84.3%) were in polytherapy, i.e., taking two or more AEDs. One hundred and eighty-one (79.0%) patients presented normal or unilateral rhythmic waves during the interictal video-EEG

and 48 (21.0%) bilateral rhythmic waves. Two hundred eleven (92.1%) and 18 (7.9%) patients presented unilateral and bilateral rhythmic waves during the ictal video-EEG, respectively. One hundred and sixty-nine (73.8%) patients showed radiological evidence of unilateral MTS on MRI, being 78 (46.1%) on the right side and 91 (53.9%) on the left, and 60 (26.2%) revealed bilateral involvement of the mesial temporal lobe. One hundred and twenty-one (52.8%) patients underwent surgical resection on the left side and 108 (47.2%) on the right side. Table 2 summarizes and compares the present study with major surgical series (>100 patients) of the 21st century for the treatment of TLE-MTS.

Seizure Control and Follow-Up

Patients were followed-up for at least two years. Overall, 144 patients (63%) were Engel I, and 200 (87%) Engel I or II. Eleven (5%) were Engel III and 18 (8%) were Engel IV. Seizure control outcomes are presented in table 3. The seizure-free survival of our series over time was illustrated through a Kaplan-Meier curve observed in Figure 1. In addition, the cumulative seizure-free survival chance obtained from the two-year follow-up of patients is showed in Figure 2.

Surgical and Neurological Complications

During the follow-up period, eleven (4.8%) patients required re-admission or prolonged hospitalization due to operative and/or neurological complications. Five patients (2.2%) presented a wound infection, one (0.4%) requiring removal of the bone flap, debridement, and delayed cranioplasty after a course of antibiotics. Four patients (1.7%) experienced bacterial meningitis from gram-positive agents and were treated with intravenous antibiotics, evolving with no additional neurological complications. Two patients (0.8%) had medical complications

after surgery consisting of mild renal insufficiency in one patient and pulmonary embolus treated with anticoagulation in another patient. Both complications resolved without further sequelae. There were no operative deaths. Mean hospital stay were 5.6 days, varying from 4 to 21 days. The surgical complications are summarized in table 4.

DISCUSSION

Epidemiology

TLE is the most common type of epilepsy that requires surgical treatment with a good seizure outcome.[11, 12] Excellent short- and long-term results of epilepsy surgery have been published.[13, 14] Table 2 summarizes the major surgical series published in the 21st century regarding the surgial management of TLE-MTS. Including the present study, twenty individual series with more than one hundred patients followed for a minimum of 6 months were reported, most from single-center. Eighteen studies (90%) were retrospective, Cukiert et al (2002)[15] designed a prospective investigation and Schramm et al (2011)[16] performed a randomized controlled trial to compere two different surgical techniques. The follow-up period ranged from 0.5 to 9 years with a seizure control varying from 54% to 88.8%. The present study observed overall results similar to those of the major surgical series. Our series included 229 patients followed during 2 years after surgery and demonstrated a seizure control in 63% of all patients enrolled on the study. Postoperative complications were observed in 4.8% of patients and no deaths occurred. Accordingly with Téllez-Zenteno et al.,[13] the median proportion of long-term seizure-free patients was 66% with temporal lobe resections, which is close to the result obtained on the present investigation.

Seizure Outcome

Overall, the majority of patients (63%) became Engel I, and 200 (87%) Engel I or II. Hardy et al.,[17] studying 118 patients with refractory epilepsy submitted to surgery, obtained 61.8% of seizure freedom, and Tanriverdi et al.[18] revealed that a favorable outcome (Engel Class I and II) was achieved in 86% of patients after 5-year follow-up.

The percentages of seizure freedom after surgery for TLE-MTS have varied from 60% to 90% in modern series,[19] and the present overall seizure outcome was consistent with that reported in the literature. A sharp decrease in seizure freedom during the 1st and 2nd postoperative year has been reported.[20] Our recrudescence rate was like some other centers with 63%, 60% and 58% seizure-free patients after 6, 12 and 24 months after surgery, respectively. The risk of relapse was less than 4% in patients who were seizure free during the initial 6 months after surgery.

Post-surgical Complications

There were no surgery-related deaths. The surgical complications rates, as shown in table 4, compares favorably with other reported rates in larger studies.[1, 21] No other neurological deficits occurred after surgery. Five (2.2%) patients had a wound infection, with one (0.4%) patient requiring removal of the bone flap, debridement, and delayed cranioplasty after a course of antibiotics. Elliott et al (2013)[19] reported a similar case of wound infection that required debridement. Two (0.8%) patients had medical complications after surgery consisting of mild renal insufficiency in one patient and pulmonary embolus treated with anticoagulation in another patient. As shown by Tanriverdi et al (2008),[18] medical complications following surgery may occur without additional sequelae when diagnosed and treated as soon as possible.

Limitations

There are some important methodological limitations in this study. Firstly, although a large number of patients were included on the present investigation, it represents less than 50% of all patients that underwent CAH for TLE-MTS in our institution. The center receives patients from all regions from Brazil and, due to its large dimensions and difficulties in transportation, the follow-up of a great amount of patients were lost. Secondly, this study is a retrospective investigation with non-randomized surgical case series without a control group. Therefore, future prospective and randomized studies with a greater number of patients are certainly necessary to confirm such findings.

CONCLUSION

In the present study, we observed that CAH was a safe and feasible surgical modality to effectively treat patients with refractory TLE-MTS treated in a tertiary Brazilian referral epilepsy center. The surgical results observed were similar to previous investigations, with adequate percentages of patients who reached adequate seizure control associated with low rates of surgical and medical complications.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

TABLES, FIGURES AND LEGENDS

TABLE 1: Demographic and clinical data for 229 patients who underwent ATL-AH for MTS.

Table 1. Demographic and clinical data for 229 patients who underwent ATL-AH for MTS.

Variables	Value*
Age (mean±SD)	39.9±11.57
Gender	
-Male	105 (46%)
-Female	124 (54%)
Handedness	
- Right	221 (97%)
- Left	8 (3%)
Risk Factors	
- None	172 (75%)
- Febrile seizures	30 (13%)
- Head trauma	27 (12%)
Pharmacotherapy	
-Mono	36 (16%)
-Poli	193 (84%)
Interictal EEG	
- Unil./Normal	181 (79%)
- Bilateral	48 (21%)
Ictal EEG	
- Unilateral	211 (92%)
- Bilateral	18 (8%)
MRI	
- Unilateral MTS	169 (74%)
- Bilateral MTS	60 (26%)
Surgery side	
- Left	121 (53%)
- Right	108 (47%)

*Mean values are presented as the mean ±SD. All other values are the number of patients with the percentage in parentheses.

TABLE 2: Major surgical series (≥100 patients) of treatment of mesial temporal sclerosis in the 21st century.

Table 2. Major surgical series (≥100 patients) of treatment of mesial temporal sclerosis in the 21st century.

Authors	Year	No. of Patients	Design	Surgery type	Follow-up (years)	Seizure freedom	Complications
Hennessy et al. [22]	2001	116	Retro	ATL-AH	5.2	67%	-
Cukiert et al. [15]	2002	100	Prosp	ATL-AH	2	89%	2%
Clusmann et al. [23]	2002	132	Retro	SelAH + ATL-AH	3.2	68.9%	5.2%
Hardy et al. [17]	2003	118	Retro	ATL-AH	3.8	61.8%	-
Wieser et al [24]	2003	151	Retro	SelAH	7.2	74%	7.7%
Jasnzky et al. [11]	2005	171	Retro	ATL-AH	2	71%	-
Jeong et al. [10]	2005	227	Retro	ATL-AH	5	75.2%	-
Cohen-Gadol et al. [1]	2006	113	Retro	ATL-AH	6.2	79%	4%
Paglioli et al. [25]	2006	161	Retro	SelAH + ATL-AH	5.8	88.8%	0%
Bate et al. [26]	2007	114	Retro	SelAH + ATL-AH	1	54%	6.1%
Alpherts et al. [27]	2008	100	Retro	SelAH + ATL-AH	0.5	58%	-
Aull-Watschinger et al. [28]	2008	135	Retro	SelAH + ATL-AH	5	79.1%	-
Tanriverdi et al. [18]	2008	100	Retro	SelAH + ATL-AH	5	64%	-
Tezer et al. [29]	2008	109	Retro	ATL-AH	4.8	76.1	20.2%
Uijl et al. [30]	2008	484	Retro	SelAH + ATL-AH	1	74%	-
Elsharkawy et al. [2]	2009	269	Retro	ATL-AH	9	75.5%	5%
Ramos et al. [31]	2009	105	Retro	SelAH	3	83%	-
Schramm et al. [16]	2011	186	RCT	SelAH + ATL-AH	1	71.5%	-
Elliott et al. [19]	2013	116	Retro	ATL-AH	6.9	88.8%	2.7%
Current study	2014	229	Retro	ATL-AH	2	63%	4.8%

Retro: Retrospective; Prosp: Prospective; RCT: randomized controlled trial; SelAH: Selective amygdalo-hippocampectomy; ATL-AH: Standard anterior temporal lobectomy with amygdalohippocampectomy.

TABLE 3: Seizure outcomes by modified Engel outcome classification after ATL-AH in 229 patients with MTS.

Table 3. Seizure outcomes by modified Engel outcome classification after ATL-AH in 229 patients with MTS.

Class	Modified Engel Description	No. of Patients (%)
I	Seizure free; rare; non disabling	144 (63%)
II	>90% reduction in seizure frequency	56 (24%)
III	50-90% reduction in seizure frequency	11 (5%)
IV	<50% reduction in seizure frequency	18 (8%)

ATL-AH: Standard anterior temporal lobectomy with amygdalohippocampectomy; MTS: Mesial temporal lobe sclerosis.

TABLE 4: Operative and neurological complications following ATL-AH.

Table 4. Operative and neurological complications following ATL-AH.

	Number	Percentage
Wound infection	5	2.2%
Meningitis	4	1.7%
Medical complication	2	0.8%
Total	11	4.8%

ATL-AH: Standard anterior temporal lobectomy with amygdalohippocampectomy.

FIGURE 1: Kaplan-Meier seizure-free survival curve.

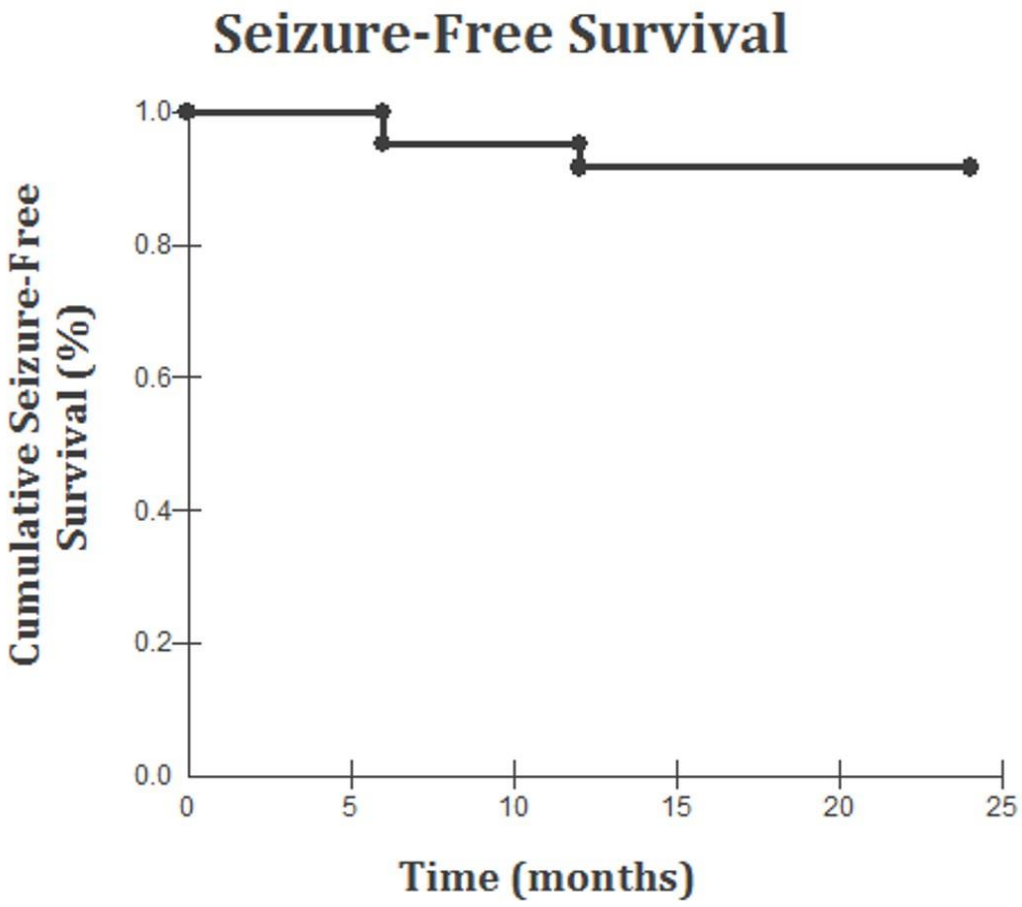
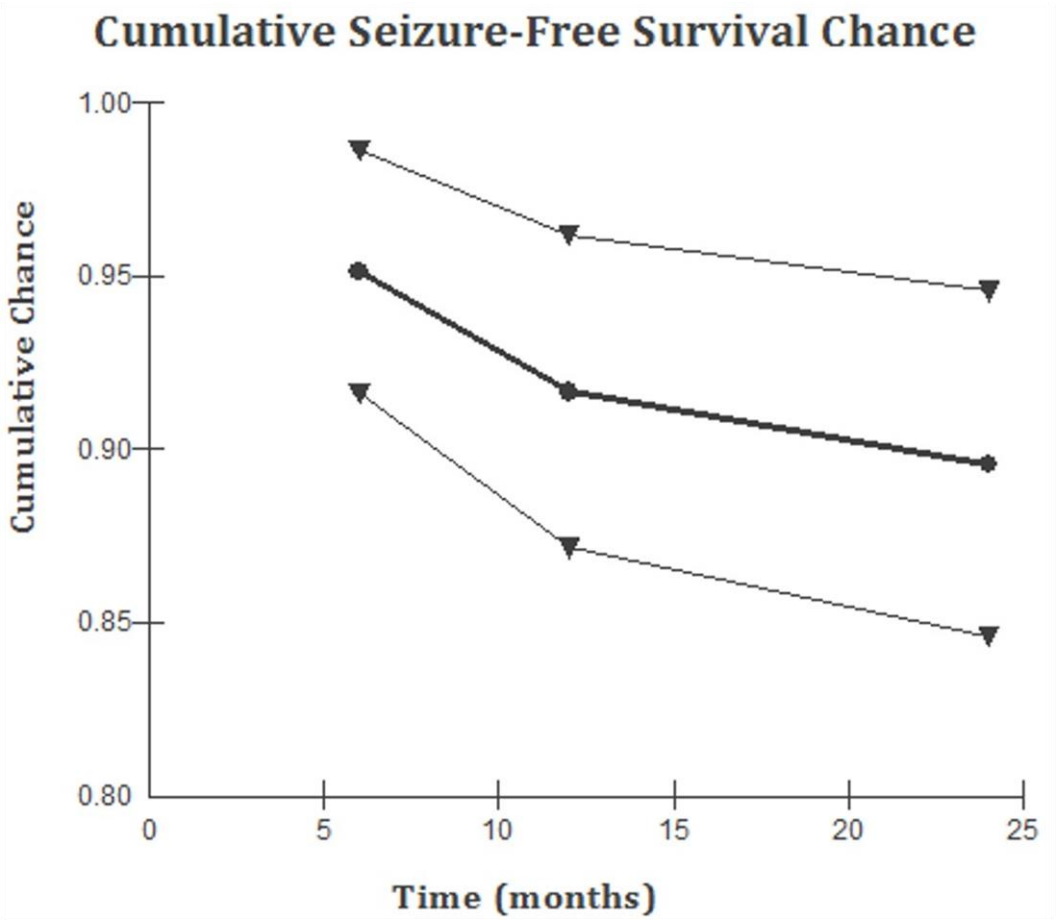


FIGURE 2: Cumulative seizure-free survival chance.



REFERENCES

1. 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 Apr;104(4):513-24.
2. 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 Jun;110(6):1135-46.
3. Falconer MA, Taylor DC. Surgical treatment of drug-resistant epilepsy due to mesial temporal sclerosis. Etiology and significance. Arch Neurol. 1968 Oct;19(4):353-61.
4. Falconer MA, Serafetinides EA. A follow-up study of surgery in temporal lobe epilepsy. J Neurol Neurosurg Psychiatry. 1963 Apr;26(2):154-65.
5. Falconer MA, Serafetinides EA, Corsellis JA. Etiology and pathogenesis of temporal lobe epilepsy. Arch Neurol. 1964 Mar;10:233-48.
6. Wiebe S, Blume WT, Girvin JP, Eliasziw M. Effectiveness and Efficiency of Surgery for Temporal Lobe Epilepsy Study Group. A randomized, controlled trial of surgery for temporal-lobe epilepsy. N Engl J Med. 2001 Aug 2;345(5):311-8.
7. Josephson CB, Dykeman J, Fiest KM, Liu X, Sadler RM, Jette N, et al. Systematic review and meta-analysis of standard vs selective temporal lobe epilepsy surgery. Neurology. 2013 Apr 30;80(18):1669-76.
8. Hu WH, Zhang C, Zhang K, Meng FG, Chen N, Zhang JG. Selective amygdalohippocampectomy versus anterior temporal lobectomy in the management of

mesial temporallobe epilepsy: a meta-analysis of comparative studies. J Neurosurg. 2013 Nov;119(5):1089-97.

9. Janszky J, Janszky I, Schulz R, Hoppe M, Behne F, Pannek HW, et al. Temporal lobe epilepsy with hippocampal sclerosis: predictors for long-term surgical outcome. Brain. 2005 Feb;128(Pt 2):395-404.
10. Jeong SW, Lee SK, Hong KS, Kim KK, Chung CK, Kim H. Prognostic factors for the surgery for mesial temporal lobe epilepsy: longitudinal analysis. Epilepsia. 2005 Aug;46(8):1273-9.
11. Janszky J, Janszky I, Schulz R, Hoppe M, Behne F, Pannek HW, et al. Temporal lobe epilepsy with hippocampal sclerosis: predictors for long-term surgical outcome. Brain. 2005 Feb;128(Pt 2):395-404
12. Engel J Jr. Mesial temporal lobe epilepsy: what have we learned? Neuroscientist. 2001 Aug;7(4):340-52.
13. Téllez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. Brain. 2005 May;128(Pt 5):1188-98.
14. Jaramillo-Betancur H, Jiménez ME, Massaro-Ceballos M, Cortés-Silva E, Restrepo-Marín DM, Mora-López O, et al. Risk factors for seizure recurrence and short term outcome after epilepsy surgery for mesial temporal sclerosis. Rev Neurol. 2009 Aug 16-31;49(4):175-80.
15. Cukiert A, Buratini JA, Machado E, Sousa A, Vieira J, Forster C, et al. Seizure-related outcome after corticoamygdalohippocampectomy in patients with refractory temporal

lobe epilepsy and mesial temporal sclerosis evaluated by magnetic resonance imaging alone. Neurosurg Focus. 2002 Oct 15;13(4):ecp2.

16. Schramm J, Lehmann TN, Zentner J, Mueller CA, Scorzin J, Fimmers R et al. Randomized controlled trial of 2.5-cm versus 3.5-cm mesial temporal resection in temporal lobe epilepsy--Part 1: intent-to-treat analysis. Acta Neurochir (Wien). 2011 Feb;153(2):209-19.

17. Hardy SG, Miller JW, Holmes MD, Born DE, Ojemann GA, Dodrill CB, et al. Factors predicting outcome of surgery for intractable epilepsy with pathologically verified mesial temporalsclerosis. Epilepsia. 2003 Apr;44(4):565-8.

18. Tanriverdi T, Olivier A, Poulin N, Andermann F, Dubeau F. Long-term seizure outcome after mesial temporal lobe epilepsy surgery: cortical-amygdalohippocampectomy versus selective amygdalohippocampectomy. J Neurosurg. 2008 Mar;108(3):517-24.

19. Elliott RE, Bollo RJ, Berliner JL, Silverberg A, Carlson C, Geller EB, et al. Anterior temporal lobectomy with amygdalohippocampectomy for mesial temporal sclerosis: predictors of long-term seizure control. J Neurosurg. 2013 Aug;119(2):261-72.

20. McIntosh AM, Wilson SJ, Berkovic SF. Seizure outcome after temporal lobectomy: current research practice and findings. Epilepsia. 2001 Oct;42(10):1288-307.

21. Behrens E, Schramm J, Zentner J, König R. Surgical and neurological complications in a series of 708 epilepsy surgery procedures. Neurosurgery. 1997 Jul;41(1):1-9; discussion 9-10.

22. Hennessy MJ, Elwes RD, Rabe-Hesketh S, Binnie CD, Polkey CE. Prognostic factors in the surgical treatment of medically intractable epilepsy associated with mesial temporalsclerosis. Acta Neurol Scand. 2001 Jun;103(6):344-50.

23. Clusmann H, Schramm J, Kral T, Helmstaedter C, Ostertun B, Fimmers R et al. Prognostic factors and outcome after different types of resection for temporal lobe epilepsy. J Neurosurg. 2002 Nov;97(5):1131-41.

24. Wieser HG, Ortega M, Friedman A, Yonekawa Y. Long-term seizure outcomes following amygdalohippocampectomy. J Neurosurg. 2003 Apr;98(4):751-63.

25. Paglioli E, Palmini A, Portuguez M, Paglioli E, Azambuja N, da Costa JC, et al. Seizure and memory outcome following temporal lobe surgery: selective compared with nonselective approaches for hippocampal sclerosis. J Neurosurg. 2006 Jan;104(1):70-8.

26. Bate H, Eldridge P, Varma T, Wieshmann UC. The seizure outcome after amygdalohippocampectomy and temporal lobectomy. Eur J Neurol. 2007 Jan;14(1):90-4.

27. Alpherts WC, Vermeulen J, van Rijen PC, da Silva FH, van Veelen CW. Dutch Collaborative Epilepsy Surgery Program. Standard versus tailored left temporal lobe resections: differences in cognitive outcome? Neuropsychologia. 2008 Jan 31;46(2):455-60

28. Aull-Watschinger S, Pataraia E, Czech T, Baumgartner C. Outcome predictors for surgical treatment of temporal lobe epilepsy with hippocampal sclerosis. Epilepsia. 2008 Aug;49(8):1308-16.

29. Tezer FI, Akalan N, Oguz KK, Karabulut E, Dericioglu N, Ciger A, et al. Predictive factors for postoperative outcome in temporal lobe epilepsy according to two different classifications. Seizure. 2008 Sep;17(6):549-60

30. Uijl SG, Leijten FS, Arends JB, Parra J, van Huffelen AC, Moons KG. Prognosis after temporal lobe epilepsy surgery: the value of combining predictors. Epilepsia. 2008 Aug;49(8):1317-23.

31. Ramos E, Benbadis S, Vale FL. Failure of temporal lobe resection for epilepsy in patients with mesial temporal sclerosis: results and treatment options. J Neurosurg. 2009 Jun;110(6):1127-34.

32. Hildebrandt M, Schulz R, Hoppe M, May T, Ebner A. Postoperative routine EEG correlates with long-term seizure outcome after epilepsy surgery. Seizure 2005; 14:446-51.

B. ARTIGO CIENTÍFICO 2

ARTIGO CIENTÍFICO 2

Título: Shorter epilepsy duration is associated with better seizure outcome in temporal lobe epilepsy surgery.

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ABSTRACT

Introduction: Epilepsy is the most common chronic neurological disease in the general population.

Objetive: The aim of the present study is to investigate the influence of patient's age at surgery and seizure onset on surgical outcome of temporal lobe epilepsy (TLE) in a Brazilian tertiary epilepsy center.

Method: A retrospective observational investigation was performed with data collection from a cohort of consecutive patients surgically treated in the epilepsy clinic of Faculdade de Medicina de Sao Jose do Rio Preto (FAMERP), a Brazilian tertiary referral epilepsy center, from January 2000 to March 2012. Patients were divided accordingly to their age at surgery (< or ≥50 years) and to epilepsy duration at surgery (< or > 10 years).

Results: At the moment of the study, 533 underwent multidisciplinary investigation of epilepsy at our center and 229 (43%) were included. One-hundred and eleven of 179 patients (62%) were classified as Engel I in the group with <50 years old, whereas 33 of 50 (66%) as Engel I in the group with ≥50 years old group ($p=0.82$). From the total of patients seizure free (Engel I), 88 (61%) reported epilepsy duration inferior to 10 years and 56 (39%) superior to 10 years ($p<0.01$). From the total of patients not seizure free (Engel II, III and IV), 36 (42%) reported epilepsy duration inferior to 10 years and 49 (58%) superior to 10 years ($p<0.01$).

Conclusion: We observed that a shorter epilepsy duration at surgery is an important risk factor that must be considered before surgical management of MTS. Early recognition and surgical treatment of patients with refractory TLE-MTS may improve seizure outcome.

Key-words: Mesial temporal sclerosis; age at surgery; epilepsy duration at surgery; seizure outcome.

INTRODUCTION

Epilepsy is the most common chronic neurological disease, affecting 0.4 to 1% of general population. The cumulative incidence of seizure is thought to be almost 10% to age 74 years, and the lifetime likelihood of receiving a diagnosis of epilepsy is almost 3%.[1] Temporal lobe epilepsy (TLE) is the most common epilepsy syndrome, observed in almost 40% of epilepsy patients. Several risk factors are associated with epilepsy, such as prolonged childhood febrile seizure, *status epilepticus*, CNS infections, head trauma, neoplasm, perinatal/vascular insults, mesial temporal lobe sclerosis (MTS), an a family history of epilepsy.[2-4] These risk factors are thought to result in brain injury at a molecular level, leading to either biologic or morphologic changes over years, ultimately leading to the development of refractory epilepsy.[5] Epilepsy surgery has been shown to be an effective treatment, especially for patients with refractory TLE associated to MTS (TLE-MTS), providing 60 to 70% of seizure remission.[6-9] Therefore, determining pre-surgical prognostic factors for TLE-MTS is important for identifying ideal candidates and predicting the prognosis for individual patients. The aim of the present study is to investigate the influence of patients' age at surgery and age at seizure onset on surgical outcome of TLE-MTS patients accompanied in a Brazilian tertiary center.

METHODS

Study Delineation

A retrospective observational was conducted with data collection consecutive patients with TLE-MTS treated in the Epilepsy service of Faculdade de Medicina de Sao Jose do Rio

Preto (FAMERP), a Brazilian tertiary referral center, between January 2000 to March 2012. Patients with neuroradiological evidence and neuro-pathological confirmation of diseases other than MTS, as well as additional potential epileptogenic MRI-lesions, where excluded from the study. Clinical data were obtained retrospectively from the patient records and files. For all patients with the diagnosis of MTS on MR images, the following data were collected: gender, age at surgery, handedness, type and number of AEDs used and results of formal neuropsychological evaluation. In addition, non-invasive video-EEG data and side of surgery were registered.

Pre-surgical evaluation

All patients were submitted to non-invasive video-EEG monitoring using the Stella system, Neuro Workbench software and a Nihon Kohden hardware to record and later evaluated all the epileptic events. Every patient was analyzed by an experienced epileptologist as an integral part of inpatient assessment. Patients were also 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 below of the normal performance of age-matched controls.

Brain MRI was obtained accordingly with a specific epilepsy protocol using a 1.5 Tesla Scanner, Philips. Displaying the sagittal 3D T1-weighted gradient-echo sequences, the next sequences were an axial and coronal fluid-attenuated inversion recovery (FLAIR) 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). All MRIs were

analyzed by an experienced neuroradiologist who confirmed the visual radiological diagnosis of MTS, which was determined to be present if atrophy, an increased T2-weighted signal, a decreased T1-weighted signal and a disrupted internal structure of the hippocampus were present, accompanied by atrophy of the amygdala and/or temporal pole signal alteration on visual inspection of the MRI pictures.

Biopsy specimens were obtained from all patients who underwent surgical treatment, and standardized neuropathological analyses were performed. Surgical specimens were microscopically analyzed using hematoxylin-eosin staining. MTS was diagnosed via pathological findings: cell loss in the CA3 and CA1 pyramidal cells and dentate hilar neurons with relative sparing of the dentate granular cells and CA2 pyramidal cells. The pathologist reported their findings independently of clinical or imaging data. Patients with dual pathology (MTS plus another epileptogenic lesion) were excluded.

Surgical Technique

The surgical approach was similar for all patients, and only one neurosurgeon experienced in surgery for epilepsy (SCS Jr.) performed all patients' surgeries. Patient positioning includes placing a shoulder roll to elevate the trunk and then turning the head 15-20 degrees from the midline so that the operative side is up. The head is slightly extended to bring the sylvian fissure to a perpendicular plane to the operating approach. Finally, dropping the vertex down toward the floor improves surgeon access to mesial structures and allows less retraction on the temporal lobe. A reverse question mark incision was made from just above the zigoma extending back in the temporal region. An anterior temporal craniotomy was performed respecting the anatomical landmarks of the temporal lobe from the root of the zygoma to the

anatomic keyhole. The anterior and lateral remaining bone was removed by drilling down to the limits of the medial fossa floor. At the end of the craniotomy, all bone edges were waxed as necessary, any exposed air cells sealed and take-up sutures were performed before opening the dura-mater to prevent epidural bleeding. A maximum of 4.0 to 5.0 cm of the anterior lateral temporal lobe was resected. The mesial resection included amygdala removal and the anterior 2.0 to 3.0 cm of the hippocampus.

Post-surgical follow-Up

Follow up investigation were carried out in operated MTS patients 6, 12 and 24 months after surgery. At the 12 months follow up, all 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 (including auras), i.e. Engel IA, or not seizure-free (Engel IB-IV). All of the Engel subcategories are described in Table 1. Operative mortality was defined as death within 30 days of surgery.

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

The statistical analyses were performed with SPSS software (IBM, Chicago, IL, USA). Data collected from all patients were organized in tables and figures. Averages are expressed as the means ±SD for parametric data and as median values for nonparametric data. We considered the patients' age as "age groups" and we use the $R2$ coefficient for study its correlation with

postoperative outcome of patients. Next, we considered the patients age at surgery as a variable category (< or ≥50 years) and Pearson Chi-squared coefficient for correlation study was used. For statistical analysis, we performed the chi-square test to compare to groups for epilepsy duration. A p-value<0.05 was considered statistically significant.

RESULTS

Pre-surgical Demographic and Clinical Characteristics

At the moment of the study, 533 patients underwent multidisciplinary investigation of epilepsy at our center and 229 (43%) fulfilled the inclusion criteria. Most patients excluded from the study did not reach a minimum follow up of six months. In table 2, data descriptive analysis is presented with contingency tables, confidential intervals and hypothesis tests.

Seizure Control and Follow-Up

In Figure 1 and 2 and table 3 and 4, seizure-outcome data accordingly to a descriptive analysis of Engel Classification for patients with <50 and ≥50 years old following surgery are presented. Analyzing the correlation between variables through Pearson chi-square test (significance level α=0.05), we observed that patients' age at surgery had no influence in post-surgical outcome (p-value=0.82). Table 5 shows the association between post-surgical seizure outcome (Engel classification) and age distribution. Table 6 and Figure 3 show a descriptive analysis of surgical prognosis accordingly to the age at surgery.

In table 7 and Figure 4, the post-surgical seizure outcome distribution accordingly to epilepsy duration at surgery is presented. From the total of patients seizure free (Engel I), 88 (61%) reported epilepsy duration at surgery less than 10 years and 56 (39%) higher than 10

years ($p<0.001$). In addition, from the total of patients not seizure free (Engel II, III and IV), 36 (42%) reported epilepsy duration inferior to 10 years and 49 (58%) superior to 10 years ($p<0.001$).

DISCUSSION

In the present study, we focused our investigation regarding the influence of age at surgery and seizure onset on the surgical outcome of patients with TLE-MTS treated in a Brazilian referral epilepsy center. MTS is the most common pathological abnormality found in patients with refractory TLE,[10-13] presenting a prevalence of 50% to 70%.[14, 15] Studies have confirmed that MTS is a chronic disease characterized by prominent neuronal loss and fibrillary gliosis at the level of hippocampal pyramidal cell layer, but the pathophysiological mechanisms of hippocampal sclerosis are not fully understood.[16, 17] Early surgery is usually recommended since refractory epilepsy may lead to cognitive impairment, poor quality of life, psychosocial dysfunction, and increased morbidity and mortality. If refractoriness is detected early in the course of the disease, aggressive drug therapy or early surgery can improve the responsiveness to treatment and minimize such adverse effects.[7, 18] However, there is a lack of information regarding factors that predict the clinical outcome of patients surgically treated for TLE-MTS.

Jeong et al[19] and Junna et al[20] observed that a younger age at surgery was predictive of a favorable post-surgical outcome. Additionally, Sirven el at[21] studying a large number of patients undergoing temporal lobectomy, observed that patients younger than 50 had a higher likelihood of seizure freedom compared with those older than 50 years, although the procedure was considered safe and beneficial in both groups. On the other hand, a Brazilian investigation reported no statistical difference of age at surgery in the post-surgical outcome after temporal lobectomy.[22] In the present study, we also observed no statistical difference regarding the

outcome between patients < or > than 50 years at surgery (table 6), although the procedure proved to be safe beneficial to both groups, which is in accordance with literature.[21].

Varoglou et al[23] recognized the early seizure onset as a poor prognostic feature for epilepsy control. Other studies have observed that a longer epilepsy duration before surgical treatment predicted worse seizure outcome.[19,22] However, Baldauf et al. did not observe such findings.[24] In the present study, we found that epilepsy duration longer than 10 years before surgery represented a risk factor for a worse seizure control. In fact, literature studies have highlighted that longer seizure duration could predispose patients to structural and microbiological changes in other brain areas not involved in the primary epileptogenic zone, and probably leading these patients to persist with disabling seizures.[19-24] However, further clinical and experimental investigations are necessary to validate this hypothesis.

There are several methodological aspects in the present findings, which should be interpreted in the context of a number of limitations. Firstly, although a large number of patients were included on the present investigation, it represented less than 50% of all patients that underwent surgery for TLE-MTS at our institution. Since the epilepsy center receives patients from all regions from Brazil and, due to its large dimensions and difficulties in transportation, the follow-up of a great amount of patients were lost. Secondly, this study is a retrospective investigation with non-randomized surgical case series without a control group. Therefore, future prospective and randomized studies with a greater number of patients are certainly necessary to confirm such findings.

CONCLUSION

To conclude, the present study highlights that the seizure duration at surgery is an important risk factor that must be considered before surgical management of patients with refractory TLE-MTS. Early recognition and surgical treatment of patients with refractory TLE-MTS may improve seizure outcome and patient's quality of life.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

TABLES, FIGURES AND LEGENDS

TABLE 1: Engel's classification of post-surgical outcome.

Table 1. Engel's classification of post-surgical outcome.

Class I: Free of disabling seizures [a]
A. Completely seizure-free since surgery
B. Nondisabling simple partial seizures only since surgery
C. Some disabling seizures after surgery, but free of disabling seizures for at least two years
D. Generalized convulsions with AED* discontinuation only
Class II: Rare disabling seizures ("almost seizure-free")
A. Initially free of disabling seizures but has rare seizures now
B. Rare disabling seizures since surgery
C. More than rare disabling seizures since surgery, but rare seizures for the last two years
D. Nocturnal seizures only
Class III: Worthwhile improvement [b]
A. Worthwhile seizure reduction
B. Prolonged seizure-free intervals amounting to greater than half the follow-up period, but not < 2 years
Class IV: No worthwhile improvement
A. Significant seizure reduction
B. No appreciable change
C. Seizures worse

[a]Excludes early post-surgical seizures (first few weeks); [b]Determination of "worthwhile improvement" requires quantitative analysis of additional data, such as the percent seizure reduction, cognitive function and quality of life; * AED: antiepileptic drugs.

Table 2: Preoperative clinical characteristics of patients with MTS according to age distribution.

Table 2. Preoperative clinical characteristics of patients with MTS according to age distribution.

Variables	<50 years-old n=179 (78.1%)	≥50 years-old n=50 (21.9%)	C.I. 95%	*p*-Value
Gender				
- Male	83 (46%)	22 (44%)	-0.14;0.18	0.6
- Female	96 (54%)	28 (56%)	-0.18;0.14	0.4
Handedness				
- Right	173 (97%)	48 (96%)	-0.04;0.07	0.6
- Left	6 (3%)	2 (4%)	-0.07;0.04	0.3
Risk factors				
- Febrile seizure	28 (16%)	2 (4%)	-0.04,0.2	0.9
- Traumatic brain injury	10 (6%)	17 (34%)	-0.1;0.1	0.5
Pharmacotherapy				
- Mono	28 (16%)	9 (18%)	-0.14;0.1	0.3
- Combined	151 (84%)	41 (82%)	-0.1;0.14	0.6
Ictal EEG				
- Unil./Normal	166 (93%)	45 (90%)	-0.06;0.12	0.2
- Bilateral	13 (7%)	5 (10%)	-0.12;0.06	0.7
Interictal EEG				
- Unilateral	146 (82%)	36 (72%)	-0.04;0.24	0.92
- Bilateral	33 (18%)	14 (28%)	-0.24;0.04	0.08
Surgery side				
- Left	85 (47%)	24 (48%)	-0.17;0.15	0.4
- Right	94 (53%)	26 (52%)	-0.15;0.17	0.5

MTS: mesial temporal lobe sclerosis; C.I.: Confidential interval.

TABLE 3: Patient's age and postoperative outcome (Engel I, II, III and IV).

Table 3. Patient's age and postoperative outcome (Engel I, II, III and IV).

	N	Mean Age	Standard deviation	Minimum	1st Quartile	2nd Quartile	3rd Quartile	Maximum
I	144	39.7153	11.9162	10	31.75	40	49	68
II	56	42,0714	10,69689	16	35	41,5	50	63
III	11	39,9094	8,826144	23	36,5	39	44,5	58
IV	18	34,8333	10,81793	13	28,75	37	39,75	61
Total	229	39	11,55	10	33	40	48	68

TABLE 4: Patient's age and postoperative outcome (Engel Ia, Ib, Ic, Id).

Table 4. Patient's age and postoperative outcome (Engel Ia, Ib, Ic, Id).

	N	Mean Age	Standard deviation	Minimum	1st Quartile	2nd Quartile	3rd Quartile	Maximum
Ia	117	39,77777	12,5692	10	31	40	49	68
Ib	14	39,7143	8,08375	27	35,25	40	42	58
Ic	10	38,6	8,743	27	31,5	37	45,25	52
Id	3	41	9,4163	32	34,5	37	45,5	54
Total	144	39.7153	11.9162	10	31.75	40	49	68

TABLE 5: Postoperative outcome distribution according to age groups.

Table 5. Postoperative outcome distribution according to age groups.

Age	I	II	III	IV	Total
10–19	7	3	0	3	13
20–29	21	3	1	2	27
30–39	39	17	5	8	69
40–49	44	18	4	4	70
50–59	28	11	1	0	40
60–69	5	4	0	1	10
Total	144	56	11	18	229

TABLE 6: Descriptive analysis of surgical outcome according to the age at the time of surgery (follow-up: 2 years).

Table 6. Descriptive analysis of surgical outcome according to the age at the time of surgery (follow-up: 2 years).

Surgical Prognosis	Age at Surgery (years) < 50	≥ 50	C.I 95%	p-value
Ia	89(50%)	28(56%)	[-0.22, 0.10]	0.23
Ib	12(7%)	2(4%)	[-0.04, 0.10]	0.81
Ic	8(4%)	2(4%)	[-0.06, 0.06]	0.5
Id	3(2%)	1(2%)	[-0.04, 0.04]	0.5
II	41(23%)	15(30%)	[-0.21, 0.07]	0.17
III	10(5%)	1(2%)	[-0.02, 0.08]	0.88
IV	16(9%)	1(2%)	[0.01, 0.13]	0.99
Engel Ia vs Others (Ib,Ic,Id,II,III,IV)				
Engel Ia	89(49%)	28(56%)	[-0.23, 0.09]	0.19
Outros (Ib,Ic,Id,II,III,IV)	90(51%)	22(44%)	[-0.09, 023]	0.81
Engel I vs Others (II,III,IV)				
Engel I	112(63%)	33(66%)	[-0.18, 0.12]	0.35
Others (II,III,IV)	67(37%)	17(34%)	[-0.12, 0.18]	0.65

C.I.: Confidential interval.

TABLE 7: Seizure outcome according to early (<10 years) and late (≥10 years) epilepsy onset.

Table 7. Seizure outcome according to early (<10 years) and late (≥10 years) epilepsy onset (follow-up: 2 years).

	Epilepsy Duration *		Total
	< 10 years	≥ 10 years	
Seizure free	88 (61%)	56 (39%)	144
Not Seizure free	36 (42%)	49 (58%)	85

Seizure free=Engel I; Not Seizure free = Others (Engel II, III and IV); * Chi-square test, p<0.001

FIGURE 1: Boxplot – Patient's age and postoperative outcome (Engel I, II, III and IV).

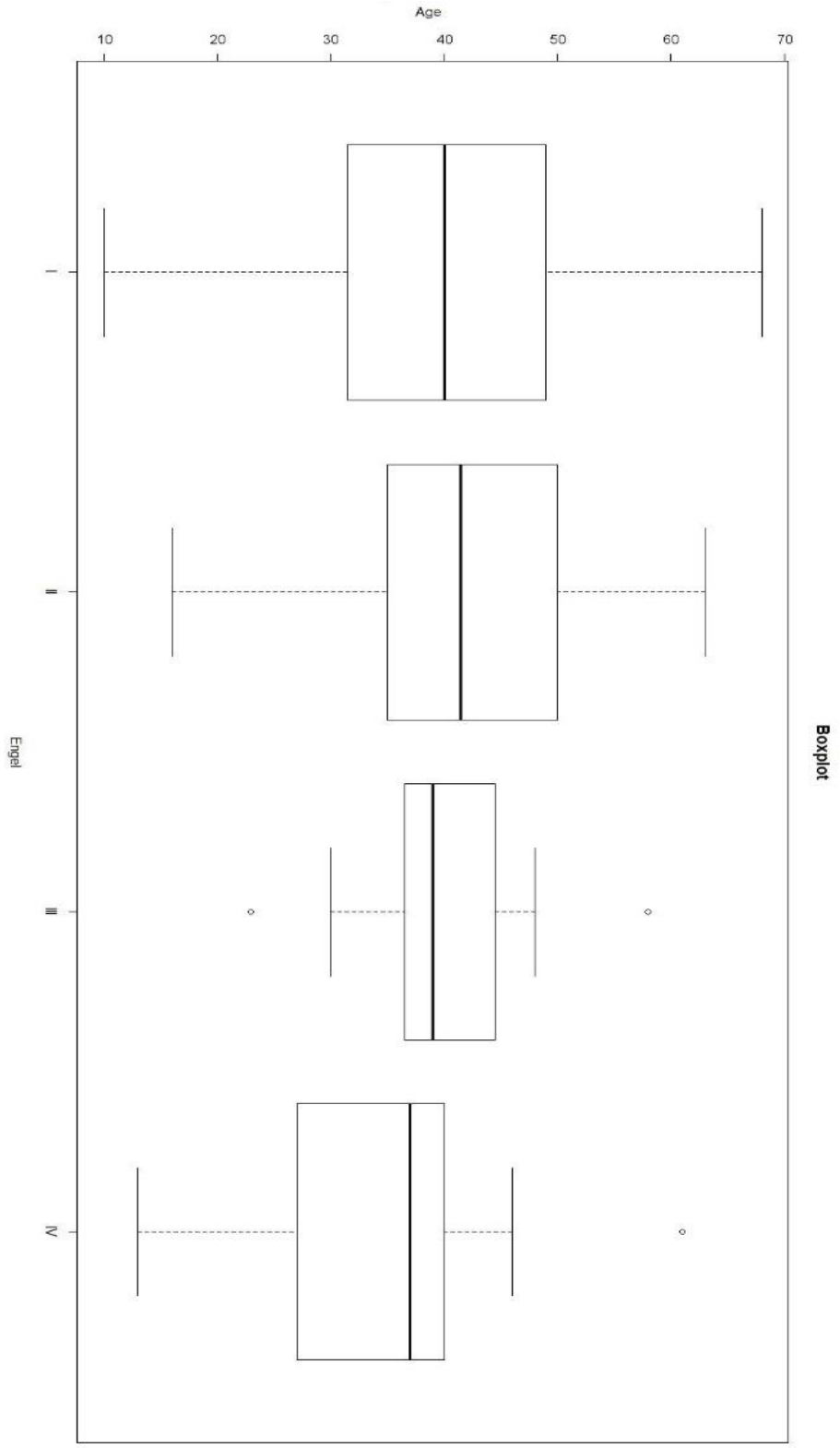


FIGURE 2: Boxplot – Patient's age and postoperative outcome (Engel Ia, Ib, Ic, Id).

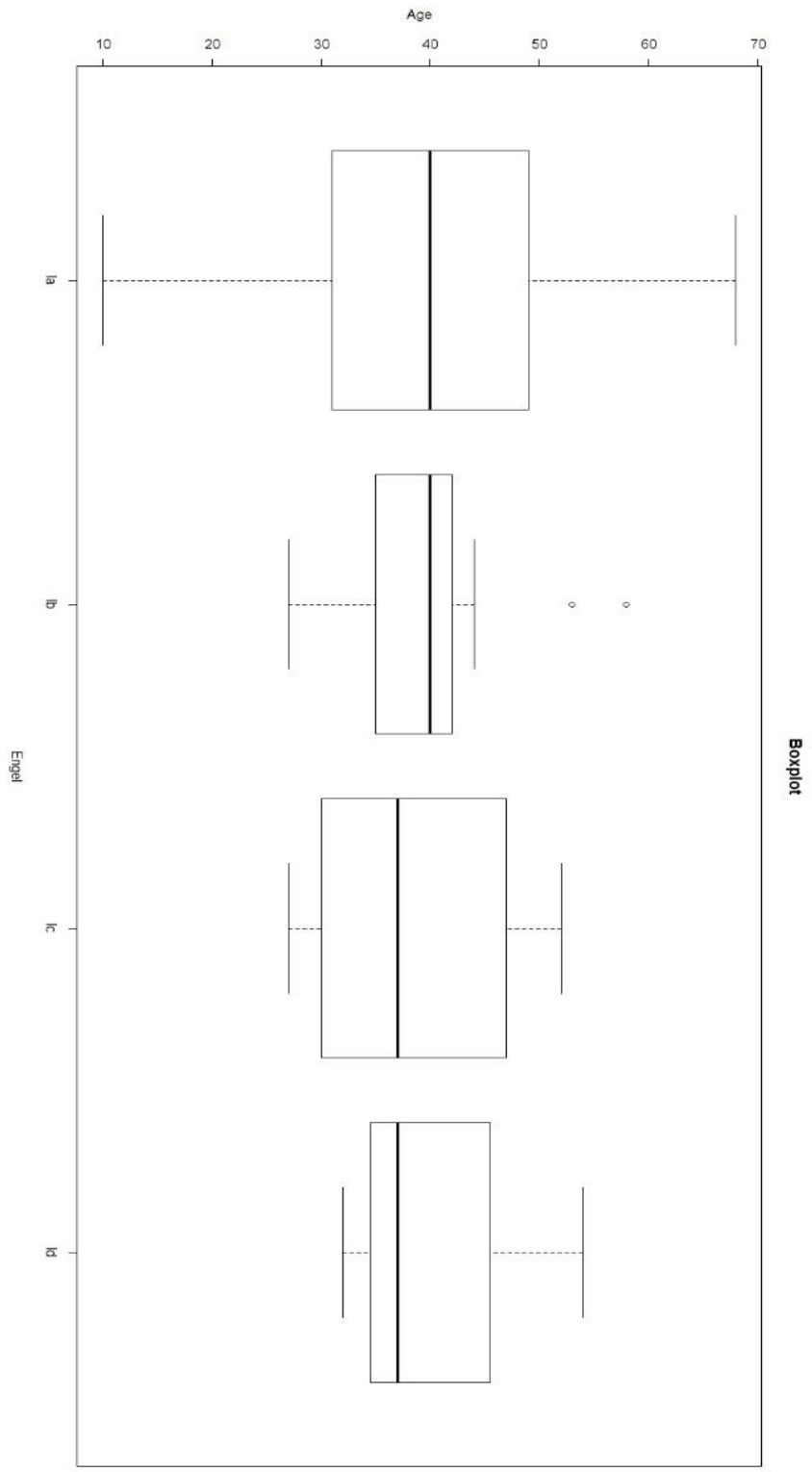


FIGURE 3: Graphic of postoperative outcome distribution according to age groups (follow-up: 2 years).

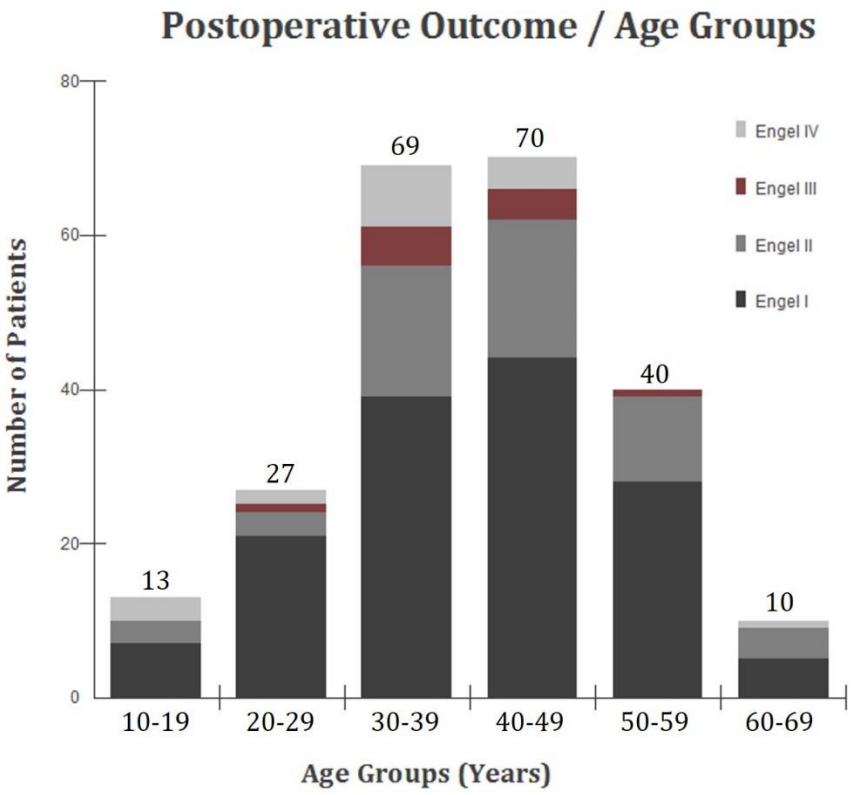
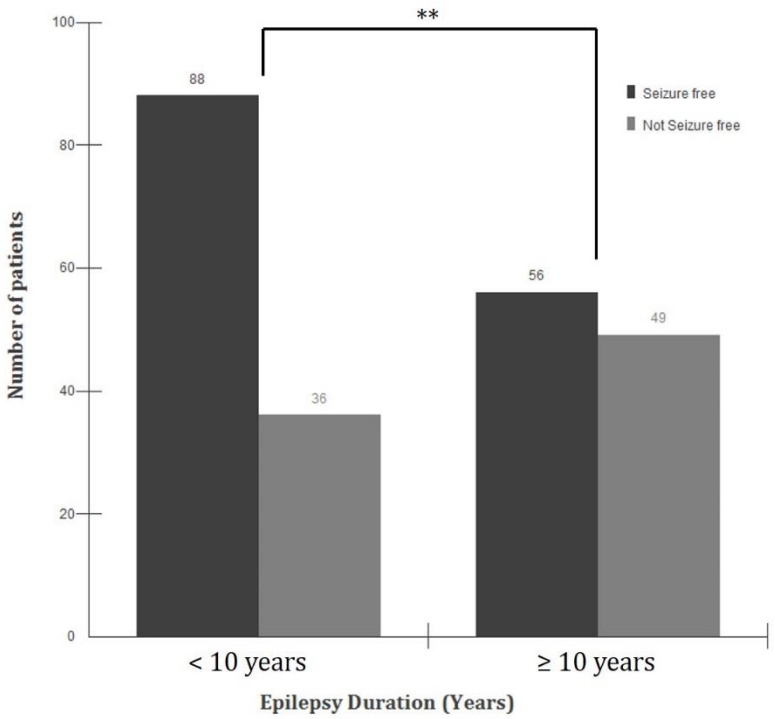


FIGURE 4: Graphic of seizure outcome according to early (<10 years) and late (≥10 years) epilepsy onset. (** *p*-value: 0.0089). Seizure free=Engel I; Not Seizure free = Others (Engel II, III and IV). (Follow-up: 2 years)



REFERENCES

1. Hauser WA, Annegers JF, Rocca WA. Descriptive epidemiology of epilepsy: contributions of population-based studies from Rochester, Minnesota. Mayo Clin Proc. 1996 Jun;71(6):576-86.

2. Fanciulli M, Di Bonaventura C, Egeo G, Fattouch J, Dazzo E, Radovic S, et al**.** Suggestive linkage of familial mesial temporal lobe epilepsy to chromosome 3q26. Epilepsy Res. 2014 Feb;108(2):232-40.

3. Tezer FI, Akalan N, Oguz KK, Karabulut E, Dericioglu N, Ciger A, et al. Predictive factors for postoperative outcome in temporal lobe epilepsy according to two different classifications. Seizure. 2008 Sep;17(6):549-60.

4. Burneo JG, Black L, Martin R, Devinsky O, Pacia S, Faught E, et al. Race/ethnicity, sex, and socioeconomic status as predictors of outcome after surgery for temporal lobe epilepsy. Arch Neurol. 2006 Aug;63(8):1106-10.

5. Herman ST. Epilepsy after brain insult: targeting epileptogenesis. Neurology. 2002 Nov 12;59(9 Suppl 5):S21-6.

6. 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 Apr;104(4):513-24.

7. Engel J Jr, McDermott MP, Wiebe S, Langfitt JT, Stern JM, Dewar S, et al. EarlyRandomized Surgical Epilepsy Trial (ERSET) Study Group. Early surgical

therapy for drug-resistant temporal lobe epilepsy: a randomized trial. JAMA. 2012 Mar 7;307(9):922-30.

8. Fiest KM, Sajobi TT, Wiebe S. Epilepsy surgery and meaningful improvements in quality of life: Results from a randomized controlled trial. Epilepsia. 2014 Jun;55(6):886-892.
9. Wiebe S, Blume WT, Girvin JP, Eliasziw M. Effectiveness and Efficiency of Surgery for Temporal Lobe Epilepsy Study Group. A randomized, controlled trial of surgery for temporal-lobe epilepsy. N Engl J Med. 2001 Aug 2;345(5):311-8.
10. Kim WJ, Park SC, Lee SJ, Lee JH, Kim JY, Lee BI, et al. The prognosis for control of seizures with medications in patients with MRI evidence f or mesial temporalsclerosis. Epilepsia. 1999 Mar;40(3):290-3.
11. Semah F, Picot MC, Adam C, Broglin D, Arzimanoglou A, Bazin B, et al. Is the underlying cause of epilepsy a major prognostic factor for recurrence? Neurology. 1998 Nov;51(5):1256-62.
12. Stephen LJ, Kwan P, Brodie MJ. Does the cause of localisation-related epilepsy influence the response to antiepileptic drug treatment? Epilepsia. 2001 Mar;42(3):357-62.
13. Van Paesschen W, Duncan JS, Stevens JM, Connelly A. Etiology and early prognosis of newly diagnosed partial seizures in adults: a quantitative hippocampal MRI study. Neurology. 1997 Sep;49(3):753-7.

14. Lee DH, Gao FQ, Rogers JM, Gulka I, Mackenzie IR, Parrent AG, et al. MR in temporal lobe epilepsy: analysis with pathologic confirmation. AJNR Am J Neuroradiol. 1998 Jan;19(1):19-27.

15. Margerison JH, Corsellis JA. Epilepsy and the temporal lobes. A clinical, electroencephalographic and neuropathological study of the brain in epilepsy, with particular reference to the temporal lobes. Brain. 1966 Sep;89(3):499-530.

16. Bernasconi A. Magnetic resonance imaging in intractable epilepsy: focus on structural image analysis. Adv Neurol. 2006;97:273-8.

17. Cendes F, Caramanos Z, Andermann F, Dubeau F, Arnold DL. Proton magnetic resonance spectroscopic imaging and magnetic resonance imaging volumetry in the lateralization of temporal lobe epilepsy: a series of 100 patients. Ann Neurol. 1997 Nov;42(5):737-46.

18. Langfitt JT, Wiebe S. Early surgical treatment for epilepsy. Curr Opin Neurol. 2008 Apr;21(2):179-83.

19. Jeong SW, Lee SK, Hong KS, Kim KK, Chung CK, Kim H. Prognostic factors for the surgery for mesial temporal lobe epilepsy: longitudinal analysis. Epilepsia. 2005 Aug;46(8):1273-9.

20. Junna MR, Buechler R, Cohen-Gadol AA, Mandrekar J, Christianson T, Marsh WR, et al. Prognostic importance of risk factors for temporal lobe epilepsy in patients undergoing surgical treatment. Mayo Clin Proc. 2013 Apr;88(4):332-6.

21. Sirven JI, Malamut BL, O'Connor MJ, Sperling MR.
Temporal lobectomy outcome in older versus younger adults. Neurology. 2000 Jun 13;54(11):2166-70.

22. Prevedello DM, Sandmann MC, Ebner A. Prognostic factors in mesial temporal lobe epilepsy surgery. Arq Neuropsiquiatr. 2000 Jun;58(2A):207-13.

23. Varoglu AO, Saygi S, Acemoglu H, Ciger A. Prognosis of patients
with mesial temporal lobe epilepsy due to hippocampal sclerosis. Epilepsy Res. 2009 Aug;85(2-3):206-11.

24. Baldauf CM, Cukiert A, Argentoni M, Baise-Zung C, Forster CR, Mello VA, et al. Surgical outcome in patients with refractory epilepsy associated to MRI-defined unilateral mesial temporal sclerosis. Arq Neuropsiquiatr. 2006 Jun;64(2B):363-8.

4. CONCLUSÃO

CONCLUSÃO

1. A esclerose mesial temporal foi observada com maior frequência entre indivíduos na faixa etária de 30 a 50 anos, sem predominância de gênero, com uma proporção de 1:1,18 entre o sexo masculino e o feminino.

2. Não foi observada diferença estatística significativa na evolução clínica pós-operatória da frequência das crises convulsivas entre indivíduos com mais de 50 anos ou menos de 50 anos.

3. A duração da epilepsia antes do procedimento cirúrgico é um importante fator prognóstico no controle das crises convulsivas, sendo os pacientes com menos de 10 anos de crises convulsivas os com melhor resposta terapêutica. Desta forma, o diagnóstico precoce de epilepsia refratária e o encaminhamento correto a um centro especializado no tratamento cirúrgico da epilepsia do lobo temporal, parece favorecer o controle clínico das crises convulsivas.

5. REFERÊNCIAS BIBLIOGRÁFICAS

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1. Scott RA, Lhatoo SD, Sander JW. The treatment of epilepsy in developing countries: where do we go from here? Bull World Health Organ. 2001;79(4):344-51.
2. Meinardi H, Scott RA, Reis R, Sander JW; ILAE Commission on the Developing World. The treatment gap in epilepsy: the current situation and ways forward. Epilepsia. 2001 Jan;42(1):136-49.
3. Fernandes JG, Schmidt MI, Monte TL, Tozzi S, Sander JWAS. Prevalence of Epilepsy: The Porto Alegre Study. Epilepsia 1992;33(3):132.
4. de Bittencourt PR, Adamolekum B, Bharucha N, Carpio A, Cossío OH, Danesi MA, et al. Epilepsy in the tropics: II. Clinical presentations, pathophysiology, immunologic diagnosis, economics, and therapy. Epilepsia. 1996 Nov;37(11):1128-37.
5. Machado MF, da Rocha Neto OG, Carvalho JRSA. Epilepsia em remissão: estudo da prevalência e do perfil clínico-epidemiológico. Rev Neurocienc 2007; 15 (2): 135-40.
6. Sander JW, Shorvon SD. Epidemiology of the epilepsies. J Neurol Neurosurg Psychiatry. 1996 Nov;61(5):433-43.
7. Placencia M, Shorvon SD, Paredes V, Bimos C, Sander JW, Suarez J, et al. Epileptic seizures in an Andean region of Ecuador. Incidence and prevalence and regional variation. Brain. 1992 Jun;115 (Pt 3):771-82.

8. Li SC, Schoenberg BS, Wang CC, Cheng XM, Zhou SS, Bolis CL. Epidemiology of epilepsy in urban areas of the People's Republic of China. Epilepsia. 1985 Sep-Oct;26(5):391-4.

9. Burneo JG, Cavazos JE. Neurocysticercosis and epilepsy. Epilepsy Curr. 2014 Jan;14(1 Suppl):23-8.

10. Ba-Diop A, Marin B, Druet-Cabanac M, Ngoungou EB, Newton CR, Preux PM. Epidemiology, causes, and treatment of epilepsy in sub-Saharan Africa. Lancet Neurol. 2014 Oct;13(10):1029-1044.

11. Szaflarski JP, Nazzal Y, Dreer LE. Post-traumatic epilepsy: current and emerging treatment options. Neuropsychiatr Dis Treat. 2014 Aug 11;10:1469-77.

12. Bruno E, Bartoloni A, Zammarchi L, Strohmeyer M, Bartalesi F, Bustos JA, et al. Epilepsy and neurocysticercosis in Latin America: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2013 Oct 31;7(10):e2480.

13. Jallon P. Epilepsy in developing countries. Epilepsia. 1997 Oct;38(10):1143-51.

14. Rondón J, Betancourt X, Conteras A. Real prevalence of epilepsy in a mental health programme in Merida,Venezuel. Rev Salud Publica (Bogota). 2008 Aug-Oct;10(4):643-9.

15. Almeida Filho N. Epidemiologia social das epilepsias no Brasil. In: Sena, PG, editor. Novas achegas sobre a epilepsia. Salvador: UFBA, Centro Editorial e Didático; 1980. p. 57-76.

16. da Costa JC, Oliveira MLK, Panta RMG. Epilepsia na Infância. Acta Médica ATM. 1982;142:142-79.

17. Marino Jr. R, Cukiert A, Pinho E. Aspectos epidemiológicos da epilepsia em São Paulo. Um estudo da prevalência. Arq Neuropsiquiatr. 1986;44(3):243-54.

18. Borges MA, Barros EP, Zanetta DM, Borges AP. Prevalence of epilepsy in Bakairi indians from Mato Grosso State, Brazil. Arq Neuropsiquiatr. 2002 Mar;60(1):80-5.

19. Shorvon SD. The delivery and cost of medical services for people with epilepsy. In: Hopkins A, Shorvon S, Cacino G, editors. Epilepsy. London: Chapman and Hall; 1995. p. 605-14.

20. World Health Organization. The global burden of mental and neurological problems. Geneva: WHO; 1999. (Fact Sheet, 217).

21. Hauser WA, Annegers JF. Epidemiology of epilepsy. In: Laidlaw J, editors. A textbook of epilepsy. Edinburgh: Churchill Livingstone; 1993. p. 23-45.

6. ANEXOS

FACULDADE DE MEDICINA DE SÃO JOSÉ DO RIO PRETO
DEPARTAMENTO DE CIÊNCIAS NEUROLÓGICAS
CENTRO DE CIRURGIA DA EPILEPSIA DO HOSPITAL DE BASE

AVALIAÇÃO NEUROFISIOLÓGICA

IDENTIFICAÇÃO

Nome: **Lateralidade:**

Prontuário: **Naturalidade:**

Idade: **Procedência:**

Sexo: **Estado Civil:**

Cor:

HISTÓRIA DA MOLÉSTIA ATUAL

ANTECEDENTE PESSOAL

ANTECEDENTE FAMILIAR

MEDICAÇÕES EM USO

MEDICAÇÕES JÁ UTILIZADAS

EXAME FÍSICO GERAL

EXAME NEUROLÓGICO

EXAMES COMPLEMENTARES

MVEP (Monitorização por Vídeo-Eletroencefalograma Prolongado):

RESSONÂNCIA MAGNÉTICA:

AVALIAÇÃO NEUROPSICOLÓGICA:

Resultados das funções cognitivas avaliadas especificamente

Função	Testes Utilizados	Pontuação Esperada	Pontuação Obtida	Resultados
Atenção	Dígitos (WAIS-III)			
	Trilhas B			
Visuoconstrução	Cubos (WAIS-III)			
Linguagem	BNT			
	Fluência Verbal (FAS)			
	Vocabulário (WAIS-III)			
	Fluência Animais			
Memória e				

Aprendizagem	Histórias - WMS			
	Reprodução Visual			
	Figura de Rey			
QI Total	WAIS-R			

Conclusão:

SPECT-basal

DIAGNÓSTICO:

CONCLUSÃO DA AVALIAÇÃO NEUROFISIOLÓGICA

_____ _____

NEUROLOGISTA CHEFE RESIDENTE / NEUROLOGIA

São José do Rio Preto, ____ / ____ / _____.