Original Article

Non-image Guided Selective Amygdalohippocampectomy for Refractory Mesial Temporal Lobe Epilepsy

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ABSTRACT

Background: Temporal lobe epilepsy is the most frequent type of treatment-resistant epilepsy. Mesial temporal sclerosis (MTS) is the most common recognized cause of temporal lobe epilepsy (TLE). Only half of patients responds to medical treatment. Surgery is the only effective treatment for mesial temporal sclerosis epilepsy in case of failure of medical treatment with a success rate of 60% - 90%. Objective: is to assess the feasibility of performing selective amygdalohippocampectomy without image guidance for refractory mesial temporal lobe epilepsy cases caused by hippocampal sclerosis.

Patients and Methods: Twenty six patients (fifteen females and eleven males) with age range 11-64 years, with intractable temporal lobe epilepsy, after proper evaluation; clinical, magnetic resonance imaging (MRI) and video electroencephalography, all selected cases had minimally invasive non-image guided selective amygdalohippocampectomy. Results: Precipitating factors were evident in 46,15% of cases; subdivided as follows: 26,92 % had febrile seizure (the most common), 11,53% had head trauma, 3,84% had encephalitis and 3,84% had perinatal asphyxia. The preoperative median weekly seizure frequency was two. 53,84% of cases had CPS with secondary generalization and 46,15% of cases had complex partial seizures (CPS) without secondary generalization. Patients used a median of 2 antiepileptic medications (AEDs) preoperatively. Seizure control outcomes at the last follow up revealed by modified Engel outcome (table III): 65,38% of cases were Engel Class I, 11,53% of cases were Engel Class II, 15,38% of cases were Engel Class III and 7,69% of cases were Engel Class IV. Single case developed wound infection. 38,46% of cases had complete AED cessation, 53,84% had reduction in AED doses and 7,69% had no change in AED regimen.

Conclusion: Selective amygdalohippocampectomy is a safe, precise, easy and effective surgical procedure, without the necessity of image guidance or larger resection, in properly selected cases with refractory mesial temporal lobe epilepsy due hippocampal sclerosis.

INTRODUCTION

Temporal lobe epilepsy is the most frequent type of treatment-resistant epilepsy.\textsuperscript{19,22,23} Mesial temporal sclerosis (MTS) is the most common recognized cause of temporal lobe epilepsy (TLE), only 50% of cases respond to medical treatment.\textsuperscript{18} A randomized, controlled trial demonstrated the superior efficacy of surgery over prolonged medical therapy for TLE\textsuperscript{20,27} and rates of seizure freedom after surgery range from 60% to 90% in most studies.

Various centers use different definitions of seizure freedom, assess seizure freedom at different times of follow-up, and use different statistical methods. Such discrepancies likely explain the wide variation in seizure freedom after surgery for MTS and the factors that predict the outcome.\textsuperscript{25,26}

PATIENTS AND METHODS

This study included twenty six patients (fifteen females and eleven males), age range 11 to 64 years, with intractable temporal lobe epilepsy, defined as failure of at least two trials of antiepileptic monotherapy and one combination therapy at therapeutic levels over two years at least, all cases were managed in Kasr Al Aini Hospital, Cairo university, Egypt, between June 2003 and January 2009 after having detailed informed consent.

All patients underwent a standard presurgical evaluation that included 1) demographic information 2) history and physical examination including epilepsy evaluation, the results of which were used to guide the surgical decision. The surgical procedure was performed without the use of image guidance.
characteristics, mean weekly seizure frequency, treatment history and current antiepileptic medications with full description of the seizure semiology; 3) video-electroencephalography (EEG) ictal and interictal were a prerequisite prehand and before admission to Kasr Al Ainy Hospital; 4) magnetic resonance imaging (MRI) with T1- and T2-weighted and Flair sequences to assess for hippocampal atrophy and increased T2 signal.

Selection criteria included patients with classic findings consistent with MTS such as complex partial seizures (CPS), epileptiform activity arising in the mesial temporal structures, and unilateral hippocampal atrophy with or without a T2 hyperintense signal (Figure 1,2,3,4).

Surgical technique:

The patient is positioned supine with the head held in position in 3-pin fixation, rotated 90 degrees to the opposite side and parallel to the floor, 4 cm linear scalp incision above the root of the zygoma, 2,5 cm in front of the auricle. The temporalis fascia and muscle is incised and retracted. Craniotomy is performed and dura opened and flapped inferiorly. Transverse cortical incision in the middle temporal gyrus that is 3.0 cm behind the tip of the temporal lobe and in an area free of cortical vessels. The corticectomy is generally 2.5 cm in length, followed by temporal lobe dissection toward the temporal horn until it is entered. With gentle brain retraction an optimal view of the intraventricular anatomy is evident, and key anatomical structures are identified. The parahippocampal gyrus is resected beginning with subpial resection of the uncus and then advancing medially and posteriorly. With resection of the anterior uncus, the incisura is visualized, and superiorly the internal carotid artery and third nerve can be seen through the pia. The choroidal fissure is identified. Care must be taken to ensure that the dissection is not carried superior to the choroidal fissure. The hippocampus is then mobilized laterally and resected beginning anteriorly, with care to preserve the anterior choroidal artery, and carried posteriorly to the level of the tectal plate. Once the hippocampal resection is completed, the cerebral peduncle and anterior choroidal artery are visualized through the pia. Careful hemostasis is obtained. In stepwise fashion the dura is closed, bone flap fixed, temporals muscle reapproximated, and scalp closed in layers to the skin.

Pathological examination:

Mesial temporal sclerosis 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 pathologists reported their findings without clinical or imaging data.

Follow up:

All patients underwent follow-up after surgery for four years, data on seizure frequency and AED regimens were recorded at each visit. Neurological and non-neurological complications were recorded. Epilepsy outcomes were assessed at each visit using a modified Engel scale17 Engel I: seizure free with or without aura, Engel II: greater than 90% reduction in seizure frequency, Engel III: 50%-90% reduction in seizure frequency; and Engel IV: less than 50% reduction in seizure frequency. Routine interictal EEG was performed, and antiepileptic medications were managed at the discretion of the treating epileptologist.

RESULTS

The studied cases were analyzed demographically and clinically (Table 1): fifteen cases were females and eleven cases were males with age range of 11 – 64 years, the mean age at seizures onset was 13,3 years with age range 1 – 42 years. Hippocampal sclerosis was left sided in sixteen cases (61,53%) and right sided in ten cases (38,46%). Precipitating factors were encountered in twelve cases (46,15%); subdivided as follow: seven cases (26,92 %) had febrile seizure as the most common, three cases (11,53%) had head trauma, single case (3,84%) had encephalitis and another case (3,84%) had perinatal asphyxia. The preoperative median weekly seizure frequency was two. Fourteen patients (53,84%) had CPS with secondary generalization and twelve patients (46,15%) had CPS without secondary generalization. Patients used a median of two AEDs preoperatively. Regarding significance of risk factors only SGS and postoperative early seizures were statistically significant; P value in case of SGS; at the end of the first year was p=0,033 and at the last follow up p=0,056, for postoperative early seizures p=0,003 at the end of the first year, while at the last follow up p=0,002. Seizure control outcomes at the last follow up by modified Engel outcome (table 2) revealed: seventeen cases (65,38%) were Engel Class I, three cases (11,53%) were Engel Class II, four cases (15,38%) were Engel Class III and two cases (7,69%) was Engel Class IV. There were no operative deaths and no neurological deficits occurred after surgery, only single case developed wound infection managed by repeated dressings and antibiotics according to culture and sensitivity. Regarding AED cessation, ten cases (38,46%) had complete AED cessation, fourteen cases (53,84%) had reduction in AED doses and only two cases (7,69%) had no change in AED regimen.
Table 1: Demographic and clinical data of patients

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<table>
<thead>
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<tr>
<td>Sex (female/male)</td>
<td>15 (57.69%) / 11 (42.3%)</td>
</tr>
<tr>
<td>Mean age at seizures onset in years</td>
<td>13.3 y (1 – 42 y)</td>
</tr>
<tr>
<td>Mean age at surgery</td>
<td>38.3 y (11 – 64 y)</td>
</tr>
<tr>
<td>Lateralization (left/right)</td>
<td>16 (61.53%) / 10 (38.46%)</td>
</tr>
<tr>
<td>Precipitating factors:</td>
<td>12 (46.15%)</td>
</tr>
<tr>
<td>Febrile seizures</td>
<td>7 (26.92%)</td>
</tr>
<tr>
<td>Head trauma</td>
<td>3 (11.53%)</td>
</tr>
<tr>
<td>CNS infection</td>
<td>1 (3.84%)</td>
</tr>
<tr>
<td>Perinatal insult</td>
<td>1 (3.84%)</td>
</tr>
<tr>
<td>Median seizure frequency per week</td>
<td>2</td>
</tr>
<tr>
<td>Median number of antiepileptic drugs</td>
<td>2</td>
</tr>
<tr>
<td>Secondary seizure generalization</td>
<td>14 (53.84%)</td>
</tr>
</tbody>
</table>

Table 2: Modified Engel classification of cases

<table>
<thead>
<tr>
<th></th>
<th>End of first year</th>
<th>End of 2nd year</th>
<th>End of 3rd year</th>
<th>End of 4th year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engel I</td>
<td>80.69%</td>
<td>73.07%</td>
<td>69.23%</td>
<td>65.38%</td>
</tr>
<tr>
<td>Engel II</td>
<td>7.69%</td>
<td>11.53%</td>
<td>15.38%</td>
<td>11.53%</td>
</tr>
<tr>
<td>Engel III</td>
<td>7.69%</td>
<td>11.53%</td>
<td>7.69%</td>
<td>15.38%</td>
</tr>
<tr>
<td>Engel IV</td>
<td>3.84%</td>
<td>3.84%</td>
<td>7.69%</td>
<td>7.69%</td>
</tr>
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Fig. 1 a&b: a: Coronal MRI T2-weighted image with right sided hippocampal atrophy, b: Postoperative axial MRI T2-weighted image after transcortical non-image guided selective amygdalohippocampectomy.

Fig. 2 a&b: a: Coronal MRI T2-weighted image with right sided hippocampal atrophy, b: Postoperative coronal MRI T1-weighted image after transcortical non-image guided selective amygdalohippocampectomy.
DISCUSSION

Temporal lobe epilepsy is the most common type of intractable partial epilepsy. The typical substrate associated with medial temporal lobe epilepsy (MTLE) is hippocampal sclerosis (HS) accounting for 60% to 70% of cases. The etiology of HS remains unclear. Histologically, severe neuronal loss and gliosis are observed, especially in the CA1, CA3, and CA4 subfields of the hippocampus. Recurrent sprouting of mossy fibers is also seen. In most patients, the epileptogenic focus involves the mediobasal structures of the temporal lobe. These structures include the hippocampus, amygdala, uncus and parahippocampal gyrus. Antiepileptic drugs usually suppress secondary generalized seizures successfully, but 50% of patients or more will continue to have partial seizures. When seizures persist, surgery is an effective treatment for MTLE associated with hippocampal sclerosis (HS). Either anterior temporal lobectomy (ATL) or selective amygdalohippocampectomy (SEAH) is the treatment of choice. The surgical results in HS are gratifying; seizure freedom is achieved in 60% to 90% of patients, with low morbidity and the findings of HS, both preoperatively by MRI and postoperatively by histology and electrophysiology, predict higher seizure-free outcomes.

In this study we report the surgical outcome of patients with MTLE due to HS, who underwent standard pre and postoperative evaluations and a uniform surgical procedure, which is transcortical selective amygdalohippocampectomy without navigation guidance. This approach is employed in cases of medically refractory temporal lobe epilepsy of mesial temporal origin. There is no universally agreed upon definition of medically refractory or treatment-resistant epilepsy. Many
authors use a working definition of failure of at least two trials of antiepileptic drug monotherapy and one combination therapy when used at therapeutic levels over 1-2 years, this was the protocol we followed in our study; however, a variety of definitions have been employed. In practice, many patients have failed much more extensive medication trials over much more extended time periods. Most commonly, suitable candidates are selected based on convergent lines of evidence implicating unilateral mesial temporal structures as the epileptogenic region. Consolidated with compatible ictal semiology and neurological history. Video-EEG monitoring should confirm ictal semiology and stereotyped ictal onset on scalp EEG consistent with mesial temporal origin. Intercital EEG may show concordant unilateral or bilateral (usually ipsilateral predominant) epileptiform discharges. MRI often demonstrates an abnormality in the mesial temporal structures: most commonly hippocampal atrophy with or without mesial temporal signal change on T2-weighted or FLAIR sequences. Patients with exclusively mesial temporal foreign tissue lesions (e.g., low grade tumor) or neurodevelopmental abnormalities may also be good candidates for this procedure but not included in our study. Additional studies may be used including positron emission tomography (PET), magnetoencephalography (MEG) and ictal single photon emission computed tomography (SPECT). Particularly in non-lesional cases, if standard evaluation, supplemented by specialized imaging studies, defines a unilateral temporal lobe onset, intracranial EEG monitoring may be required for distinguishing mesial from temporal neocortical onset so as to determine whether SEAH is indicated or ATL is mandatory. None of our cases was non-lesional in MRI. The intracarotid amobarbital test (IAT) or Wada test was first described in 1960 by Wada and Rasmussen and was originally conceived to obtain functional information concerning language prior to surgery and was later adapted to assess memory. Worse functioning of one temporal lobe (as measured by memory performance) suggests greater underlying damage from chronic epilepsy. A Wada memory asymmetry between involved and uninvolved hemispheres of as little as 25% can differentiate medial versus lateral neocortical TLE. Compared with non-MTS patients with TLE, Wada memory testing may be more specific for MTS patients, possibly due to direct involvement of the mesial temporal structures, regions known to be involved in proper memory functioning.

Others have reported that significant asymmetry between the hemispheres on Wada memory testing can predict seizure control after surgery in children and adults. Greater memory asymmetries on Wada testing between the ipsilateral and contralateral hemispheres, and the Wada results were concordant with the side of operation in about 80% of patients, and may result from hippocampal dysfunction by chronic epilepsy impairing functioning while the other temporal lobe is anesthetized by amytal. Other centers have reported similar rates of correlation between Wada testing and noninvasive studies (80%–90%) and hippocampal volume. Greater disparity on Wada testing and hippocampal volumetric analyses were inversely correlated with memory decline after surgery (greater dysfunction in the involved hemisphere) and predicted seizure control. Based on previous studies, IAT offers important localization information and prognostication in terms of postoperative deficits (memory and language) and seizure freedom. Some contend that IAT is obsolete and can be replaced by preoperative language and memory testing by functional MRI. Others stated that noninvasive functional studies such as functional MRI cannot predict the amnestic risk after temporal lobectomy as accurately as IAT. Functional MRI memory protocols are lagging behind language assessments, and results of memory testing with this noninvasive modality are limited to small series.

In our study we did not depend on IAT to investigate patients preoperatively. As brief historical background; Paulo Niemeyer reported selective resection of mesial temporal structures for intractable epilepsy in 1958. In a letter to his colleague Henri Gastaut, he related “because the focus of this epilepsy is usually in the nucleus amygdalae, in Ammon’s horn, or in the hippocampus of gyrus, I resected these 3 structures via a transventricular approach, almost without touching the temporal cortex”. The fascinating history of his pioneering work in neurosurgery in Brazil is related in a recent historical article by Cavalcanti et al. Subsequently Wieser and Yasargil popularized a transsylvian approach to SEAH and reported outcomes of large numbers of patients who underwent this procedure.

Other approaches including subtemporal and variants of the transcortical approach have been described. Use of SEAH became more widespread in the 1990s in tandem with increased utilization of intraoperative neuronavigation systems. There are data comparing SEAH and anterior temporal lobectomy (ATL) in terms of seizure control. Selective amygdalohippocampectomy was suggested with advantages of reduced risk of cognitive side effects and injury to the optic radiation. A poorer psychosocial outcome for ATL was reported compared to more selective techniques. Two recent studies have also compared seizure outcomes for ATL and SEAH. A better outcome (Engel I and II) was reported more frequently in ATL than SEAH, giving 66% improvement versus 44%. Ozkara et al. reported an overall seizure outcome of 72.1% in Engel I and 56.4% in ILAE I (International League Against Epilepsy) at the
last available follow-up in a patient group operated on either by SEAH or ATL and the prognosis was found to be better with ATL surgery according to Engel, but not according to ILAE classification. A more recent study reviewed 53 studies addressing the extent of resection in surgery for TLE and concluded that SEAH appears to have similar seizure outcome but a better cognitive outcome than temporal lobectomy. 51 In our study, at the last follow up 65.38% were classified in Engel I, 11.53% as Engel II and 15.38% as Engel III and 7.69% of the patients were Engel IV. There is little evidence to suggest that different approaches to SEAH result in different seizure-free outcomes. 38 There are some small reports suggesting that seizure-free outcomes following SEAH are less robust in children compared with adults. 9,13 Several studies have investigated the prognostic factors for surgery outcome, but no clear risks have been identified. Other studies have shown that epilepsy duration and age at surgery seem to be the most important predictors for surgical outcome. 21,25,27 However, after statistical adjustments were made for other factors, duration of the disease and age at surgery had no significant effect on the outcome. 48,41 In addition, the age at onset was not found to be associated with seizure recurrence. 21,27,40 However, a lack of obvious abnormality, or the presence of diffuse pathology, and secondary generalized seizures (SGS) were shown to be risk factors for postoperative recurrence. 40 Early postoperative seizures are another factor that has been shown to be associated with relapses. 39 In our study both preoperative SGS and postoperative early seizure were the only statistically significant factors indicative of seizure recurrence. According to Ozkara et al, 44 AED cessation was reported in 42.7% of patients at the sixth year for both ATL and SEAH. Weisers and Hane 58 reported 36.1% five years after SEAH. This was achieved in 38.46% of our patients at the last follow-up. An additional 53.84% had a reduction in their treatment. Similarly, Wieser et al 59 reported an overall treatment reduction in 70% of their patients.

**CONCLUSION**

This study shows that non-image guided selective amygdalohippocampectomy is a safe, precise, easy and effective surgical procedure for refractory mesial temporal lobe epilepsy caused by hippocampal sclerosis, without the necessity of image guidance or larger resection, with satisfactory outcome comparable to image guided procedures and to anterior temporal lobectomy.

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