Failure of temporal lobe resection for epilepsy in patients with mesial temporal sclerosis: results and treatment options

Clinical article

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Methods

In 1998 the University of South Florida in Tampa, Florida established a Comprehensive Epilepsy Center. Between 1998 and 2006, > 300 surgical interventions have been performed for the management of epilepsy (exclud-
Regarding vagus nerve stimulation. A prospective data registry was established in 1998 for the evaluation and treatment of intractable epilepsy. More than 250 procedures from this registry were temporal lobe resections. A retrospective review of these charts identified 145 patients who underwent selective anterior mesial temporal lobe resections for the treatment of MTLE in the setting of preoperative radiographic findings suggestive of MTS. Of those patients, only 105 of them were considered "ideal" candidates and met the following criteria for the study: 1) syndrome of MTLE as characterized by complex partial seizures with the typical clinical semiology of mesial origin (epigastric or psychic auras); 2) video-EEG findings compatible with unilateral ictal temporal lobe activity; 3) preoperative MR imaging findings suggestive of MTS (no evidence of dual pathological entities); and 4) minimum follow-up duration of 2 years.

Patients underwent a relatively standardized preoperative workup, which was initiated with long-term video-EEG monitoring. Patients were monitored in our epilepsy unit, and those who were found to have unilateral epileptiform temporal activity underwent further workup. High-resolution MR imaging performed using a 1.5-T magnet with attention to the temporal lobes consisted of axial and coronal T2-weighted and FLAIR images. A board-certified neuroradiologist reviewed all neuroimaging studies. Patients who demonstrated MR imaging findings suggestive of MTS were included in this study. Abnormal signal on FLAIR and T2-weighted images, and decreased volume and loss of anatomical configuration of the hippocampal formation are considered the hallmarks of radiographically confirmed MTS.

Interictal PET scans and/or ictal SPECT were obtained to corroborate a physiological abnormality in the mesial temporal lobe. A PET scan demonstrates hypometabolism in the epileptogenic brain, whereas SPECT scanning measures alteration in the blood flow in the epileptic tissue. Neuropsychological testing was done routinely to assess for neurological impairment. Finally, a Wada test was also performed in all patients. This test was done to assess for language dominance and memory impairment. Once this workup was completed, each case was discussed at a multidisciplinary epilepsy conference and surgical treatment was decided upon.

Our surgical technique consisted of a selective anterior mesial temporal resection via a transcortical approach. An extensive anterior temporal resection was not performed; thus the superior and middle temporal gyri were preserved in all patients. The intention was to remove the hippocampus and surrounding structures (parahippocampus) to the level of the superior colliculi. Complete resection of the uncus and partial resection (> 80%) of the amygdala were also performed. Surgeries were all performed by the senior author (F.L.V). Pathological specimens were sent for analysis in all cases, and the final reports were compatible with gliosis and neuronal loss, corroborating the diagnosis of mesial sclerosis.

All patients underwent postoperative MR imaging studies at the 3-month follow-up to document resection of the mesial structures. Surgical outcome was based on the Engel modified classification, as follows: Class I, seizure free or residual auras; Class II, rare disabling seizures (< 3 complex partial seizures per year); Class III, worthwhile seizure reduction; and Class IV, no worthwhile improvement. Patients were divided into 2 categories: Group A (Engel Class I or II) and Group B (Engel Class III or IV). Inclusion in Group B was considered to signify a major failure of surgical intervention.

A treatment algorithm was followed for failed temporal lobe surgery (Fig. 1). As an initial step, a repeat Phase I evaluation consisting of video-EEG monitoring was performed in all surgical failures (Group B). Seizure recurrence was divided, based on ictal electrophysiology, into 3 major groups: ipsilateral temporal, contralateral temporal, and extratemporal. Each group involves a different pathway in our surgical algorithm. A Phase II evaluation (invasive EEG monitoring with subdural strips or depth electrodes) is considered prior to further intervention if there are any concerns regarding ictal onset localization. A second operation was considered in those patients with localized epileptiform activity. The reoperation was performed with the aid of intraoperative electrocorticography and usually involved an extended neocortical resection in those cases with persistent ipsilateral temporal lobe epilepsy. Placement of a VNS was considered in those patients in whom a further resective procedure was thought not to be effective. A retrospective analysis was performed in those patients to identify predictors of surgical failure.

Results

A retrospective analysis was performed for the 105 patients who met the inclusion criteria. Adequate control of seizures was achieved in 92% of our patient population (Class I or II, Group A) at the last follow-up visit (mean 36 months, range 24–84 months) (Fig. 2). A significant finding was that there was no cross-over between groups (A and B) after the initial 1-year follow-up period. Although Group A (Engel I or II) total numbers remained constant throughout the follow-up period, there was a trend of 1–2% per year of decreased seizure-free outcome (Engel I → II).

Only 8 patients did not achieve a significant improvement (Class III or IV, Group B). All major failures (Group B) occurred within 1 year of surgery (range 3–9 months). All surgical failures had similar preoperative workup results, and there were no major differences in their preoperative clinical and radiographic findings when compared with Group A. A typical pattern for MTLE of unilateral rhythmic theta (4–7 Hz) discharges that were localized to the temporal lobe and beginning within 30 seconds of clinical onset was the norm for all patients. Interictal recordings also lateralized to the ipsilateral side. None of our patients had a clinical semiology to suggest bitemporal onset, such as ipsilateral or bilateral versive head turning (such a strong lateralizing sign would have prohibited a direct temporal resection without invasive studies). In all 8 patients a PET scan demonstrated temporal hypometabolism ipsilateral to the ictal onset on EEG. Wada testing was compatible with mesial temporal dysfunction (significant short-term memory asymmetry) in the ipsilateral temporal lobe. None of these patients had a clinical history of encephalitis, trauma, or status epilepticus, conditions that
Failure of temporal lobe resection

have been associated with increased risk of failure after temporal resections.16,19,22,40,44,47,50 Febrile seizures were a common finding in our patient population, but were not limited to the ones in whom surgery failed. In addition, no dual pathological entity was seen on follow-up radiographic evaluation (high-resolution MR imaging).

A statistical analysis was done using the Fisher exact test or the chi-square test when appropriate. Age at the time of surgery (mean 32 years, range 14–45 years), age at onset (mean 11 years, range 3–18 years), duration of epilepsy (mean 20 years, range 8–34 years), preoperative seizures recorded on video-EEG (Phase I evaluation) (mean 7, range 4–10), sex (5 female, 3 male patients), and side of surgery (4 each on the left and right sides) were not statistically significant predictors for failure when compared with Group A (p > 0.05). Nevertheless, we understand that due to the small sample size in Group B, the power of the analysis is low.

Patients in whom initial surgical intervention failed (Group B, 8 patients) were studied again by the epilepsy team according to a specified protocol (Fig. 1). In Group B, seizures recurred within 1 year, concordant with previous reports of failed surgical therapy.5,13,38,55 No early recurrence (< 30 days) was seen in this group. Electrophysiological reevaluation with surface electrodes in these patients ranged from ipsilateral temporal spikes to contralateral temporal findings (Table I). No cases of extratemporal ictal onset were identified on EEG recordings.

Five patients (62.5%) presented with ipsilateral recurrent temporal lobe seizures. Resection of mesial structures was achieved in all but 1 patient (12.5%), as demonstrated by high-resolution MR imaging. This patient had undergone an intentional partial resection of the mesial structures. Neuropsychological testing had raised questions about his ability to support memory function with resection of the left hippocampus, despite results of a Wada test that suggested mesial dysfunction in the affected temporal lobe. This patient had seizure control for 3 months following this partial resection. On repeat evaluation, video-EEG monitoring pointed to the residual mesial structures as the epileptogenic zone. Total resection of his mesial structures in a subsequent surgery improved seizure control to Engel Class I. This was not unexpected, because previous reports have suggested improved outcomes with resection of retained mesial structures in temporal lobe epilepsy.5,13,57 No postoperative sequela was documented in this patient.

![Fig. 1. Algorithm for the management of failed temporal lobe surgery. All patients undergo postoperative MR imaging studies at the 3-month follow-up. A Phase I evaluation (video-EEG) is performed as an initial step in cases of surgical failure. Invasive EEG recordings (Phase II evaluation) are considered if the surface electrode data are inconclusive.]

![Fig. 2. Histogram demonstrating surgical outcomes based on Engel outcome scale. Group A comprises Engel Class I or II, and Group B is made up of Engel Class III or IV. The number of major failures (Group B) remained constant throughout the follow-up period. N = number of patients (at the 3-, 4-, and 5-year follow-up; the number of patients decreases each time because fewer have reached that cutoff point).]
TABLE 1: Repeat evaluation in 8 patients with TLE in whom initial mesial temporal resection failed

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Initial Patho Findings</th>
<th>Clinical History</th>
<th>Postop EEG Findings</th>
<th>Postop MRI Findings</th>
<th>Reop Result</th>
<th>Reop Patho Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>lt MTS dejá vu, CPsz</td>
<td>ipilat temporal</td>
<td>residual mesial structures</td>
<td>Engel I</td>
<td>MTS</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>rt MTS febrile sz, CPsz</td>
<td>contralat temporal</td>
<td>abnormal signal, contralat mesial structures</td>
<td>VNS, Engel III</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>rt MTS CPsz</td>
<td>contralat temporal</td>
<td>adequate resection</td>
<td>VNS, Engel II</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>rt MTS CPsz &amp; rare GTCS</td>
<td>contralat temporal</td>
<td>abnormal signal, contralat mesial structures</td>
<td>VNS, Engel III</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>lt MTS febrile sz, CPsz</td>
<td>ipsilat temporal</td>
<td>adequate resection</td>
<td>Engel II</td>
<td>nonspecific gliosis</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>lt MTS CPsz</td>
<td>ipsilat temporal</td>
<td>adequate resection</td>
<td>Engel III</td>
<td>nonspecific gliosis</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>rt MTS CPsz &amp; rare GTCS</td>
<td>ipsilat temporal</td>
<td>adequate resection</td>
<td>Engel I</td>
<td>nonspecific gliosis</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>lt MTS CPsz</td>
<td>ipsilat temporal</td>
<td>adequate resection</td>
<td>Engel III (SUD)</td>
<td>nonspecific gliosis</td>
<td></td>
</tr>
</tbody>
</table>

* CPsz = complex partial seizure; GTCS = generalized tonic-clonic seizure; NA = not applicable; patho = pathological; SUD = sudden unexplained death (Patient was found dead 6 months after the reoperation.); TLE = temporal lobe epilepsy.

Excluding the patient who had retained mesial structures, a volumetric analysis of the other 7 patients in Group B was performed. Using standard software provided by GE’s Volume Viewer 2, version Vox Tool 6.4.52E, volumetric MR images were acquired using a 1.5-T MR imager. This software uses 3D reconstructions of axial, sagittal, and coronal T1-weighted MR images to calculate the volume of a selected area, in our case the resection cavity. Volume values of the resected cavity demonstrated a mean volume of 10.5 cm³, with a range between 8.4 and 12.3 cm³. This finding was compared with 30 consecutive patients from Group A (mean volume 10.7 cm³, range 8–12.8 cm³). The hippocampal/parahippocampal resection between groups failed to demonstrate a significant difference in the resection cavity (p > 0.05).

On repeat Phase I evaluation, 4 patients (50%) in Group B had persistent ipsilateral temporal EEG findings with similar clinical semiology, despite adequate resection of mesial structures, as documented by MR imaging (Table 1). All patients underwent a second operation consisting of an extended neocortical resection along the previous resection cavity in the temporal lobe. The second operation was performed with the aid of intraoperative electrocorticography. In the case of limited intraoperative electrophysiological data, a standard 5.5-cm resection from the temporal tip was performed to include the basal and lateral cortical structures, with the intent to preserve the superior temporal gyrus. Pathological specimens in this situation were compatible with nonspecific gliosis. Fifty percent (2 of 4) of these patients had improved outcomes with reoperation (Engel Class I or II). One patient was found dead of unexplained natural causes at 6 months after reoperation, without ever achieving adequate seizure control (Engel Class III).

The 3 remaining patients (37.5%, Group B) had EEG findings compatible with contralateral temporal lobe epilepsy. There was no preoperative discordant information in these patients to suggest bilateral disease. Only 1 of these 3 patients had bilateral interictal spikes, with > 80% predominance to the surgical side in the preoperative workup. This finding was also seen in our general population and was not limited to the patients in whom initial surgical intervention failed. Postoperative MR imaging studies demonstrated abnormal radiographic signal (increased FLAIR intensity) in the contralateral mesial temporal lobe in 2 of these 3 patients in whom initial temporal resection failed. This finding was not detected on the preoperative high-resolution MR imaging study. The significance of this finding remains unknown. All patients in this group had an impaired baseline verbal memory function, but there was no significant decline in short-term memory performance documented in the initial postoperative follow-up evaluation. Because of the nature of their disease, no further resection was recommended. Instead, all 3 patients underwent VNS implantation to help control their epilepsy. Improved seizure control was achieved in 1 (33%; Engel Class II) (Table 1).

Based on our clinical findings, the most common postoperative EEG finding in patients in whom mesial temporal lobe resections for MTS failed are ipsilateral temporal lobe discharges, as evidenced in 62.5% of our patients (including the one with residual mesial structures). Similar findings have been identified in recent reports (Table 2). No evidence of dual pathological entities such as cortical dysplasia was identified in the pathological specimens. Unfortunately, contralateral temporal lobe ictaliform activity was another major cause for surgical failure (37.5%). No cases of extratemporal ictal onset were identified in this group of patients after reevaluation. In this series, all but one patient had adequate resection of mesial structures, as evidenced by postoperative MR imaging, eliminating this factor as a common cause for failure.

Discussion

Patients with MTLE and radiographic findings suggestive of unilateral MTS are the ideal candidates for mesial temporal lobe resections. Medical treatment alone will fail in 75% of these patients, whereas surgery results in seizure control rates in up to 90%. Unfortunately, some patients do not have a significant improvement of their condition after surgery, even with complete resection of the suspected epileptogenic zone. Surgical failures remain a challenge to the epilepsy treatment team.

No major clinical risk factors were identified in our group of patients. Major surgical failure usually occurred within 1 year. Age, sex, and duration of epilepsy were not
different in each clinical group. Electrophysiology and radiographic findings were similar between groups. Surgical approach was similar in all patients, and there was no significant difference between resection volumes in each group. The search for clinical predictors of surgical failures has shown limited success.52 Many factors have been studied as predictors of outcome in these patients, including the following: duration of epilepsy; age at operation; history of febrile seizures; and presence of a known cause of epilepsy such as significant head trauma, tuberous sclerosis, presence of ventriculoperitoneal shunt, arteriovenous malformations, CNS infection, global hypoxia, or infantile hemiparesis.16 Unfortunately, results have been inconclusive. In a retrospective study by Hardy et al., only a history of status epilepticus was found to be a significant predictor of poor outcome. In our experience, a history of recurrent status epilepticus suggests extensive and multifocal epilepsy, which is not typically found in temporal lobe epilepsy. However, we realize that because surgical intervention failed in only 8 patients in our series, it is possible that additional patients would be required to identify preoperative predictors of failure. Preoperative volumetric analysis of both temporal lobes (mesial structures) perhaps will offer some insight in cases of bitemporal disease; unfortunately those measurements were not always available in our current study. Nevertheless, the cause of failure lies in the pathological substrate of this group of patients. However, these patients should not be considered absolute failures of surgical management; instead they should be studied once again to determine why surgery failed and to decide if further surgical intervention is indicated.

Failure of Temporal Lobe Resection: What to Do?

Favorable outcomes following repeat epilepsy surgery have been reported in the following types of patients: 1) those with residual epileptogenic structures and concordant findings on repeat EEG studies; and 2) those in whom reoperation extended the prior resection. Unfavorable outcomes occurred in the following cases: 1) patients with epileptogenesis distant from the original site of resection; 2) patients with multifocal abnormalities detected on EEG recordings; 3) patients with a history of encephalitis (especially after the age of 4 years); and 4) patients in whom recurrent seizures developed within 1 month postoperatively (early failures).5,13,16,17,41,45,46,57

Based on our treatment algorithm, a repeat Phase I (video-EEG) evaluation should be performed as an initial step when seizures recur. Video-EEG recordings in combination with the clinical semiology should give an accurate location of ictal onset. It will also rule out non-epileptic seizures, which may occur in a small percentage of patients.9,14,35

It is our experience as well as others’ that reoperation might be of benefit in selected patients (Table 3). We believe that further surgical intervention can be considered for those patients with ipsilateral temporal seizures, with or without residual mesial structures, and for those with new extratemporal seizures if a lesion or epileptogenic cortex can be identified. For patients with persistent ipsilateral seizure onset, extension of the cortical resection along the surgical scar seems to be beneficial ~ 50–60% of the time. For those patients with contralateral temporal seizures or nonlocalizable seizure onset, a VNS may be implanted as a surgical option. Our preliminary experience using the VNS as a salvage surgical intervention in patients with MTS has been of limited success. There are no large series reporting the use of VNSs for failed surgery in MTS cases.23,24 Outcome has not improved in the few cases reported.15

In contrast with previous reports of failure in patients with MTS,5,13,17,45,57 surgery failed in only one case in our series, due to incomplete resection of the mesial structures. It has been suggested that removal of the mesial structures (hippocampal/parahippocampal gyrus) to the level of the superior colliculi allows for better seizure control in patients with temporal lobe epilepsy.5,13,57,58 The residual hippocampus can remain epileptogenic. As long as a “critical mass” is present, epileptogenesis is a possibility.1 In 1991, Awad et al.5 reported 6 of 10 patients who demonstrated epileptogenicity in the residual mesial temporal structures. In 2000, Hennessy et al.17 reported 5 of 20 patients with residual mesial structures (Table 2). Both authors acknowledged that incomplete resection of mesial structures is a potential cause of treatment failure.

Germano et al.23 published a series of 40 patients who underwent reoperation on the temporal lobe for recurrent seizures (Table 3). After a second operation to complete resection of the mesial structures, 63% of the patients were seizure free or had only rare seizures. Salanova et al.48 reported that 57% of their patients were seizure free after a repeat surgery to complete mesial resection. Wyler et al.37 reported 52% and Awad et al.5 60% improvement

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**TABLE 2: Literature review of failure rates and postoperative ictal findings in patients with MTS**

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Patients w/ MTS</th>
<th>Tx Failures w/ MTS</th>
<th>Ipsilat Temporal Sz</th>
<th>Contralat Temporal Sz</th>
<th>Extratemporal Sz</th>
<th>Residual Structures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kilpatrick et al., 1999</td>
<td>56</td>
<td>8 (14)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hennessy et al., 2000</td>
<td>165</td>
<td>20 (12)</td>
<td>12 (60)</td>
<td>5 (25)</td>
<td>2 (10)</td>
<td>5</td>
</tr>
<tr>
<td>Schwartz &amp; Spencer, 2001</td>
<td>NR</td>
<td>5</td>
<td>4 (80)</td>
<td>1 (20)</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Hardy et al., 2003</td>
<td>118</td>
<td>9 (7.6)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Gonzalez-Martinez et al., 2007</td>
<td>NR</td>
<td>7</td>
<td>1</td>
<td>4 (57)</td>
<td>1 (14)</td>
<td>1</td>
</tr>
<tr>
<td>Present study</td>
<td>105</td>
<td>8 (8)</td>
<td>5 (62.5)</td>
<td>3 (37.5)</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

* NR = not reported.
in similar series of patients with temporal lobe epilepsy and retained mesial structures. Recurrent seizures in these patients most likely originate from the residual hippocampus. It appears that reoperation in these patients is beneficial, at least in 50–60% of cases.

Nevertheless, patients who undergo complete resection of the mesial structures and continue to have ipsilateral temporal seizures pose a diagnostic and management dilemma. Imaging studies frequently reveal no anatomical abnormalities, making it difficult to identify the epileptogenic zone and therefore plan further treatment. The role of invasive EEG recordings with strips, grids, or depth electrodes in this group is not clear. In addition, unawareness of the pathological substrate behind the recurrent seizures makes planning further interventions very difficult.

An extended neocortical resection may be indicated in patients with unilateral MTS in whom initial resection fails and whose seizures can be localized to the ipsilateral temporal lobe. Results of reoperation are difficult to predict because there are few series published in this particular group of patients. In a recent study by Gonzalez-Martinez et al., reoperation consisted of extending the previous resection margin in patients with MTS. It only led to good outcomes in 3 (30%) of 10 patients. However, on further analysis, 4 of these 10 patients were found to have contralateral temporal epileptic activity, explaining their poor outcomes and demonstrating the importance of repeating EEG studies prior to planning further resections in so-called surgical failures. In our series 2 of 4 patients who initially had complete resection of the mesial structures improved to Engel Class I or II with an extended neocortical resection along the basal and lateral cortex of the previous resection cavity. Despite an EEG recording that clearly localized the recurrent seizures to the ipsilateral temporal lobe, the pathological specimens from this group were consistent with non-specific gliosis. The significance of this finding is unclear. Surgical scarring as a cause of recurrent epilepsy remains a controversial subject. Most likely the pathological explanation for failure in these patients is occult epileptogenic areas that are not seen on current diagnostic studies and that may represent neuronal developmental problems such as focal cortical dysplasia.

Unfortunately, contralateral temporal lobe epilepsy remains a frequent finding in patients in whom initial temporal lobe resection failed. Limited knowledge of the pathophysiological features of MTS has prevented us from identifying factors that precipitate neuronal loss and gliosis of the hippocampal formation. The pathogenesis of MTLE is associated with an event that probably injures the hippocampus at some time prior to habitual seizure onset. This event likely affects both hippocampi in an asymmetrical way. Febrile seizures have been recognized as a common offender, but controversy still exists regarding the etiological relationship between MTS and epilepsy. Some investigators view hippocampal sclerosis as the primary cause of temporal lobe epilepsy, whereas others interpret the changes to be the result of chronic seizure activity. Regardless of its origin, it appears that MTL-E is a bilateral disease with a broad range of lateralization.

Autopsy series corroborate the theory that a high proportion of patients with epilepsy, 47–86% of cases, suffer from bitemporal hippocampal sclerosis. Volumetric MR imaging studies suggest that most patients with MTLE have some degree of bilateral, asymmetrical hippocampal disease. As a result, a high proportion of patients in whom surgery fails demonstrate contralateral temporal epileptiform activity, and in some cases there are significant MR imaging findings to suggest MTS. Gonzalez-Martinez et al. reported on 4 of 7 patients with contralateral temporal epileptiform activity, and in some cases there are significant MR imaging findings to suggest MTS. Gonzalez-Martinez et al. reported on 1 of 5, and Hennessy et al. on 5 of 20 in their respective series of surgical failures (Table 2). In our series, 3 (37.5%) of 8 patients developed contralateral temporal lobe seizures. In these cases, EEG data identified the contralateral mesial structures as the new epileptogenic zone. The events leading to activation of this new epileptogenic area are not understood. Unfortunately, this group of patients is not eligible for further resective surgery because bilateral mesial temporal resections may result in devastating cognitive and behavioral deficits. Further therapeutic options are limited to medical therapy and possible placement of a VNS.

Extratemporal seizure origin is not a common cause of treatment failure for patients with hippocampal sclerosis. The number of documented cases in the literature is small (Table 2). We did not identify any cases of extratemporal ictal onset, but in other series it has been identified as a cause of failure. Assuming that the localization of the epileptogenic focus was initially accurate, the pathological substrate of these cases probably involves the activa-

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients w/ MTS</th>
<th>No. of Patients w/ Reop</th>
<th>Success Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wyler et al., 1989</td>
<td>NR</td>
<td>23</td>
<td>52</td>
</tr>
<tr>
<td>Awad et al., 1991</td>
<td>NR</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>Germano et al., 1994</td>
<td>NR</td>
<td>40</td>
<td>63</td>
</tr>
<tr>
<td>Schwartz &amp; Spencer, 2001</td>
<td>5</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>Abosch et al., 2002</td>
<td>3</td>
<td>3</td>
<td>34</td>
</tr>
<tr>
<td>Salanova et al., 2005</td>
<td>NR</td>
<td>21</td>
<td>57</td>
</tr>
<tr>
<td>Gonzalez-Martinez et al., 2007</td>
<td>10</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>Present study</td>
<td>8</td>
<td>5</td>
<td>60</td>
</tr>
</tbody>
</table>

* Engel Class I or II.
tion of a new or occult epileptogenic area(s). For patients with temporal lobe epilepsy, these new areas most likely represent dual pathological entities not diagnosed on the initial neurophysiological and radiographic studies.

The presence of dual pathological entities in patients with MTS has been well described in the literature. Some authors have found a 15–30% incidence of this type of dual pathological entity in their series of patients with temporal lobe epilepsy. In this situation, both the dysplastic temporal neocortex and the sclerotic hippocampus can be epileptogenic. It appears that the contribution of the hippocampus to seizure generation corresponds to the degree of hippocampal pathological involvement, whereas even mild forms of cortical dysplasia can be epileptogenic. This finding has major prognostic implications for patients who undergo selective temporal lobe surgery, because MR imaging may not detect mild neuronal and cortical changes that have epileptogenic potential.

In general, there are 3 main reasons why epilepsy surgery, regardless of pathological findings, can fail. These are as follows: 1) inaccurate localization/mapping of the epileptogenic focus, usually seen in early failures (< 30 days); 2) incomplete resection of the epileptogenic focus; and 3) occult or new epileptogenic areas.

Because of the lack of clinical findings as predictors of poor outcome, to understand better the reasons for failure, attention should be placed on the pathological substrate of this group.

It is clear that larger series of cases of surgical failure in patients with MTS are certainly needed before more conclusions are drawn. Further understanding of the pathophysiological features and mechanisms of epileptogenesis of MTS is necessary. Accurate identification of the epileptogenic area is critical for success. The evolving field of MEG and advanced neuroimaging (3-T MR imaging) may play an essential role in identifying epileptic activity in patients with intractable epilepsy. Brain shifts following resection may cause gross distortions of topographic anatomy, which may cause false localization on scalp EEG recordings. In these situations MEG may be superior to scalp EEG, because magnetic fields are not distorted by skull defects. In addition, MEG has been used successfully in identifying residual epileptogenic zones in patients in whom MR imaging reveals no residual abnormality and scalp EEG results are not lateralizing.

Conclusions

Surgical treatment of MTLE associated with MTS results in control of epilepsy in the vast majority of patients. Unfortunately, major failures do occur, usually within 1 year of surgery. Reasons for the failure of temporal lobe surgery are multifactorial and difficult to predict based on clinical and physiological evaluations. Nevertheless, the cause of failure appears to lie in the pathological substrates in this group of patients, which include the generation of an epileptogenic focus in the form of dual pathological entities, scar tissue, or contralateral temporal epileptogenesis. Incomplete resection of the epileptogenic zones in the form of residual hippocampus is no longer a common cause for surgical failures. A protocol of repeat evaluation and reoperation results in improved seizure control in properly selected patients.

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Disclaimer

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