Prognostic factors and outcome after different types of resection for temporal lobe epilepsy

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Object. It is unknown whether different resection strategies for temporal lobe epilepsy (TLE) produce alterations in seizure control or neuropsychological performance.

Methods: A series of 321 patients who underwent surgery for TLE between 1989 and 1997 was submitted to a univariable and multifactorial analysis of clinical, electrophysiological, neuroimaging, neuropsychological, and surgical factors to determine independent predictors of outcome. Until 1993, most patients with TLE underwent standard anterior temporal lobectomy (ATL); beginning in 1993, surgical procedures were increasingly restricted to lesions detected on magnetic resonance (MR) imaging and the presumed epileptogenic foci: for example, amygdalohippocampectomy (AH) or lesionectomy/corticectomy began to be used more often.

The mean follow-up duration in this study was 38 months. Two hundred twenty-seven patients were classified as seizure free (70.7%), and 36 patients had rare and nondisabling seizures (11.2%); these groups were summarized as having good seizure control (81.9%). Twenty-four patients attained more than 75% improvement (7.5%), and no worthwhile improvement was seen in 34 cases (10.6%); these groups were summarized as having unsatisfactory seizure control (18.1%).

On unifactorial analysis the following preoperative factors were associated with good seizure control (p < 0.05): single and concordant lateralizing focus on electroencephalography studies, low seizure frequency, absence of status epilepticus, concordant lateralizing memory deficit, clear abnormality on MR images, suspected ganglioglioma or dysembryoplastic neuroepithelial tumor (DNT), and absence of dysplasia on MR images. Stepwise logistic regression revealed a model containing five factors that were predictive for good seizure control (p < 0.1): 1) clear abnormality on MR images; 2) absence of status epilepticus; 3) MR imaging–confirmed ganglioglioma or DNT; 4) concordant lateralizing memory deficit; and 5) absence of dysplasia on MR images. Seizure outcome was mainly correlated with diagnosis and clinical factors. No significant differences were found regarding different resection types performed for comparable tumors. Neuropsychological testing revealed better postoperative results after limited resections compared with standard ATL, especially with regard to attention level, verbal memory, and calculated total neuropsychological performance.

Conclusions. Different strategies for surgical approaches in TLE result in equally good outcomes. Seizure outcome is mainly dependent on the diagnosis and clinical factors, whereas the neuropsychological results are more beneficial after resections limited to an epileptogenic lesion and focus.

Key Words • temporal lobe epilepsy • neuropsychology • predictive factor • epilepsy surgery • magnetic resonance imaging • S

URGICAL treatment of medically refractory TLE as a standard modality has improved during the last decades. Generally, seizure relief was achieved in more patients in series published after 1990 compared with earlier trials. Surgical morbidity and mortality rates were reduced, for example, after the introduction of micro-neurosurgical methods.

Numerous predictive factors were identified in earlier studies, whereas publications from recent years generally contain fewer items, probably as a result of increasing knowledge and thus avoiding surgery in unsuitable candidates. A single unilateral lesion detectable on MR images, or unilateral hippocampal sclerosis and exclusively ipsilateral epileptiform ictal and interictal EEG activity seem to be most predictive for excellent outcome. A variety of factors have been attributed to surgical success: for example, a history of febrile seizures, age at onset, and seizure types and frequency, but none of these findings was consistently confirmed in other studies.

With increasing ability to demonstrate even subtle structural lesions by using high-resolution MR modalities plus elaborate electrophysiological monitoring, the concept of tailoring the resection just to the epileptic focus and lesion has evolved. Nevertheless, ATL is still the most widely performed standard resection for TLE. With respect to mesial TLE, it is still a matter of discussion whether limited resections (for example, AH) are beneficial in terms of side effects, postsurgical memory performance, and seizure relief.
During the last 10 years a number of epilepsy surgery centers have changed their resection strategies. Since 1994, we have increasingly performed more limited resections and more AHS while reducing the number of ATLs, whenever presurgical evaluation demonstrated a localized lesion and epileptogenic area within the temporal lobe, for example, in pure mesial TLE.

So far it is unknown whether this change in resection strategy has led to alterations in patient outcome, in terms of seizure relief or neurological or neuropsychological features. Moreover, a comprehensive multifactorial analysis of prognostic factors with respect to different surgical strategies for TLE is not available. This information is necessary for preoperative patient counseling, especially because the surgical strategy is one of few covariates that can be voluntarily modified. This study was initiated to examine the influences of group experience, advances in MR imaging technology, resection strategies, and other clinical factors on seizure outcome and neuropsychological performance, by using uni- and multifactorial analysis.

**Clinical Material and Methods**

**Patient Population**

Between 1989 and 1997, a total of 456 consecutive patients underwent temporal lobe resections for medically intractable TLE in the epilepsy surgery program at the University of Bonn. Of these, four patients died postoperatively of causes unrelated to surgery. Minimal requirements for inclusion in the study were as follows: 1) complete clinical and electrophysiological data sets; 2) preoperative MR images available for review; and 3) follow-up duration of at least 12 months. One hundred thirty-one patients had to be excluded, most of them because of nonavailability of preoperative MR images for review or lack of follow-up information, resulting in a total of 321 patients.

**Presurgical Evaluation**

All patients had suffered well-documented chronic and medically intractable TLE for more than 1 year and had undergone adequate trials of at least two first-line antiepileptic drugs before they were referred for presurgical evaluation. All patients underwent continuous, noninvasive video scalp EEG monitoring, including sphenoidal electrodes, to determine ictal and interictal focal activity. Data used for this analysis included the following clinical and demographic information for each patient: 1) age at epilepsy manifestation; 2) duration of epilepsy; 3) age at operation; 4) presence of febrile seizures; 5) other medical history; 6) neurological status; 7) seizure type; and 8) seizure frequency. The EEG data were classified according to the location of interictal epileptiform EEG activity and ictal onset. For missing information, patient charts were reviewed and the data were updated. Intraoperative cortiography was only applied in two cases. Intracranial recordings were performed, mostly in combination, in 161 patients as follows: amygdalohippocampal depth electrodes were used in 121 patients, subdural strip electrodes in 145 patients, and a subdural grid electrode in 11 patients. The details of procedures used for invasive recordings at this center have been described previously. A global Wada test evaluation was regularly done in the first patient cohort (1989–1992), but was increasingly omitted thereafter, so that features derived from Wada testing are not included in this study. Noninvasive EEG recordings are mostly not specifically affected in the Wada setting, and better memory prediction can be obtained by means of cognitive potentials recorded with hippocampal depth electrodes. Thus, Wada testing is presently only applied to determine speech dominance in neocortical epilepsy in which the lesion or focus is close to presumed speech areas.

Presurgical MR imaging was performed using a 1.5 tesla unit (Philips Gyroscan model S15; Philips Medical Systems, Eindhoven, NL). Axial and sagittal $T_1$-weighted images (TR 500–600 msec, TE 15–25 msec, slice thickness 4–8 mm) and axial and coronal $T_2$-weighted images (TR 2–2.5 msec, TE 80–120 msec, slice thickness 4–8 mm) were obtained routinely. Spin-echo sequences were also usually performed. If a tumor was suspected, additional axial and coronal $T_2$-weighted images with and without Gd-dihydrenetramine pentaacetic acid were acquired using similar parameters. The MR images were reviewed by a neuroradiologist (B.O.) who is experienced in the field of epilepsy and who was blinded to the clinical and outcome data. At review, MR imaging data were classified as follows: MTS, lesion, or presumed diagnosis (ganglioglioma, DNT, other tumor, dysplasia, or other). Furthermore, MR images were subjectively classified into three categories according to their quality (low, medium, or high).

Neuropsychological testing of intelligence, attention, visual and verbal memory, language, and higher verbal and visual reasoning was routinely performed, as described before. Attention was assessed by use of a letter cancellation test and a standardized composite score of speed and precision was chosen for analysis.

Memory assessments included the following tests: verbal memory was assessed by a verbal learning and memory test that requires serial learning with immediate recall after each learning trial, free recall after distraction and a delay of 30 minutes, and finally recognition of the words to be learned from among alternatives. Analysis of these tests was based on learning over five trials, loss of learned items after delay, and recognition. Visual memory was assessed using a graphic learning test, which requires learning and reproduction of a list of nine designs in six learning trials. With respect to language-related functions, naming was assessed using a confrontation naming subtest of the Aachen Aphasic Test, a German test battery for aphasia; the number of errors was recorded for analysis. Verbal comprehension was assessed using the Token Test, which is also a subtest of the Aachen Aphasic Test; the number of errors was recorded for analysis. Verbal fluency was assessed using a written word fluency test, a subtest of a German test of intelligence (Subtest 6 of the Leistungsprüfsystem). Verbal reasoning was assessed using two subtests of another German test of intelligence (Intelligenz Struktur Test): one requires the detection of words from among alternatives that do not belong to the same semantic category as the test words, and the other requires detection of two words from among alternatives that belong to the same superordinated semantic category. Visual construction–oriented tests were as follows: visual construction was assessed using the Block Design subtest of the Wechsler Adult Intelligence Scale, which requires construction of designs of varying complexity. Mental imagination and rotation were assessed.
using another subtest of the German test of intelligence (Subtest 8 of the Leistungsprüfsystem), which requires transformation of two-dimensional figures into three-dimensional objects and mental rotation of the objects.26

For the comprehensive purpose of this study, only results involving the major factors of attention, visual memory, and verbal memory were taken into account. All neuropsychological results were classified into six categories ranging from 0 (far below average) to 5 (far better than average), with the difference between two neighboring categories being 1 standard deviation. Categories 2 and 3 were considered to be in the range of normal average.23 A difference of at least 1 standard deviation in preoperative verbal and visual memory performance was considered to be lateralizing to the side of the poorer performance. Postoperative changes of more than one category were judged to indicate a significant change in performance, according to retest reliabilities evaluated in nonsurgically treated patients with epilepsy.23 The summing of postoperative differences in the tests for attention, visual memory, and verbal memory was considered to be a means to assess the total neuropsychological outcome. The outcome was categorized as worsening, unchanged performance, and improvement compared with the respective preoperative findings.

Surgical Procedures

From 1989 to 1992 (first cohort, 96 patients), ATL with removal of the mesiotemporal structures was chosen as the standard procedure for treating mesial TLE, as well as for most other cases of TLE. The resection line extended 4.5 to 5.5 cm from the temporal pole in the nondominant and 4.5 cm in the dominant hemisphere, including the superior temporal gyrus. For patients with lateral lesions and absence of clinical and electrophysiological mesiotemporal features, we performed lateral lesionectomies or corticectomies only. Temporodorsal and basal lesions were treated using a temporodorsal lesionectomy and corticectomy, with additional removal of hippocampus and amygdala in selected cases. During 1993 and 1994 (second cohort, 84 patients) resections were increasingly limited, facilitated by the demonstration of presumably epileptogenic lesions and localization of the epileptogenic focus on high-resolution MR imaging, after their detection on invasive and noninvasive EEG recordings.

During this period, transsylvian AH, as introduced by Yasargil, et al.,56 replaced ATL for the treatment of mesial TLE; the new procedure was performed as follows: after microsurgical preparation and 3-cm anterior opening of the sylvian fissure with preservation of arterial and venous vessels, the temporal horn of the lateral ventricle was opened by incision of the temporal stem to an extent of approximately 1.5 cm. After identification of the hippocampus and amygdala, first the caput hippocampi and the amygdala were resected en bloc, and additionally the uncus was removed using ultrasonic aspiration. In a second step, we performed an en bloc preparation of the corpus hippocampi together with the parahippocampal gyrus, preserving the arachnoid layers covering the cisterna ambiens. Finally, the vessels in the hippocampal fissure were prepared, coagulated, and cut. The lateral resection border is the sulcus collateralis, and the posterior resection should reach the middle or even the dorsal brainstem level. In most cases after en bloc resection, some millimeters of hippocampal tissue have to be removed by ultrasonic aspiration to reach the planned dorsal extent of resection.

Starting in 1995, resections for pure mesial TLE were performed using selective AH exclusively, and for most other cases only lateral neocortical lesionectomies or combined mesial and lateral resections were used (third cohort, 141 patients).55,57 In general, intracerebral lesions, either detected on MR images or visible intraoperatively, were completely excised in addition to removal of an adjacent 5 to 10 mm of epileptogenic tissue, unless the region of ictal onset overlapped eloquent areas. Gross-total tumor removal was achieved in all cases. In patients with tumors we regularly obtained a first postoperative MR image at 3 or 12 months postsurgery, and at 1- or 2-year intervals thereafter for screening of tumor recurrence.

Surgical procedures included AH (138 patients), ATL with hippocampectomy (98 patients), purely lateral temporal lesionectomy and corticectomy (58 patients), and lesionectomy and corticectomy plus additional hippocampectomy (27 patients). Three patients underwent additional multiple subpial transections in adjacent epileptogenic eloquent areas. There were 167 procedures performed on the right and 154 on the left. Eight patients with recurrent seizures underwent further resections, mostly for completion of hippocampal or parahippocampal tissue removal. Successful seizure control (Class I) was attained in four of these eight patients.

Histological Examination

The resected specimens were histopathologically examined using methods that have been described previously.54 A standard neuropathological protocol was generally used for all epilepsy surgery cases. Hematoxylin and eosin–stained sections were available for all cases. In most cases, Nissl stains and combined hematoxylin and eosin and luxol fast-blue stains were also available. In selected cases, additional special staining was performed. Tumors were classified according to the revised WHO classification scheme31 of tumors of the nervous system. The diagnosis of AHS and dysplastic malformations was made as previously described for temporal lobe specimens in epilepsy.54 Different subtypes of dysplastic malformations were grouped together as cortical dysplasias.

Outcome Data

Follow-up information on seizure outcome and neurological status was obtained either from the last regular annual outpatient visit or from standardized telephone interviews performed by one of the authors (H.C.). Patients were assigned to one of four outcome classes according to the rankings of Engel, et al.,19 based on their last postoperative seizure status. The scale is as follows: Class I, seizure free or only auras since surgery; Class II, rare seizures (fewer than two/year or only nondisabling nocturnal seizures); Class III, reduction of seizure frequency more than 75%; and Class IV, unchanged (< 75% reduction of seizure frequency). For further analysis, Class I and II outcomes were usually summarized as good or satisfactory seizure control, whereas Classes III and IV were listed as unsatisfactory seizure control.
TABLE 1
Demographic and clinical characteristics of 321 patients with TLE

<table>
<thead>
<tr>
<th>Factor</th>
<th>No. of Patients (%)</th>
<th>Years</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>sex</td>
<td>male 157 (48.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>female 164 (51.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>age at op</td>
<td></td>
<td>29.7</td>
<td>2–62</td>
</tr>
<tr>
<td>yrs from seizure onset</td>
<td>all patients 11.8</td>
<td>0.1–48</td>
<td></td>
</tr>
<tr>
<td></td>
<td>patients w/ neoplasia 13.3</td>
<td>1–37</td>
<td></td>
</tr>
<tr>
<td></td>
<td>patients w/ AHS or dysplasia 10.0</td>
<td>0.1–42</td>
<td></td>
</tr>
<tr>
<td>preop epilepsy duration</td>
<td>history 17.9</td>
<td>1–54</td>
<td></td>
</tr>
<tr>
<td>history</td>
<td>febrile convulsions 46 (14.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>trauma 23 (7.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>infection 24 (7.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>familial seizures 27 (8.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>neurological status</td>
<td>normal 291 (90.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>impaired 30 (9.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>seizure type</td>
<td>auras 236 (73.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>simple partial seizures 97 (30.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>complex partial seizures 308 (96.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>generalized seizures 130 (40.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>other 3 (0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>no. of seizure types</td>
<td>1 115 (35.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 140 (43.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;2 61 (20.6)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data Collection and Statistical Analysis

The potentially prognostic factors that we documented were analyzed with respect to their prediction of good seizure outcome. The data were prospectively collected in three data banks and retrospectively analyzed. For unifactorial analysis between groups defined by the outcome, the Student t-test was used for statistical comparison of continuous prognostic variables if the distribution was normal, and the Wilcoxon test was used if it was not. Dichotomous discrete variables were analyzed using the chi-square test or the Fisher exact test. Testing for significant trends was done with the Cochran–Armitage trend test. For multifactorial analysis, a stepwise logistic regression model was applied. Prognostic variables were included in the multifactorial analysis if the unifactorial analysis resulted in a probability level less than 0.05. Forward stepwise logistic regression was performed with critical probability levels of 0.1 for inclusion and 0.3 for exclusion of factors from the model by using adjusted chi-square statistics. The result was confirmed using a backward stepwise regression.

Results

Follow-Up Findings

The mean follow-up duration was 38 months (12–108 months); 279 patients (86.9%) had a follow-up of more than 2 years. A total of 227 patients (70.7%) were classified as seizure free (Class I), and 36 patients (11.2%) had rare and nondisabling seizures (Class II); these classes were grouped together as satisfactory seizure control (263 patients, 81.9%). Twenty-four patients (7.5%) were categorized in Class III, and no worthwhile improvement was reached in 34 (10.6%, Class IV); these classes were grouped together as unsatisfactory seizure control.

Clinical Findings and Demographic Data

Demographic and clinical data are summarized in Table 1. Patients with AHS or dysplasias had an earlier onset compared with those who had tumor-associated epilepsies (p = 0.034). Seizure frequencies varied over a wide range: complex partial seizures occurred at a median of seven per month (range 0.1–240), and simple partial seizures at a median of seven per month (range 0.1–240). The median frequency of secondary generalization, if present, was 0.2 per month. A history of febrile convulsions was significantly more common in patients with AHS (38 individuals, 28.1%), than in those without AHS (eight patients, 4.3%; p = 0.001).

Interictal EEG studies revealed primary specific EEG activity exclusively in the ipsilateral temporal lobe in 182 cases (56.7%), and in other ipsilateral areas in four cases (1.2%). In 68 patients (21.2%) bilateral temporal interictal activity was observed, in eight patients (2.5%) we found multifocal interictal activity, and in 59 patients (18.4%) interictal EEG findings remained elusive. An ipsilateral temporal ictal EEG focus was documented in 283 patients (88.2%), whereas 10 patients (3.1%) had other primary ictal EEG foci, and in 28 patients (8.7%) no information about

TABLE 2
Presurgical factors and seizure outcomes in 321 patients (unifactorial analysis)*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Classes I &amp; II</th>
<th>Classes III &amp; IV</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>all patients</td>
<td>263 (81.9)</td>
<td>58 (18.1)</td>
<td></td>
</tr>
<tr>
<td>clin, EEG, &amp; npsych findings</td>
<td>105 (85.4)</td>
<td>18 (14.6)</td>
<td>0.001 (+)</td>
</tr>
<tr>
<td>history of status epilepticus</td>
<td>4 (33.3)</td>
<td>8 (66.7)</td>
<td>0.001 (+)</td>
</tr>
<tr>
<td>discordant ictal EEG focus</td>
<td>19 (63.3)</td>
<td>11 (36.7)</td>
<td>0.011 (−)</td>
</tr>
<tr>
<td>discordant interictal EEG finding</td>
<td>52 (76.5)</td>
<td>16 (23.5)</td>
<td>0.187 NS</td>
</tr>
<tr>
<td>preop neurological deficit</td>
<td>21 (70.0)</td>
<td>9 (30.0)</td>
<td>0.068 NS</td>
</tr>
<tr>
<td>MR findings†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>low-quality image</td>
<td>16 (66.7)</td>
<td>8 (33.3)</td>
<td>0.043 (−)</td>
</tr>
<tr>
<td>no structural abnormality</td>
<td>6 (46.2)</td>
<td>7 (53.8)</td>
<td>0.001 (−)</td>
</tr>
<tr>
<td>neoplasia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>100 (89.3)</td>
<td>12 (10.7)</td>
<td>0.014 (+)</td>
</tr>
<tr>
<td>ganglioglioma or DNT</td>
<td>85 (92.4)</td>
<td>7 (7.6)</td>
<td>0.002 (+)</td>
</tr>
<tr>
<td>MTS‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total</td>
<td>116 (80.0)</td>
<td>29 (20.0)</td>
<td>0.414 NS</td>
</tr>
<tr>
<td>unilat</td>
<td>105 (80.2)</td>
<td>26 (19.8)</td>
<td>0.688 NS</td>
</tr>
<tr>
<td>bilat</td>
<td>11 (78.6)</td>
<td>3 (21.4)</td>
<td>0.478 NS</td>
</tr>
<tr>
<td>dual lesions</td>
<td>28 (70.0)</td>
<td>12 (30.0)</td>
<td>0.036 (−)</td>
</tr>
<tr>
<td>dysplasia</td>
<td>46 (71.9)</td>
<td>18 (28.1)</td>
<td>0.19 (−)</td>
</tr>
</tbody>
</table>

* See Outcome Data for explanation of Engel categories. Classes I and II combined represent satisfactory outcomes, whereas Classes III and IV together represent unsatisfactory outcomes. Comparison of p values; factor present compared with factor not present, with direction of effect indicated; (+) denotes better seizure outcome and (−) means worse seizure outcome. Abbreviations: clin = clinical; npsych = neuropsychological; NS = not significant.

† Frequencies of MR findings and histological diagnoses cannot be directly compared, because MR data contain a fraction of missed and wrong diagnoses.

‡ As diagnosed on MR imaging.

Class III, and no worthwhile improvement was reached in 34 (10.6%, Class IV); these classes were grouped together as unsatisfactory seizure control (58 patients, 18.1%).

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ictal EEG activity was available. Thirty patients (9.3%) had additional ictal EEG foci, mostly in the contralateral temporal lobe.

Factors relevant to outcome are shown in Table 2. As shown in Fig. 1, of the clinical and electrophysiological factors, some were significantly associated with worse outcomes, for example: a secondary ictal EEG focus (p = 0.011), history of status epilepticus (p = 0.001), and higher seizure frequencies (p = 0.031). Two other factors were relevant, but not significant: contralateral interictal EEG activity (p = 0.187) and a preoperative neurological deficit (p = 0.068). Other factors did not correlate with outcome.

Neuroimaging Findings

On review, the quality of the brain MR images was found to be good in 179 patients, sufficient in 118, and of low quality in 24. In 308 patients (96%), structural abnormalities were demonstrated, whereas in the remaining 13 no abnormalities were detected. The most common finding was unilateral MTS (131 patients); MTS was found to be bilateral in 14 patients, and in 10 additional individuals the existence of MTS remained uncertain. In 40 patients with suspected MTS, an accompanying neocortical temporal lesion was demonstrated (MR imaging–confirmed dual lesion rate, 25.6%). Of 112 MR images on which neoplastic lesions were diagnosed, 92 were thought to be gangliogliomas or DNTs, 20 were other gliomas, and the diagnosis for 25 additional lesions remained uncertain. Sixty-four cortical dysplasias were suspected from MR findings, but in 42 of these cases the diagnosis was thought to be uncertain.

Comparing all the diagnoses of suspected lesions on MR imaging, including the uncertain cases and the histologically confirmed diagnoses in these patients, MR sensitivity was 96% for gangliogliomas or DNTs, and specificity was 68% for these lesions. The MR sensitivity was 95% for AHS, and specificity was 88% for this entity. The MR sensitivity was 78% for the group with cortical dysplasias, and specificity was 36%.

Relevant factors for outcome are shown in Table 2. Of the neuroimaging factors, low-quality MR images and lack of structural abnormality were significantly associated with worse outcome, as well as diagnosis or suspicion of any dysplasia or dual disease entities. The patients with neoplasias on MR imaging, and especially the subgroup with ganglioglioma or DNT, experienced extraordinarily good seizure relief rates. In patients with unilateral MTS we attained average results. The outcome was only insignificantly worse in 14 patients with bilateral MTS, but in the 40 patients in whom dual lesions were demonstrated on MR images, the success rate was significantly lower (70% good seizure control).

Histopathological Findings

A clear histopathological diagnosis was obtained in 312 (97.2%) of 321 patients; in four additional patients some unspecific cell loss and gliosis was described, and five were classified as unclear. There were 116 neoplastic findings (36.1%), 193 specimens with nonneoplastic lesions or AHS (60.1%), and three specimens were classified as normal (0.9%).

The most frequent diagnosis was AHS; it was the leading pathological finding (126 patients). In 19 of these patients with AHS additional pathological findings were described, as follows: seven cortical dysplasias, two DNTs, and 10 nonspecific gliosis, scars, cysts, or dysplastic neurons. In addition, AHS was judged to be a secondary finding in nine patients with lesions, resulting in a total of 135 cases with AHS. Thus, histologically proven dual lesions were found in 28 cases, accounting for 20.7% of patients with AHS. Fifty other nonneoplastic histopathological findings were obtained: 41 were cortical dysplasias and nine were cavernous hemangiomas.

All neoplasias except three were low-grade tumors: gangliogliomas (56 tumors: 52 WHO Grade I, three WHO Grade II, and one WHO Grade III); DNT (16 tumors: all WHO Grade I); and 44 other gliomas (19 astrocytomas in WHO Grade I, eight astrocytomas in WHO Grade II, one astrocytoma in WHO Grade III, one glioblastoma in WHO Grade IV, nine oligoastrocytomas in WHO Grade II, two oligodendrogliomas in WHO Grade II, and four pleomorphic xanthoastrocytomas in WHO Grade II).

Analyzing the presence or absence of histological factors, seizure outcome was better if gangliogliomas or DNTs were present (94.4% good seizure control; p = 0.044), and worse with cortical dysplasias present (68.3% good seizure control; p = 0.038), compared with all other diagnoses. Seizure outcome was similar with AHS (84.9% good seizure control; p = 0.263) and other neoplasias present (79.6% good seizure control; p = 0.408).

Neuropsychological Findings

In 285 of 321 patients, neuropsychological data from preoperative and 1 year postoperative testing were available. Unifactorial analysis with respect to seizure outcome revealed that a concordant lateralization of impaired function (123 patients) was associated with better outcome results (85.4% in Classes I and II), compared with 51 patients who had discordant lateralization (76.5% in Classes I and II; chi-square test, p = 0.001). Patients with no lateralizing neuropsychological features (111 individuals) attained intermediate results (82.9% in Classes I and II).
Postoperative attentional performance was improved in 41.4% of patients, unchanged in 49.8%, and deteriorated in 8.8% (Table 3). Multifactorial logistic regression analysis revealed that postoperative attentional performance was dependent on the patient’s preoperative performance on the same test (p = 0.001), seizure control (p = 0.001), and surgical procedure (p = 0.011): the rate of improvement was higher in patients with preoperatively weaker performance, good seizure control was associated with gains in attentional performance, and after ATL patients showed less gain and more loss compared with AH and lateral lesionectomy or corticectomy, with or without additional hippocampal removal.

Postoperative testing of visual memory revealed similar rates of improvement and deterioration for each of the surgical approaches (Table 3). Logistic regression analysis showed a dependency on the preoperative performance (p = 0.001) and age at surgery (p = 0.018): a better performance preoperatively and older age were associated with worse postoperative results. Subgroup analysis revealed that patients with poor visual memory performance preoperatively and operations on the left side (81 individuals) had a higher rate of postoperative improvement when undergoing limited resections (60.4%) compared with standard ATL (28.6%, p = 0.002), whereas the improvement rate was 38% for either approach with surgery on the right side.

Verbal memory function improved in 19.3% of patients, was stable in 46.3%, and deteriorated in 34.4%, documenting that verbal memory was the most critical item, with the lowest rate of improved and the highest rate of deteriorated results (Table 3). There were considerable differences in verbal memory outcome, depending on preoperative performance, age at surgery, side of operation (p = 0.001 for all three), and surgical approach (p = 0.094), as revealed by logistic regression analysis: preoperatively weakly performing patients and younger patients tended to improve, operations on the right side and approaches other than ATL were associated with lower deterioration rates. The higher rates of deterioration after ATL (43.4%) compared with AH (30.9%) and lesionectomy/corticectomy (29.2% with AH and 30.8% without AH) is significant (p = 0.044).

The total performance score showed an improvement in 43.9% of patients, stable results in 21.4%, and a deterioration in 34.7% (Table 3). The lowest rate of improvement (33.7%) and the highest rate of deterioration (44.6%) were found after ATL, whereas AH and lesionectomies or corticectomies with or without hippocampectomy showed significantly better results (improved 42.3–58.3%, deteriorated 25–36.5%; p = 0.05). Generally, the rate of gains increased from 35.7% in the first (1989–1992) to 43.4% in the third patient cohort (1995–1997), whereas the deterioration rate dropped from 35.7 to 27.9%.

Procedures, Experience, and Complications

There were no significant differences in outcomes between types of surgery for the whole time period (Table 4): a satisfactory seizure outcome was obtained in 79.6% of patients who underwent ATL, in 83.4% of those treated with AH, in 74.1% of those who underwent lateral lesionectomy and hippocampectomy (only 27 of 321 patients), and in 86.2% of those with purely lateral neocortical resections. Subclassification of the surgical approaches according to histopathological findings reveals striking differences: surgery for dysplastic lesions always results in lower success rates, whereas resections for tumors lead to extraordinarily good results. This tendency cannot be found in the smallest patient group (lesionectomies with hippocampectomy), probably because of the small group size and a heterogeneous patient population. When comparing the two different resection types used for treatment of mesial TLE with AHs, no significant difference in seizure outcome was found between ATL and AH.

As shown in Table 5, outcome with respect to seizure
control did not differ when we compared the patient cohorts from the three time periods (1989–1992, 96 patients; 1993–1994, 84 patients; and 1995–1997, 141 patients); Table 5 also demonstrates increasing application of AH instead of ATL for the treatment of mesial TLE. Moreover, the number of purely lateral resections for neocortical TLE increased meanwhile from 12.5 to 23.4%. The outcome data in the respective periods show some variations, especially in the smaller samples, but in general the outcome results were stable during the study period.

There were no intraoperative deaths in this series. Among the 329 neurosurgical interventions, 28 surgical complications occurred (8.5%), all without permanent sequelae (for example, meningitis [1.5%], subdural hematoma [0.6%], and thrombosis [1.2%]). Neurological complications occurred in 17 (5.2%) of 329 interventions; eight of these complications resulted in transient morbidity (2.4%), and nine in permanent morbidity (2.7%).

Predictors of Seizure Relief: Multifactorial Logistic Regression Analysis

For multifactorial testing 36 patients in whom neuropsychological data were not available were omitted. The following five factors were found to be independently correlated with satisfactory seizure control in the remaining 285 patients: 1) no history of status epilepticus; 2) a concordant lateralization of memory impairment; 3) a clearly pathologic MR image finding; 4) ganglioglioma or DNT on MR imaging; and 5) no dysplasia—for detailed information see Table 6. Exclusion of neuropsychological data and thus inclusion of 321 patients for analysis revealed an additional contribution of the factor “no secondary seizure focus” to the prediction of seizure relief (p = 0.041; odds ratio 0.372; 95% confidence interval 0.151–0.914). There were no relevant changes concerning the other factors.

The multifactorial analysis revealed no additional factors for the three patient cohorts, nor for the subgroups treated with ATL, AH, and lesionectomy or corticectomy with or without hippocampectomy. Nevertheless, because of the smaller numbers of patients, not all parameters derived from 321 total patients reached significant levels within the subgroups.

Discussion

Study Group and Demographics

We included in this study 321 of 456 patients who underwent surgery for TLE. Patient exclusion was mostly on account of missing MR images for review, but in many of these cases there were other data missing as well. We do not think that a study bias resulted from this, because the seizure outcome in 450 patients with a mean follow-up duration of 41 months (range 3–118 months) was virtually identical to that reported here. The lower limit for follow up was set at 12 months postsurgery, but in 279 patients (87%) the follow-up duration was 24 months or more. Seizure outcome is believed to be stable after 12 months.57

Seizure Outcome

After the introduction of surgical treatment for drug-resistant TLE, Bengzon, et al.,4 were the first to define prognostic criteria for surgical success. With the introduction of new diagnostic tools, especially video EEG monitoring and MR imaging, success rates increased from less than 50%.6,15 In this study, which is the largest single-center surgical TLE series in the era of MR imaging, a seizure-free outcome was found in 71% of patients and 11% had only rare and nondisabling seizures, resulting in good seizure control in 82% of patients. Eighteen percent of patients had unsatisfactory seizure control; 7.5% of them had a reduction of seizure frequency of more than 75%, and 10.5% had a frequency reduction of less than 75%. This is well in line with other studies with TLE.6,15,36,40 Similar or slightly better success rates were recently described for pure mesial TLE37,28,46 and for purely neocortical TLE.15 Outcome is comparable to the multicenter results reported at the 1992 Palm Desert Conference, where seizure-free outcome was reported in 68% of nearly 4000 patients with TLE, whereas the success rate was reported to be approximately 55% before 1985.15

Clinical and EEG Factors

Febrile convulsions, seizure types, patient’s age at surgery, age at onset, and duration of epileptic disorder were not associated with seizure outcome, and thus did not contribute to the multifactorial procedure. Several authors have

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described a history of febrile convulsions as positively correlated with outcome.27 Prolonged childhood febrile convulsions are thought to be associated with the occurrence of AHS.10 In our study, febrile convulsions occurred in 28% of patients with AHS, but in only 4% with other histological findings. In more than 80% of the patients in this sample who had febrile convulsions, AHS was found in the hippocampal specimens. Therefore, a history of febrile convulsions seems to be mainly a surrogate for the existence of hippocampal sclerosis.

In this study, a history of status epilepticus correlated strongly with poor surgical results and thus contributed to the multifactorial model. This correlation has not been reported before, probably because the rate for a history of status epilepticus is relatively low (3.7% in our study) and thus large study populations are necessary to discriminate a correlation with outcome data. A tendency toward prolonged seizure activity may be a hint about general proconvulsive properties of the brain. Seizure frequency depends on the rate of “successful” propagation of epileptiform activity from the focus to surrounding structures.

Foldvary, et al.,16 found a cutoff line at 20 seizures per month for good outcome, whereas in our study we documented a steadier relationship between increasing seizure frequency and poor outcome. Preexisting neurological deficits were found in less than 10% of cases, and the difference in good outcome rates was not impressive (70% compared with 83%), with a borderline significance, but this feature revealed an unexpectedly independent contribution in the multifactorial procedure. We suppose that a neurological deficit not only serves as an indicator for a circumscribed cerebral lesion, but possibly also for more global or more severe malfunction.

A secondary ictal EEG focus, mostly in the contralateral temporal lobe, was associated with a worse outcome; this confirms previous findings.27,46 On the other hand, in our study we were unable to reproduce the negative implications of contralateral interictal EEG activity, which has been described as a major factor associated with recurrence of seizures after surgery, even in a smaller sample of our own patients.2,27,40,46 An explanation may be the necessary categorization and the presumed consecutive loss of subtle differences in EEG data for the purpose of this study. Nevertheless, in our findings contralateral interictal EEG activity occurred 1.5 times more frequently with recurrent seizures, but this difference was not significant.

**Neuroimaging Advances**

Developments in neuroimaging have contributed impressively to improved success rates in epilepsy surgery since the 1980s. In our data MR sensitivity was no different for ganglioglioma or DNT (96%), or for hippocampal sclerosis (95%), whereas specificity was better for hippocampal sclerosis (88%) than for ganglioglioma or DNT (68%). Sensitivity (78%) and specificity (36%) were lower for dysplasias. These findings are comparable with those published in the literature.27,35,45

The importance of high-quality MR images was documented in our analysis of seizure outcome and MR image quality: patients with good or sufficient MR image quality had an 83% chance of good outcome, compared with only 67% in whom the MR image quality was retrospectively thought to be insufficient. We confirmed that structural abnormalities detected on MR imaging are significantly correlated with good seizure outcome (84% compared with 53% without abnormality).27,47 The finding of any tumor resulted in good seizure control in 89%; with MR imaging—confirmed diagnosis of a ganglioglioma or DNT a rate of more than 92%, good seizure control was reached. An extraordinarily good prognosis in patients with suspected gangliogliomas or DNTs has not been explicitly described before, presumably because knowledge about these rare lesions is still limited. Raymond, et al.43 reported good surgical success in 75% of 16 patients with DNT. Few series have been published on the surgical treatment of temporal and extratemporal gangliogliomas and epilepsy.35,58 The success rate with unilateral hippocampal sclerosis was 80% in our patients, which corresponds well to published data.2,3,7,27,29,40,46 whereas bilateral atrophy, bilateral normal findings, and dual lesions in our data and in the published literature resulted in less beneficial seizure outcomes.3,7,42 We found the success rates to be lower with suspected dysplasias (72%) compared with the other MR imaging–based diagnoses. This is not surprising, because cortical dysplasias are known to be accompanied by widespread changes in neuronal structure, connectivity, and function.41,42 Nevertheless, outcome was somewhat better compared with the data published on surgical treatment of epilepsy and dysplasia, which was reported to be approximately 60%.41 Data are generally difficult to compare in this respect, because the definition of dysplasia is still a matter of discussion, and even elaborate MR imaging techniques are not capable of detecting all regions of dysplastic structural abnormalities.

**Histopathological Findings**

In approximately one third of specimens different kinds of neoplasias were seen, and two thirds showed nonneoplastic lesions, of which AHS accounted for the majority (65%) of cases. The tumor incidence was 36% in our study, which is comparable with an earlier TLE series from our institution and with the rate found in other series.39,54 Dual lesions were histopathologically proven in approximately 21% of patients with AHS, which is lower compared with 25 to 30% in some previously published work.25,57 and somewhat higher compared with the rate of Cendes, et al.11 Regarding MR imaging data, dual lesions were assumed in 25.8% of patients with suspected MTS. These differences are due to the selection of study patients and the large number of purely mesial resections in our study: even if some dysplastic temporal neocortex was presumed from MR images, resections were limited to mesiotemporal structures in cases of clinically and electrophysiologically identified mesial TLE, whereas lesions suspected of being tumors were always removed. We may therefore have missed a number of dual lesions in our series, which might explain the different rates of MR imaging–suspected and histopathologically proven cases of dual lesions. Thus, our surgical approach is not suitable for a detailed analysis of the incidence, clinical relevance, and outcome in patients with documented dual lesions.

The majority of neoplasias were gangliogliomas and DNTs, which are known for their extraordinarily benign behavior and occurrence in young hosts.12,35,45,56 Patients with these diagnoses had better results (94% in Classes I and II) compared with all other histopathological subgroups, which is in line with published findings.38 The second-best out-
Prognostic factors and outcome for temporal lobe epilepsy surgery

come was found with AHS (85% in Classes I and II) and other “ordinary” gliomas (80% in Classes I and II), with no statistical difference between the two groups. The least good outcome was found with the diagnosis of cortical dysplasia (68% in Classes I and II), which corresponds to published data.41,45

Resection Strategies

We found no significant differences in seizure outcome for the three patient cohorts over time. These cohorts were chosen for size and to represent the changing policy in resection strategies. During the first period (first cohort), the majority of procedures were ATL and the rest were lateral resections, in some cases plus hippocampectomy. During the course of the second period (second cohort), ATL was progressively replaced by either AH for cases of mesial TLE, or by an increasing number of lesionectomies and corticectomies. In the third period (third cohort), whenever suitable, resections limited to the lesion and the presumed epileptic focus were performed. The limits of resection were defined by MR imaging as well as by noninvasive and invasive preoperative EEG evaluations. The relatively high rate of invasive diagnostic procedures is due to this strategy of preoperative “tailoring.” The main finding regarding these three cohorts is that, despite the reduction in the amount of resected tissue, success rates remained stable, even without intraoperative electrocorticography. This has not been shown before in a comparably large patient series from one epilepsy treatment center.

A comparison of AH and ATL performed in this series revealed a similar rate of seizure control (Table 4): approximately 70% of patients treated with AH or ATL became seizure free (Class I); and 10% (with ATL) or 14% (with AH) reached Class II, resulting in 80 and 84% rates of satisfactory seizure control. When breaking this down into procedures performed for specific lesions, the results are similar: with ATL for AHS, 90% satisfactory outcome was achieved, and the success rate for this type of lesion was 84% with AH. This difference is not significant, and might primarily result from different group sizes: 20 ATLs compared with 105 AHs were performed for AHS. The outcome was generally more dependent on the histological diagnosis; results of ATL and AH were quite comparable for tumors (92% compared with 91% satisfactory seizure control) and for dysplasia (64% satisfactory seizure control). Arruda, et al.,3 reported on a series of 74 patients with mesial TLE, in which the authors found equally good results with ATL and AH. It has been reported that the amount of tissue resected in mesiotemporal operations is crucial for surgical success in mesial TLE.36 Residual tissue is a well-known factor for seizure recurrence and is thought to be somewhat more frequent after AH compared with ATL, because of the limited view offered by AH. Reoperation for removal of residual tissue resulted in complete seizure control in four of eight patients in our study, which corresponds to published data.55 Although the findings are not significant, combined limited neocortical resections plus hippocampectomy seem to have the lowest success rates (74% satisfactory seizure control), which is reasonable, because the choice of this approach implies a combination of mesial and lateral lesions and suspected epileptogenicity. Nevertheless, with only 27 patients the sample size is too small for us to draw a conclusion, but it may be debated whether some of these patients might have profited from ATL. As expected, the outcome with lesionectomy and corticectomy for purely neocortical TLE was excellent, especially when a tumor was present (95% satisfactory seizure control).45

Complications seen in this study were as described earlier and are not different from those reported in other series.4

Neuropsychological Findings

Preoperative neuropsychological examinations revealed concordant lateralizing information in 123 of 285 patients. This was associated with significantly better outcome compared with the 51 patients who had discordant lateralization. These findings are in accordance with published data derived from intracarotid amobarbital testing for lateralization of memory deficits and its impact on seizure control.51 Other presurgically evaluated neuropsychological findings did not correlate with outcome.

Whether limited resections for mesial TLE (for example, AH) are at all beneficial compared with standard ATL is a matter of discussion. Cognitive function is known to deteriorate in many patients after temporal lobe resections for epilepsy, especially when operations are performed on the left side.28 In some studies better neuropsychological outcomes were reported after limited resections,21–23,30 and in others they were not.18 From a theoretical point of view it should be advantageous to preserve as much healthy brain tissue as possible, especially when equal seizure control can be achieved, as was shown with the present study. Katz, et al.,30 correlated the extent of resection on the left with verbal deficits, and on the right with visual deficits. Identical neuropsychological findings were described for AH and ATL.18

In contrast with these findings, differences were found with ATL, AH, and lesionectomies in an earlier study conducted at our institution: patients with ATL on the left side had a higher rate of deterioration in immediate and delayed recall, whereas after AH the deterioration rate in immediate recall was lower. Patients with left lesionectomies demonstrated better performance in all parameters.21 We were able to document the beneficial effects of limited resections, even using exclusively categorical neuropsychological data. Our results show that postoperative neuropsychological performance is highly dependent on the presurgical findings. Patients with good verbal performance and a left-sided seizure focus preoperatively tended to exhibit deterioration after surgery; the rate of deterioration was significantly dependent on the resection type (Table 3). The 43% deterioration rate in verbal memory after ATL was significantly worse, compared with only 31% after AH and 30% after lesionectomy and corticectomy with or without hippocampectomy. Compared with other surgical approaches, after ATL patients deteriorated nearly twice as often in regard to attentional performance. These data are well in line with previously published findings and argue in favor of limited resections in TLE surgery.21,22 The same conclusion can be drawn by considering the total neuropsychological performance score in the consecutive patient cohorts: with increasing use of tailored resections, the rate of improvements increased from 35.7 to 43.4%, whereas losses declined from 35.7 to 27.9%, suggesting an overall neuropsychological benefit that parallels our policy of limiting resections to the amount of tissue thought to be necessary to achieve seizure control.
Multifactorial Analysis

Of the five identified factors contributing to prediction of seizure relief, three were derived from MR images, as follows: 1) a clear pathological finding on MR images; 2) diagnosis of a ganglioglioma or DNT; and 3) absence of dysplasia. The important role of MR imaging findings is in accordance with published data, but mostly unilateral hippocampal sclerosis was found to be correlated with good outcome in multifactorial procedures.29,40 In other studies any positive MR findings were found to be relevant.2,20 Because our study involved larger numbers of patients with tumors, dysplasias, and other lesions, we were able to identify more predictive factors than have been previously described in one study. As seen in the unifactorial analysis, unilateral hippocampal sclerosis was associated with fairly good outcome results, but its significance was diminished by the presence of numerous low-grade tumors with even better prognoses.

In our study EEG findings were not entered into the multifactorial model on the first line, which might mean that their importance was lower compared with neuroimaging data. Nevertheless, an additional electroencephalographically confirmed seizure focus was associated with unsatisfactory outcome, especially when neuropsychological data were omitted. The correlation between unsatisfactory outcome and discordant EEG findings is well established,2,20 and EEG studies still play an important role in presurgical evaluation; for example, most patients with documented bilateral ictal onset are not considered to be surgical candidates. Nevertheless, it is not promising to perform resections in patients in whom no MR imaging–confirmed abnormalities are found, regardless of EEG findings.

A history of status epilepticus was predictive of unsatisfactory outcome in our study. This is not surprising, but generally the percentage of patients with TLE who experience status epilepticus is relatively small and thus did not play a major role in earlier studies. We were able to incorporate neuropsychological findings obtained with noninvasive methods into a multifactorial model of outcome prediction, and we found that concordant lateralization of memory impairment was predictive of better outcome. Memory deficits are known to provide lateralizing information, but significant findings were mostly obtained using intracarotid amobarbital testing, and so far these data have not been entered in multifactorial models.51 Multifactorial testing revealed no additional preoperative factors for the three cohorts or specific surgical approaches. As expected, not all factors reached the level of significance in all subgroups, but MR imaging parameters especially contributed significantly to all calculated models.

Conclusions

In this study we document the change in resection strategy for TLE at one institution: standard approaches were used until 1993, and after 1994 limited resections were mainly applied, especially AH for mesial TLE. Seizure outcome was no different after ATL, AH, or lesionectomy, but it was significantly dependent on the patient’s diagnosis. Good seizure control was achieved in 81.9% of patients. Logistic regression analysis revealed the following factors to be predictive for good seizure control: 1) clear abnormality on MR imaging; 2) absence of status epilepticus; 3) MR imaging–confirmed ganglioglioma or DNT; 4) concordant lateralizing memory deficit; and 5) absence of dysplasia on MR imaging. Postoperative neuropsychological testing revealed more beneficial memory results after AH and lesionectomy compared with standard ATL.

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