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Long-term outcome and predictors of resective surgery prognosis in patients with refractory extratemporal epilepsy

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ABSTRACT

Purpose: We analyzed the long-term postoperative outcome and possible predictive factors of the outcome in surgically treated patients with refractory extratemporal epilepsy.
Methods: We retrospectively analyzed 73 patients who had undergone resective surgery at the Epilepsy Center Brno between 1995 and 2010 and who had reached at least 1 year outcome after the surgery. The average age at surgery was 28.3 ± 11.4 years. Magnetic resonance imaging (MRI) did not reveal any lesion in 24 patients (32.9%). Surgical outcome was assessed annually using Engel's modified classification until 5 years after surgery and at the latest follow-up visit.
Results: Following the surgery, Engel Class I outcome was found in 52.1% of patients after 1 year, in 55.0% after 5 years, and in 50.7% at the last follow-up visit (average 6.15 ± 3.84 years). Of the patients who reached the 5-year follow-up visit (average of the last follow-up 9.23 years), 37.5% were classified as Engel IA at each follow-up visit. Tumorous etiology and lesions seen in preoperative MRI were associated with significantly better outcome ($p = 0.035$; $p < 0.01$). Postoperatively, 9.6% patients had permanent neurological deficits.
Conclusion: Surgical treatment of refractory extratemporal epilepsy is an effective procedure. The presence of a visible MRI-detected lesion and tumorous etiology is associated with significantly better outcome than the absence of MRI-detected lesion or other etiology.

1. Introduction

More than 30 percent of patients with epilepsy are refractory to antiepileptic drug treatment.[1] Partly because of this relatively high number, epilepsy surgery is an intrinsic part of the algorithm of epilepsy treatment.

The short- or long-term efficacy of various types of resections for epilepsy in different anatomical locations has been widely studied.[2–5] However, there have been only two "Class I" studies evaluating the effect of surgical treatment of epilepsy. Both of them were conducted in patients with refractory temporal lobe epilepsy (TLE). Wiebe et al.[6] published a randomized controlled study of surgery in TLE and endorsed surgery as a superior to prolonged treatment with antiepileptic drugs (AED). At one year after surgery, a statistically significant difference was confirmed between patients who underwent surgery and medically treated patients. Engel et al.[7] recently published the results of an Early Randomized Surgical Epilepsy Trial (ERSET) study of TLE patients after two failed AED treatments. Among patients with newly intractable disabling mesial TLE, resective surgery plus AED treatment resulted in a lower probability of seizures at the 2-year follow-up visit than continued AED treatment alone.

There has not been a similar controlled study focused on extratemporal epilepsy (exTLE).

Literature data report a wide range of seizure freedom in exTLE patients, varying from 25% to 80%,[2,3,8–16] Some predictive factors are believed to play roles in postsurgical outcome.

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A significantly better outcome is achieved if a lesion is identified on MRI or confirmed histologically. Several studies reported worse postoperative seizure reduction if a lesion was not found preoperatively on MRI.[2,9,16,17]

We evaluated 77 patients with refractory exTLE who underwent surgery in Epilepsy Center Brno. Our purpose was to evaluate seizure outcome following epilepsy surgery and to assess the impact of preoperative MRI, histopathological findings, number of preoperatively used antiepileptic drugs (AEDs), and other predictive factors.

2. Methods

We retrospectively analyzed all of the patients with refractory extratemporal epilepsy (exTLE) who had undergone resective surgery in St. Anne's University Hospital in Brno (Czech Republic) between August 1995 and January 2010 and who had reached at least 1 year outcome after the surgery. We identified 77 patients. Of those 77, 4 were excluded from the analysis because of lost outcome due to the death of the patients. The causes of death were: sudden unexplained death in epilepsy (SUDEP), drowning, heart attack, and traffic accident (each in one patient). We thus studied 73 patients with exTLE who achieved outcome longer than 1 year. We analyzed 40 patients who reached at least the 5-year follow-up visit in more detail. The patients' demographic data were obtained from medical charts. All patients underwent a complete preoperative evaluation to assess the extent of resection.

2.1. Video-EEG evaluation

Scalp video-EEG was recorded with the international 10–20 system with additional electrodes (anterotemporal T1, T2 and supraorbital SO1, SO2). The scalp recording was performed on the 64-channel Brain Quick system (Micromed) or the 64-channel Alien Deymed system.

Of the 73 patients, 38 (52.1%) underwent invasive EEG. Intracranial recordings with inserted depth electrodes alone were performed in 25 patients; depth electrodes in combination with subdural electrodes (strip or grid) were used in 6 patients; 4 patients were examined with subdural electrodes only. The invasive EEG had to be repeated in 3 cases. Intracerebral 5-, 10-, and 15-contact platinum semiflexible Microdeep electrodes DIXI or ALCIS (with an electrode diameter of 0.8 mm, a contact length of 2 mm, and a 1.5 mm distance between contacts) and 6- or 8-contact platinum subdural strips electrodes (Radionics) or 32-contact platinum subdural grids (Radionics) were used. The invasive video-EEG recording was performed with the 64-channel Brain Quick system (Micromed), and the 128-channel Alien Deymed system was used for intracranial video-EEG recording. Monopolar recordings (a reference electrode on the processus mastoideus) and special bipolar montages were used to evaluate the EEG activity. EEG was amplified with a bandwidth of 0.4–100 Hz at a sampling rate of 128 Hz.

2.2. Other preoperative evaluation

MRI scans were obtained using the Siemens 1.5 Tesla MRI scanner. We performed the following sequences in all patients: T1-weighted axial and coronal sections with and without contrast, T2-weighted, FLAIR-weighted, and TIR axial and coronal sections of the whole brain. MRI did not reveal a lesion in 24 (32.9%) of patients. Fluorodeoxyglucose positron emission tomography (FDG-PET) was performed in the interictal state on a Siemens tomography scanner. A complete neuropsychological evaluation was conducted on all patients. As needed, 24 of the 73 patients (32.9%) underwent interictal and ictal single-photon emission computed tomography (SPECT) to obtain the subtraction of ictal SPECT coregistred on MRI (SISCOM).

2.3. Histopathological evaluation

Evaluable formalin-fixed paraffin-embedded tissues of extra-temporal lobe resection specimens were available from all patients. All the paraffin-embedded tissue specimens, slides, and histopathology reports were retrieved from the files of the First Department of Pathological Anatomy of St. Anne's University Hospital and examined by a histopathologist. All examined resected tissues were identically treated, fixed in a 10% neutral buffered formalin, grossly inspected, measured, and cut so as to obtain representative tissue slices perpendicular to the cortical surface. Representative tissue slices were routinely processed and paraffin embedded. 5 μm thick tissue sections were stained by hematoxylin and eosin, evaluated under light microscope, and reported.

2.4. Surgery procedure

All procedures were performed in the Epilepsy Center Brno. The type and extent of the surgery was chosen individually on the basis of the preoperative evaluation. The surgical procedures included lesionectomy with resection of adjacent epileptogenic cortex, isolated lesionectomy, and corticectomy on the basis of invasive EEG, which was also performed with neocortical stimulation when the epileptogenic zone was located near the eloquent cortex. One patient underwent lobectomy and one had an extended extratemporal lesionectomy with amygdalohippocampectomy. Three patients underwent re-operation. The outcome after the re-operation was included in the study in these patients.

Preoperative electrocorticography was performed in 59 patients; 29 patients underwent fMRI; 2 patients had awake craniotomy when the lesion was located close to or involving the eloquent cortex.

2.5. Evaluation of surgical outcome

Surgical outcome was annually assessed using Engel's modified classification for 5 years after surgery and at the latest follow-up visit.[18] All patients were seen regularly (at least once per year) in the outpatient clinic and had results from at least 2 medical follow-up visits (after 1 year and at the last follow-up visit). The seizure outcome was evaluated at a given point in time (at the follow-up visit) and the time-point actually reflects the situation of the preceding entire year as well.

2.6. Statistical analysis

Statistical analysis was performed using SPSS Statistics 18. Continuous variables were summarized using standard descriptive statistics (mean and standard deviation). The statistically significant difference between epilepsy duration, the age at epilepsy onset, the age at the time of epilepsy surgery, and surgical efficacy was determined using the analysis of variance (ANOVA). A chi-square test was used to evaluate the association between histological etiology and outcomes. The chi-square test was also used to evaluate the association between preoperative MRI-detected lesions and postsurgical outcome. A p value was considered as statistically significant if $p < 0.05$.

We present the seizure outcomes of the 40 patients who reached the 5-year follow-up visit using Kaplan–Meier survival analysis.