Epilepsy Research 126 (2016) 147–156

Contents lists available at www.sciencedirect.com

Epilepsy Research

journal homepage: www.elsevier.com/locate/epilepsyres

Long-term outcome characteristics in mesial temporal lobe epilepsy with and without associated cortical dysplasia

B. Schmeiser[a,*], T. Hammen[b], B.J. Steinhoff[c], J. Zentner[a], A. Schulze-Bonhage[b]

[a] Department of Neurosurgery, University Hospital Freiburg, Breisacherstr. 64, 79110 Freiburg, Germany
[b] Department of Epileptology, University Hospital Freiburg, Breisacherstr. 64, 79110 Freiburg, Germany
[c] Epilepsy Center Kork, Landstraße 1, 77694 Kehl-Kork, Germany

ARTICLE INFO

Article history:
Received 22 June 2016
Received in revised form 27 July 2016
Accepted 29 July 2016
Available online 1 August 2016

Keywords:
Temporal lobe epilepsy (TLE)
Surgery
Seizure outcome
Predictive factors
Seizure freedom
Running down phenomenon
Focal cortical dysplasia

ABSTRACT

Object: The intention of our study was to identify predictive characteristics for long-term seizure control and running down phenomenon after surgical treatment of pharmacoresistant mesiotemporal lobe epilepsy (mTLE) with and without associated cortical dysplasia.
Materials and methods: Our study comprises a consecutive series of 458 patients who underwent surgical treatment for intractable mTLE at the Epilepsy Center Freiburg. Data evaluated included semiology, duration and frequency of seizures, results of presurgical diagnostics including video-EEG monitoring, MRI, PET and SPECT as well as postoperative seizure outcome. Results were evaluated forming two groups: Group A consisted of isolated mesiotemporal lesions. Group B comprised patients with mTLE and additional focal cortical dysplasia (FCD). Statistical evaluation was based on the Kaplan Meier survival analysis, using log-rank-tests and a multivariate regression model. Postoperative running down phenomenon was defined as seizure freedom after a period of gradual reduction of postoperative seizure frequency. This was compared to patients with ongoing epilepsy.
Results: Complete seizure freedom was achieved in 65.0% of investigated patients at 1 year and in 56.5% at long-term follow-up of ≥5 years after surgery. Corresponding results were 64.2% and 56.8% at 1 and ≥5 years, respectively in group A and 66.4% and 56.0%, respectively in group B. Predictive for favorable postoperative outcome in the total group were younger age at surgery, shorter duration of epilepsy, absence of secondarily generalized tonic-clonic seizures (SGTCS), presence of strictly ipsilateral temporal interictal epileptiform discharges (IEDs), complete resection of the lesion as well as absence of postoperative epileptiform activity and of early postoperative seizures. In subgroup analyses, patients of group A demonstrated longer postoperative seizure-free intervals with adolescent age at surgery, short duration of epilepsy before surgery and absence of SGTCS, whereas in patients of group B ipsilateral temporal seizure onset and strictly unilateral IEDs in EEG as well as complete resection were predictors for favorable seizure outcome. Furthermore, absence of early postoperative seizures and of spikes in EEG were predictive factors for long-term seizure-freedom in both subgroups.

The running down phenomenon was found in 33 (7.2%) patients. None of the parameters evaluated demonstrated significant predictive power. Only late seizure onset and neoplastic lesions showed a trend for postoperative gradual seizure reduction in multivariate analyses.
Conclusion: Depending on the presence or absence of focal cortical dysplasia in addition to mesiotemporal structural alterations, predictors of long-term seizure control differed regarding the relevant clinical and electrophysiological features. This is important for specific patient counseling in respective groups.

1. Introduction

Temporal lobe epilepsy (TLE) is the most common focal epilepsy, constituting up to 30–40% pharmacoresistant patients (Spencer and Huh, 2008). There are interesting studies dealing with the development of underlying etiologies such as focal cortical dysplasia (FCD), hippocampal sclerosis (HS) or dual pathology and corresponding clinical features. Latter include i.e. age at seizure

* Corresponding author at: Department of Neurosurgery, University Hospital, Albert-Ludwigs-University, Breisacherstr. 64, 79106 Freiburg, Germany.
E-mail addresses: barbara.schmeiser@uniklinik-freiburg.de (B. Schmeiser), thilo.hammen@uniklinik-freiburg.de (T. Hammen), BSteinhoff@epilepsiezentrum.de (B.J. Steinhoff), josef.zentner@uniklinik-freiburg.de (J. Zentner), andreas.schulze-bonhage@uniklinik-freiburg.de (A. Schulze-Bonhage).

http://dx.doi.org/10.1016/j.eplepsyres.2016.07.011
0920-1211/

onset, preoperative seizure frequency, intractability of epilepsy and postoperative seizure outcome (Levesque et al., 1991; Fauser and Schulze-Bonhage, 2015; Bocti et al., 2003; Porter et al., 2003; Kuzniecky et al., 1999; Ho et al., 1998; Cendes et al., 1995).

For patients suffering from focal intractable epilepsy, surgery has proven to be an effective option (Wiebe et al., 2001; Radhakrishnan et al., 1998; Engel et al., 1993; Engel et al., 2003) leading to seizure freedom in 60–70% (Stephen and Brodie, 2002) (Tonini et al., 2004). Despite extensive presurgical evaluation, postoperative seizure outcome varies considerably. Various predictive factors, partially controversial, have been reported to influence seizure outcome (Uijl et al., 2008; Janszky et al., 2005b; Zentner et al., 1995; Engel et al., 1993; Clusmann et al., 2002; Clusmann et al., 2004; Grivas et al., 2006; Sindou et al., 2006; Bate et al., 2007; Tanriverdi and Olivier, 2007; Paglioli et al., 2006; Mackenzie et al., 1997; Wieser et al., 2003; Schramm, 2008; Sagher et al., 2012; Armon et al., 1996; Bengzon et al., 1968; Schulz et al., 2000; Radhakrishnan et al., 1998; Hufnagel et al., 1994; Gilliam et al., 1997; McIntosh et al., 2004). To our knowledge there are only few studies which determine postoperative outcome among patients with TLE based on isolated mesiotemporal lesions and dual pathology (Savitr Sastri et al., 2014).

Previous studies showed that favorable short-term seizure outcome does not necessarily indicate long-term seizure control41, yet a subgroup of 45–55% of patients remains seizure-free up to 5 years after surgery (McIntosh et al., 2004). In addition, late seizure freedom due to running down phenomenon, defined as seizure freedom occurring after a period of gradual reduction of postoperative seizure frequency, has been reported in 5–20% of patients after temporal lobe surgery (Salanova et al., 1999; Salanova et al., 1996; Ficker et al., 1999).

The aim of our study was to determine positive predictive factors for long-term seizure free outcome (Engel Ia) including the running down phenomenon in 458 consecutive patients suffering from intractable mTLE, assessing two subgroups of isolated mesiotemporal lesions and mTLE with additional focal cortical dysplasia.

2. Materials and methods

2.1. Presurgical evaluation

This retrospective analysis comprises 458 consecutive patients with intractable mTLE who were operated at the Epilepsy Center Freiburg between 1998 and 2012. Analyzed factors include gender, age at seizure onset and surgery, duration of epilepsy, history of febrile convulsions, family history of epilepsy, seizure semiology including different subtypes of seizures and development of secondarily generalized tonic clonic seizures (SGTCS).

Presurgical evaluation included long-term video-EEG monitoring using 21-256 scalp electrodes (Rosenow and Luders, 2001). Interictal epileptiform discharges (IEDs) and at least three seizures were recorded to determine the seizure onset zone. High resolution magnetic resonance imaging (MRI) was performed using a special epilepsy protocol and included at least coronal 2D T2w and FLAIR (fluid attenuated inversion recovery) weighted images with 2–5 mm of slice thickness. 3D T1 weighted data sets [T1 flash (fast low angle shot) (Frahm et al., 1986) or T1 MPRage (magnetization prepared rapid gradient echo) (Mugler and Brookeman, 1990) sequences] with an isotropic resolution of 1 mm3. If a tumor was suspected, additional T1 weighted images with gadolinium-DTPA were acquired. If results of Video-EEG findings and MRI were inconsistent, Fluorodeoxyglucose (FDG) and Flumazenil positron emission tomography (PET) as well as interictal and ictal SPECT with Tec-99m, and/or Iomazenil were added. Decision on the surgical procedure for each patient was made in the interdisciplinary epilepsy conference regarding selective amygdalohippocampectomy, extended lesionectomy, anterior temporal lobe resection or standard temporal lobectomy.

2.2. Histopathological findings

Histopathological findings were classified in hippocampal sclerosis (HS), neoplastic and non-neoplastic lesions. HS was evaluated on the basis of the Wyler classification (Wyler et al., 1992). Neoplastic lesions were classified according the WHO classification scheme (Kleihues et al., 1993). FCD was classified according to Palmini et al. (2004).

2.3. Seizure outcome

Postoperative seizure outcome was evaluated three months after surgery and thereafter in yearly intervals according to Engel (Engel et al., 1993). Engel I: free of disabling seizures and Engel Ia: completely seizure free, Engel II: >90% seizure reduction or nocturnal seizures only, Engel III: >75% seizure reduction (worthwhile seizure reduction), and Engel IV: <75% seizure reduction (no significant improvement).

2.4. Statistical analysis

Statistical analysis was carried out using SPSS Version 22. The Kaplan–Meier survival analysis was used to estimate percentage of complete seizure control (Engel Ia) depending on the investigated predictive factors. Bivariate variables were calculated using the non-parametric log-rank test to identify prognostic indicators for postoperative seizure outcome. For analyzing the running down phenomenon bivariate analysis was carried out using the Fisher Exact or Chi2 test to compare seizure-free patients at last follow-up to those with seizure recurrence. Cox regression multivariate analyses were then affiliated to detect independent predictors. Results were considered statistically significant in case of $p \leq 0.05$. The same parameters were analyzed in patients with persisting postoperative seizures as possible predictors of the running down phenomenon using bivariate analyses.

For analysis of predictive factors the total group of 458 patients was divided into two subgroups: Group A included patients with circumscribed temporomesial lesions including isolated hippocampal sclerosis (HS), and Group B included patients with HS and additional temporopolar focal cortical dysplasia (FCD), thus reflecting dual pathology. Analyses of predictive factors for complete seizure freedom (Engel Ia) were then carried out in the total group as well as in the two subgroups. Hereby, seizures only occurring within one month after surgery, but not thereafter, were not counted for outcome analysis.

The running down phenomenon was defined as seizure freedom occurring after a period of gradual reduction of postoperative seizure frequency. For the evaluation of this phenomenon clinical findings were compared to non-seizure free patients (outcome Engel Ib–IVc).

3. Results

An overview of clinical history and findings in EEG, imaging modalities and neuropathology of the total patient cohort is displayed in Table 1, respectively in Table 2 for subgroup analysis of subgroups A and B.

3.1. Clinical findings

The total group comprised 458 patients with intractable TLE, including 217 females (47.4%) and 241 males (52.6%) who were