

## Long-term outcome of extratemporal epilepsy surgery among 154 adult patients

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**Object.** The goal of this study was to evaluate the long-term outcome of patients who underwent extratemporal epilepsy surgery and to assess preoperative prognostic factors associated with seizure outcome.

**Methods.** This retrospective study included 154 consecutive adult patients who underwent epilepsy surgery at Bethel Epilepsy Centre, Bielefeld, Germany between 1991 and 2001. Seizure outcome was categorized based on the modified Engel classification. Survival statistics were calculated using Kaplan–Meier curves, life tables, and Cox regression models to evaluate the risk factors associated with outcomes.

**Results.** Sixty-one patients (39.6%) underwent frontal resections, 68 (44.1%) had posterior cortex resections, 15 (9.7%) multilobar resections, 6 (3.9%) parietal resections, and 4 (2.6%) occipital resections. The probability of an Engel Class I outcome for the overall patient group was 55.8% (95% confidence interval [CI] 52–58% at 0.5 years), 54.5% (95% CI 50–58%) at 1 year, and 51.1% (95% CI 48–54%) at 14 years. If a patient was in Class I at 2 years postoperatively, the probability of remaining in Class I for 14 years postoperatively was 88% (95% CI 78–98%). Factors predictive of poor long-term outcome after surgery were previous surgery ( $p = 0.04$ ), tonic–clonic seizures ( $p = 0.02$ ), and the presence of an auditory aura ( $p = 0.03$ ). Factors predictive of good long-term outcome were surgery within 5 years after onset ( $p = 0.015$ ) and preoperative invasive monitoring ( $p = 0.002$ ).

**Conclusions.** Extratemporal epilepsy surgery is effective according to findings on long-term follow-up. The outcome at the first 2-year follow-up visit is a reliable predictor of long-term Engel Class I postoperative outcome. (DOI: 10.3171/JNS/2008/108/4/0676)

**KEY WORDS** • extratemporal epilepsy surgery • long-term outcome

EXTRATEMPORAL resections were more common in earlier series of epilepsy surgery.<sup>45,46</sup> In recent epilepsy series, however, these procedures account for only 15–20% of cases, whereas up to 80% of all surgical procedures involve the temporal lobe.<sup>17,18</sup> This ratio of temporal to extratemporal resections reflects not only the relatively high epileptogenicity of the temporal lobe but also the difficulties encountered in attempting to define the localization and extent of the epileptic zones in extratemporal epilepsy, which are often more diffuse and frequently overlap eloquent areas, thus preventing complete resections.<sup>17,18</sup>

Only a few reports of the long-term outcome of extratemporal epilepsy surgery have been published.<sup>62,66</sup> In a

recent report reviewing the previous studies published between 1991 and 2005 that deal with long-term seizure outcome following epilepsy surgery, the authors found that only 13% were extratemporal surgeries.<sup>66</sup> The limitations of the previous reports are that the duration of the follow-up periods varies considerably (typically a short-term follow-up is 1–2 years after surgery), a heterogeneous group of pathological entities is included, and the operative techniques have often changed over time due to the preferences of different surgeons. These factors prevent a meaningful comparison of the long-term outcomes after surgery.<sup>12,25,26,28,36,39,61,62,66,77</sup> We tried to solve this problem by investigating the long-term outcome in patient groups in whom operations were performed at the same clinic by the same preoperative and surgical teams and sorted according to the outcome into 1 of the following 3 forms: general extratemporal outcome, outcome in relation to pathological finding, and outcome in relation to resected areas.

Abbreviations used in this paper: AED = antiepileptic drug; CI = confidence interval; EEG = electroencephalography; MCD = malformation of cortical development; MR = magnetic resonance.

**Clinical Materials and Methods**

We retrospectively reviewed the records of all adult patients ( $\geq 16$  years of age) who underwent epilepsy surgery at the Bethel Epilepsy Centre between May 1991 and May 2001. There were 186 consecutive patients fulfilling our inclusion criteria: extratemporal diagnosis, resective surgery, and a follow-up period of  $> 5$  years. We excluded patients who underwent biopsy sampling only, patients with Rasmussen syndrome (progressive disease with special criteria), patients in whom EEG video monitoring was not performed, and patients who had no clear extratemporal resection. This left 154 patients who were included, 145 (94.2%) of whom had lesional and 9 (5.8%) of whom had nonlesional disease. Each of these had undergone uniform preoperative evaluation according to the same protocol.

*Patient Characteristics*

There were 91 male (59.1%) and 63 female patients (40.9%). The mean ages of the patients at seizure onset and at first and second surgery were  $12.6 \pm 10$  years (range 0.08–52 years),  $28.6 \pm 10.6$  years (range 16–59 years), and  $30.4 \pm 9.9$  years (range 16–49 years), respectively, and the mean duration of epilepsy was  $15.9 \pm 9.4$  years (range 0.8–44 years).

The clinical characteristics of these patients, with details of differences between males and females, are summarized in Table 1. The mean follow-up duration was  $8.8 \pm 2.7$  years (range 1–14 years). The values are given as the mean  $\pm$  standard deviation.

*Preoperative Evaluation*

The preoperative protocol developed at the Bethel Epilepsy Centre to identify patients who were candidates for surgery includes the patient's history and the results of physical examination, noninvasive video EEG monitoring, and invasive monitoring procedures (if results of noninvasive methods were insufficient) as well as neuropsychological evaluation, ophthalmologic assessment (visual field test), and MR imaging. Sixty-nine patients (44.8%) underwent invasive monitoring in the form of subdural grids, and 3 (1.9%) underwent semiinvasive monitoring with foramen ovale and epidural electrodes.

*Neuroimaging Modalities*

Patients underwent MR imaging performed with either a 1-T (until 1998) or 1.5-T magnet (after 1998), in which a specific protocol for epilepsy patients was used. Additional imaging methods included positron emission tomography and single-photon emission computed tomography scanning. In the majority of patients, an intracarotid amobarbital (Wada) test was done, and also functional MR imaging was performed to record speech and motor functions.

*Surgical Procedure and Postoperative Evaluation*

Extratemporal epilepsy surgery included all areas of the brain outside the temporal lobe. All patients underwent resective surgery in the form of lesionectomies, cortical

TABLE 1

*Summary of clinical characteristics and risk factors in 154 patients who underwent surgery for epilepsy\**

Variable	Male Patients	Female Patients	Total
<b>risk factor</b>			
mean age at onset	13.4 $\pm$ 10.3	11.4 $\pm$ 9.5	12.6 $\pm$ 10.0
mean duration of epilepsy	15.3 $\pm$ 9.1	17.0 $\pm$ 9.9	15.9 $\pm$ 9.4
mean age at 1st op	28.7 $\pm$ 10.3	28.4 $\pm$ 11.1	28.6 $\pm$ 10.6
mean age at 2nd op	33.5 $\pm$ 9.8	26.4 $\pm$ 9.1	30.4 $\pm$ 9.9
mean follow-up period	8.8 $\pm$ 2.9	8.7 $\pm$ 2.5	8.8 $\pm$ 2.7
<b>no. w/ characteristic (%)</b>			
febrile convulsion	4 (4.4)	1 (1.6)	5 (3.2)
head trauma	8 (8.8)	3 (4.8)	11 (7.1)
family history	3 (3.3)	0	3 (1.9)
congenital malformation	8 (8.8)	3 (4.8)	11 (7.1)
CNS infection	9 (9.9)	0	9 (5.8)
prenatal infarction	2 (2.2)	4 (6.3)	6 (3.9)
previous op	14 (15.4)	16 (25.4)	30 (19.5)
intellectual disabilities	3 (3.3)	1 (1.6)	4 (2.6)
Parry–Romberg syndrome	1 (1.1)	1 (1.6)	2 (1.3)
seizure preceded by aura	70 (76.9)	46 (73.0)	116 (75.3)
simple partial sz	11 (12.1)	10 (15.9)	21 (13.6)
complex partial sz	51 (56.0)	34 (54.0)	85 (55.2)
secondary generalized sz	46 (50.6)	26 (41.3)	72 (46.8)
combined sz	16 (17.6)	14 (22.2)	30 (19.5)
unclassified sz	4 (4.4)	2 (3.2)	6 (3.9)

\* The values for the first 5 risk factors are given in years as the mean  $\pm$  standard deviation. There were 91 male and 63 female patients in the series. Abbreviations: CNS = central nervous system; sz = seizure.

resections, and lobectomies. All operations were performed by the same surgical team.

Patients who did not have well-defined lesions or who had defined lesions but unclear extension of the epileptic focus underwent preoperative invasive monitoring. Subdural grids were used for recording interictal and ictal discharges as well as for electrical stimulation to define the limits of the functional cortex. Intraoperative electrocorticography was used routinely in the majority of the cases. Somatosensory evoked potentials were used intraoperatively in some cases.

After discharge the patients were referred to a rehabilitation clinic where EEG evaluation usually took place. Basic postoperative follow-up examinations took place 0.5 and 2 years after operation and included EEG, MR imaging, and neurological and psychological evaluation.

*Data Collection*

From the patient's medical records we abstracted the following data: age, sex, age at onset of epilepsy, epilepsy risk factors (family history, febrile convulsions, and so on), and preoperative seizure signs. From the clinic's electronic files we abstracted preoperative video EEG monitoring, sites of resection, intraoperative complications, and early postoperative complications. Long-term outcome data were abstracted from the clinic follow-up program, outpatient reports, mailed questionnaires, and telephone calls from some patients. Our questionnaire included detailed questions about auras, seizures, general quality of life, and medication. Often, family members were asked to provide the information, especially in the case of patients who had in-

tellectual disabilities and those with psychological problems. Five (3.2%) patients did not reach the follow-up endpoint (lost to follow-up), 4 (2.6%) patients died (1 [0.6%] died in status epilepticus and 3 [1.9%] died of other medical causes). Histopathological information was taken from histopathological reports in patients' files.

### Outcome Evaluation

The basic follow-up program for all patients was scheduled for 0.5 and 2 years. Seizures that occurred within 1 week after surgery were not included in this analysis. In patients who underwent multiple operations, the outcome of the second operation was used as the final outcome. Long-term outcome was evaluated using the Engel seizure outcome classification.<sup>18,69</sup>

Operations were divided into single lobar and multilobar resections. Multilobar resections were divided into the categories of posterior cortex and multilobar resections, including a combination of > 1 lobe (frontal, parietal, and temporal). Posterior cortex epilepsies encompass a group of epilepsies originating from the occipital and parietal lobe and also the occipital border of the temporal lobe, or from any combination of these regions.<sup>8,65,73</sup>

The diagnosis of lesional and nonlesional types relied on the presence or absence of pathological findings in the resected specimen.

### Statistical Analysis

Due to the variation in time elapsed before the follow-up review (range 1–14 years) for these patients, time-to-event methods were used to relate various risk factors to the maintenance of Class I outcome after surgery. Participants were censored at the time of their last follow-up evaluation or death. Kaplan–Meier methods were therefore used to estimate the probability of remaining in Class I as a function of time. The log-rank test was used to assess whether the Kaplan–Meier curves differed between subgroups of patients defined by the selected clinical criteria. Cox proportional hazard models were used to estimate hazard ratios and 95% CIs for each risk factor of interest (hereafter, referred to as CI). We reported seizure recurrence by obtaining survival estimates at 0.5, 1, 2, 5, 10, and 14 years after surgery. We used the previously described methods for all patients, for every individual group, and finally we compared each group with others.

## Results

### Overall Outcome

The majority of seizure recurrences took place during the first 2 years after surgery (Fig. 1). Overall, 77 of 153 patients were seizure free at the 2-year checkup. The number and percentage of patients in each Engel class are summarized in Table 2. The probability of Class I outcome postoperatively was 55.8% (CI 52–58%) at 0.5 years, 54.5% (CI 50–58%) at 1 year, 50.3% (CI 45–55%) at 2 years, 52% (CI 48–57%) at 5 years, 51.6% (CI 47–55%) at 10 years, and 51.1% (CI 48–54%) at 14 years. The rate of Class

I outcome remained 51.1% for 45 patients after 14 years. If the patient was in Class I at 2 years postoperatively, the probability of remaining in Class I for 14 years was 88% (CI 78–98%).

### Outcome in Relation to Lesion

In our study we found that 9 (5.8%) of the patients had nonlesional epilepsy.

The Class I outcome for patients in the lesional group at 0.5, 2, 5, 10, and 14 years was 57.2% (CI 54–60%), 55.9% (CI 52–60%), 50.7% (CI 46–54%), 53.6% (CI 49–57%), and 51.2% (CI 47–55%), respectively. For individuals in the nonlesional group it was 33.3% (CI 22–44%), 33.3% (CI 23–43%), 44.4% (CI 31–57%), 44.4% (CI 30–58%), and 50% (CI 38–62%), respectively.

The difference between the patients with lesional and nonlesional epilepsy was significant at the 1-year follow-up ( $p = 0.005$ ), but with long-term follow-up there was no significant difference ( $p = 0.07$ ; Fig. 2).

### Outcome in Relation to Resection Locations

Of the 154 patients there were 39.6% who underwent frontal lobe surgery, 50.6% underwent posterior cortex resections, and 9.7% underwent multilobar resections. Class I outcome at 0.5, 1, 2, 5, and 14 years was 50.8% (CI 46–54%), 49.2% (CI 44–54%), 47.5% (CI 41–53%), 50% (CI 44–56%), and 47.8% (CI 43–51%), respectively, in patients who underwent frontal lobe resection, whereas it was 52.6% (CI 49–55%), 51.3% (CI 46–56%), 51.9% (CI 45–57%), 56.7% (CI 51–61%), and 56.7% (CI 52–60%), respectively, in those who underwent posterior cortex resection and 46.7% (CI 40–52%), 50% (CI 40–60%), 40% (CI 30–50%), 44.4% (CI 32–56%), and 44.4% (CI 32–56%), respectively, in individuals treated with multilobar resection (Fig. 3).

### Outcome in Relation to Pathological Findings

Of the patients in this study, 34.4% had various types of neoplastic lesions, 34.4% had various types and degrees of cortical dysplasia, 12.3% had gliosis, and 8.4% had vascular malformations. Also, 3.2% had cystic lesions, 5.8% had MCD, 1.9% had hippocampal sclerosis associated with extratemporal lesions, and 2.3% had other lesions (scleroderma, Sturge–Weber syndrome, sarcoidosis, and inflammation [except in patients with Rasmussen encephalitis, who were excluded from this study]). Furthermore, 7.8% of the patients had > 1 pathological finding, including dual pathological entities.

Overall, Engel Class I outcome with cortical dysplasia at the 14-year follow-up was 52.6% (CI 46–58%); 86.7% of the patients had a favorable outcome (Classes I–III) after surgery. Overall, Class I outcome in patients with neoplastic lesions was 56% (CI 50–62%); 93.8% of the patients had a favorable outcome after surgery. Class I outcome in patients with gliosis tended to decrease over time: at the follow-up after 14 years all patients with this disease were re-assigned to other classes. The Class I outcome in patients with gliosis at 0.5, 1, 2, 5, 10, and 14 years was 57.1% (CI 47–67%), 61.9% (CI 50–70%), 52.3% (CI 42–62%), 52.3%

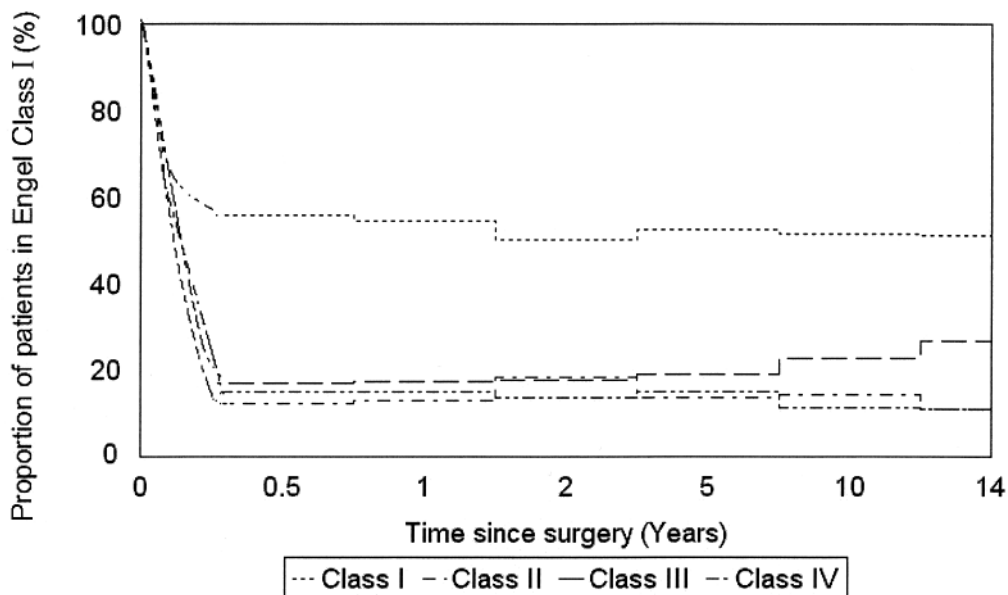


FIG. 1. Kaplan-Meier graph showing the proportion of patients in Engel Classes I-IV over 14 years of follow-up.

(CI 42–62%), 33.3% (CI 23–43%), and 0%, respectively; 66.7% of the patients had a favorable outcome after surgery. Overall, Class I outcome in patients with vascular lesions was 50% (CI 45–55%); 75% of patients had a favorable outcome after surgery (Fig. 4). In patients with dual disease, the overall Class I outcome was 33.3% (CI 23–43%); 66.7% of patients had a favorable outcome after surgery. None of the patients with MCD could be classified in Class I at the 14-year follow-up, although 66.7% of these patients benefited from surgery (Classes II and III).

*Outcome in Relation to AEDs*

The possibility of AED withdrawal was discussed with patients who had been seizure free  $\geq 2$  years and did not show epileptiform activity in the postoperative EEG studies. The final decision was made by patients or their caregivers. In our study 31.1% of 154 patients underwent AED withdrawal and maintained Class I status for  $> 2$  years; 20% had seizure recurrence after AED withdrawal; 80% of seizure recurrences occurred in the 1st year, 15% occurred in the 2nd year, and 5% occurred after  $> 2$  years. In all patients who had recurrence after AED withdrawal, the drugs were readministered to control the seizures. Of our patients, 48.9% are still receiving medical treatment: 11.1% have a reduced dose of AEDs, 17.7% receive treatment with 2 AEDs, and 20.1% are being treated with  $> 2$  drugs.

*Seizure Recurrence*

In our study there were 76 patients suffering from a relapse of seizures postsurgically. These seizures occurred in 68 patients (89.4%) within 0.5 years and in 73 patients within 2 years after epilepsy surgery. Only 3 (3.9%) of 76 patients relapsed  $> 2$  years after surgery, with a recurrence rate after the 2-year follow-up interval of 3 (13%) of 23

within the group of patients classified as Engel Class I. We observed that the number of patients and percentage of those assigned to Class I increased between 2 and 5 years of follow-up; Class I included 77 patients (50.3%) at 2 years and increased to 79 (52%) at 5 years.

If a patient was in Class I at 2 years postoperatively, the probability of remaining in this class for 14 years postoperatively was 88% (CI 78–98%).

*Prognostic Factors*

There was a significant correlation of good long-term outcome with the following findings: preoperative invasive monitoring ( $p = 0.002$ ), single operation ( $p = 0.013$ ), and surgery within the first 5 years after epilepsy onset ( $p = 0.015$ ; Fig. 5).

There was a significant correlation of poor long-term outcome associated with each of the following findings: au-

TABLE 2  
*Outcome of epilepsy surgery based on Engel classification\**

Yrs Postop	No. of Patients in Engel Class (%)			
	I	II	III	IV
0.5	86 (55.8)	19 (12.3)	26 (16.9)	23 (14.9)
1	84 (54.5)	20 (13.0)	27 (17.5)	23 (14.9)
2	77 (50.3)	28 (18.3)	27 (17.7)	21 (13.7)
5	79 (51.9)	21 (13.8)	29 (19.1)	23 (15.1)
10	32 (51.6)	9 (14.5)	14 (22.6)	7 (11.3)
14	23 (51.1)	5 (11.1)	12 (26.7)	5 (11.1)

\* Because of the difference among patients relating to time of surgery and periods of follow-up, the total number of patients for the 0.5- and 1-year intervals was 154; for 2 years it was 153; for 5 years 152; for 10 years 62; and for 14 years it was 45 patients.

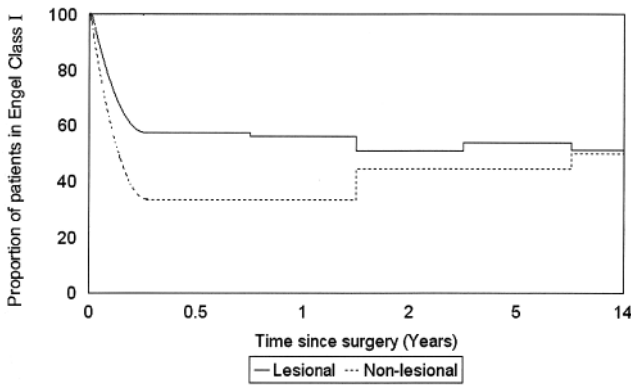


FIG 2. Kaplan-Meier graph showing the proportion of Engel Class I outcomes in lesional and nonlesional groups.

ditory auras ( $p = 0.03$ ), tonic-clonic seizures ( $p = 0.02$ ), previous surgery ( $p = 0.04$ ), and multiple operations ( $p = 0.013$ ). Patients with lesional and normal pathology had significant differences at the 1-year follow-up evaluation ( $p = 0.005$ ), but not in long-term follow-up ( $p = 0.07$ ). There was no significant difference in Class I outcome based on sex ( $p = 0.619$ ), age at surgery ( $p = 0.270$ ), age at onset ( $p = 0.562$ ), and side of surgery ( $p = 0.632$ ).

*Postoperative Complications*

There were complications in 13 (8.4%) of the patients: 3 of them (1.9%) had a persistent paresis, 6 (3.9%) had visual field defects, 1 (0.6%) had a subdural hemorrhage that needed to be evacuated, and 3 (1.9%) had bone infections (1 [0.6%] underwent surgery to remove the infected bone).

In addition, 9 patients (5.8%) suffered from transient

morbidity diagnosed during the first rehabilitation visit: 3 (1.9%) had language disturbances, 2 (1.3%) had word finding disorders, 2 (1.3%) had movement disorders, and 2 (1.3%) had frontal lobe psychological manifestations. There was no significant difference in the classification of long-term Class I outcome due to complications ( $p = 0.233$ ).

*Outcome in Patients With Multiple Operations*

Twenty-three patients (14.9%) had > 1 operation, 2 patients (1.2%) underwent an operation 3 times, and 2 patients (1.2%) received implantation of a vagus nerve stimulator.

The mean postoperative follow-up period after the reoperation was  $5.0 \pm 2.5$  years (range 0.6–12 years). The reoperation was performed at a mean of 3.25 years after the initial surgery (range 0.5–6 years). Engel Class I outcome at 0.5, 1, 2, and 5 years for patients who underwent only 1 operation was 59.1% (CI 56–62%), 55.4% (CI 51–59%), 53.2% (CI 49–57%), and 54.7% (CI 50–58%), respectively. Engel Class I outcome for patients who underwent multiple operations at 0.5, 1, 2, and 5 years was 21.7% (CI 12–30%), 26.2% (CI 16–36%), 26.2% (CI 16–36%), and 27.8% (CI 18–36%), respectively, after the first operation and 52.4% (CI 49–55%), 45% (CI 40–50%), 45% (CI 40–50%), and 42% (CI 38–46%), respectively, after the second operation. There were significant differences between numbers of Class I outcomes after first and second operations ( $p = 0.04$ ; Fig. 6).

**Discussion**

*Methodological Considerations*

The analysis of the long-term outcome is essential to as-

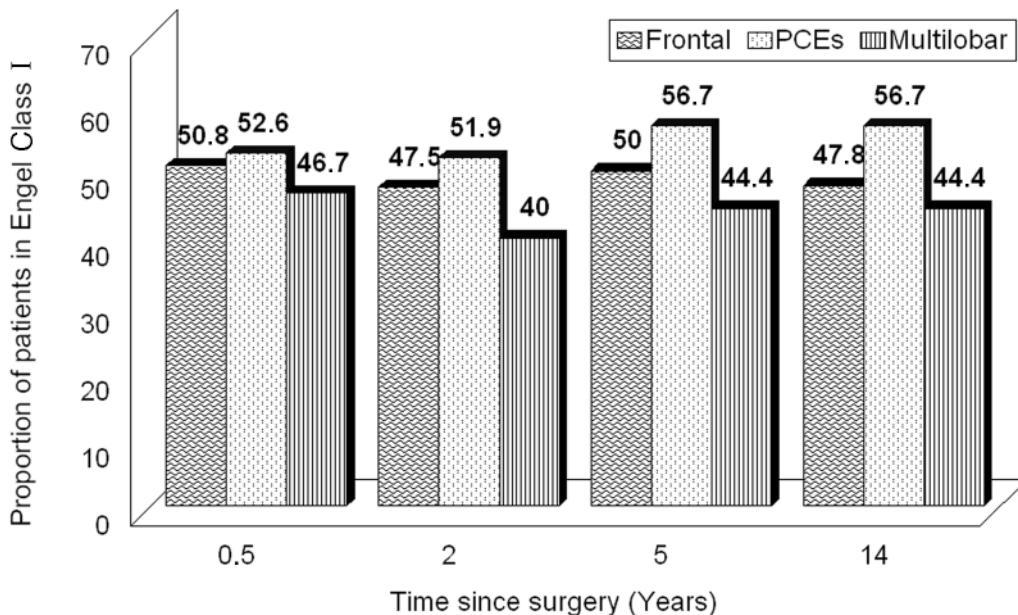


FIG 3. Bar graph showing the percentage of Engel Class I findings in different resection areas. PCEs = posterior cortex resections.

## Long-term extratemporal epilepsy surgery outcome



FIG 4. Kaplan–Meier graph showing the proportion of patients with Engel Class I outcome based on the pathological finding. FCD = focal cortical dysplasia.

sess the efficacy of epilepsy surgery. Seizure relapses may occur after initial freedom from seizures,<sup>24,75,78</sup> or, on the other hand, “running down of fits” has been reported in a substantial percentage of patients.<sup>6,50</sup> In contrast to our methodology, previous studies of extratemporal epilepsy surgery included a heterogeneous group of patients (nonlesional and lesional epilepsies) and little is known about the long-term outcome.<sup>21,62,63,66</sup> In large patient groups, diagnostic and surgical protocols usually vary over time, whereas

in our sample the preoperative diagnostic workup remained relatively unchanged and epilepsy surgery was performed by the same team. Other studies are older and do not reflect recent technological advances in diagnosis and surgery; in contrast, all of our patients had extensive EEG video monitoring, and in the majority of them high-resolution MR imaging was performed. Few studies analyze the outcome after fixed periods of time so that changes in seizure status could not be taken into account.<sup>6,54</sup> In our study we used the

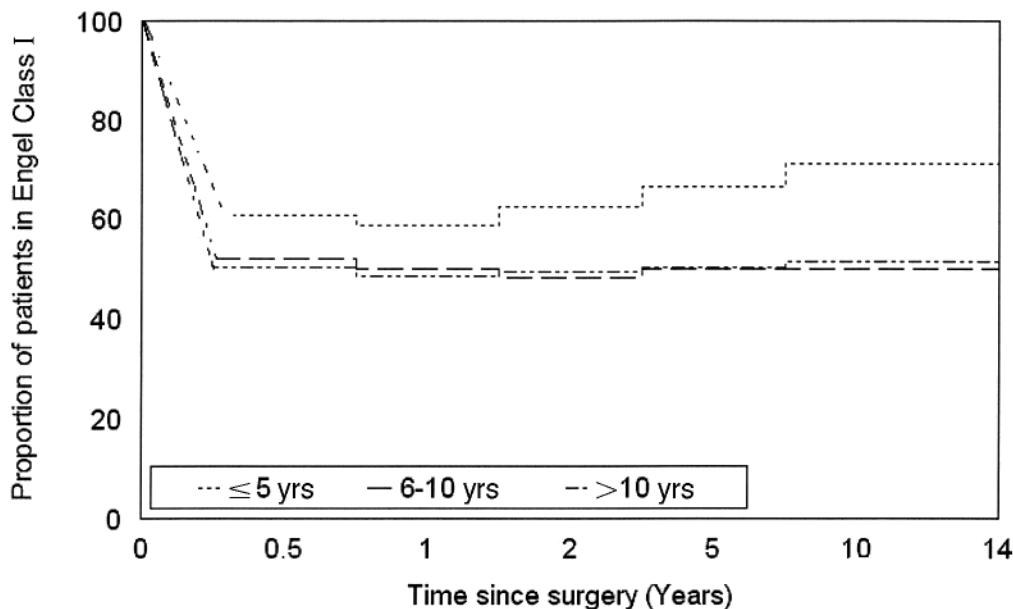


FIG 5. Kaplan–Meier graph showing the proportion of patients with Engel Class I outcome based on the preoperative epilepsy duration.

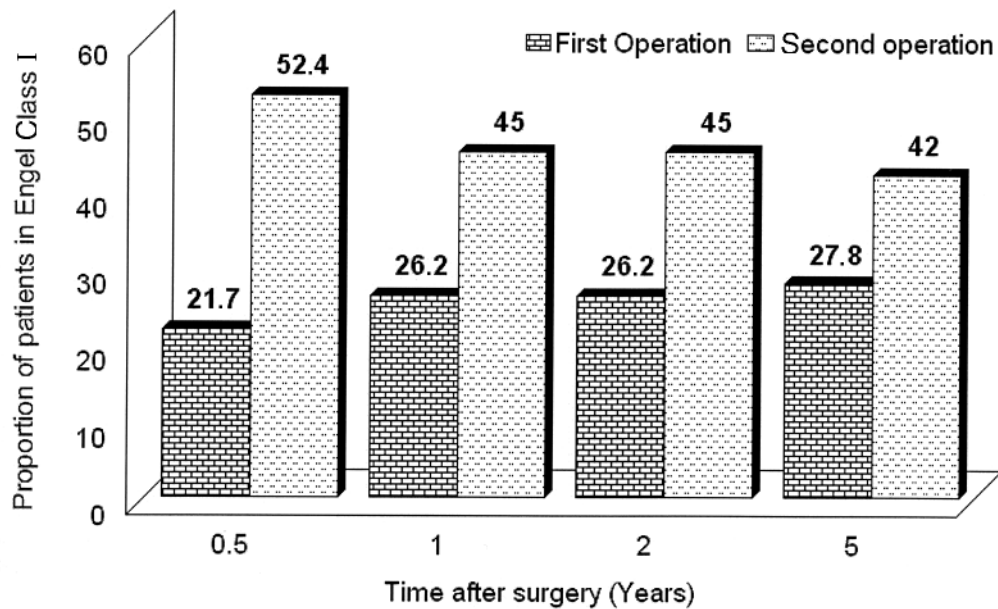


FIG 6. Bar graph showing Engel Class I outcomes after first and second operations in patients who underwent multiple surgeries.

time-to-event analysis, which allowed for better investigation of the long-term seizure outcome.

#### Seizure Outcome

In 1987 Overweg and coworkers<sup>43</sup> reported that 32% of their patients became seizure free. In other studies 40% of patients became seizure free and 30% improved.<sup>18</sup> At the first international Palm Desert Conference on epilepsy surgery in 1987, 43.2% of patients were reported to have become seizure free, 27.8% were improved, and 29.1% were unchanged. Six years later, at the second Palm Desert Conference, investigators reported that 45.1% of patients were seizure free, 35.2% improved, and 19.8% remained unchanged.<sup>18,62</sup> Recently Tellez-Zenteno and coworkers<sup>66</sup> reviewed the long-term outcome in studies conducted between 1991 and 2005; seizure-free outcome was 34% (CI 28–40%) in extratemporal resections as a group. In most studies the reported number of patients with seizure freedom is in the range of 32–45.1%.<sup>66,71</sup> Covering a longer time period, however, older studies do not reflect the current standards of epilepsy diagnosis and surgery. Most patients had not undergone high-resolution MR imaging studies with epilepsy-specific protocol, and a significant percentage of patients needed invasive monitoring with subdural or depth electrodes. In our study of the long-term outcome after extratemporal epilepsy surgery in adults, 51.1% of patients were seizure free, 88.9% had a favorable outcome (Classes I–III), and 11.1% had no appreciable change. The better outcome in our study might reflect a general improvement in extratemporal epilepsy surgery.

In nonlesional groups 33.3% of the patients were seizure free at 6-month follow-up review, but this number increased to 50% after 14 years. Previous studies reported 20–42% of patients who were seizure free among the non-

lesional groups.<sup>7,12,68,71,80</sup> Our rate was higher and increased progressively over time. The only significant finding in this group was the medication change; 77.7% changed from the preoperative treatments, and this finding may suggest that surgery can improve the response to medical treatment of patients with nonlesional epilepsy, or it may reflect the high efficacy of the more recent drugs. Our results are not conclusive, however, because the nonlesional group consisted of only 9 patients.

#### Resection Area

For frontal lobe epilepsy, in 1991 Rasmussen<sup>48</sup> reported a long-term seizure outcome of 26% of patients who became and remained seizure free. Another 30% had a marked reduction of seizures. In 2002 Zaatreh et al.<sup>79</sup> reported that 35.1% of patients in Class I and 32.4% of patients in Class II had tumor-related frontal lobe epilepsy. The Commission for the Neurosurgery of Epilepsy reported freedom from seizures in up to 41.2% of patients in 1997.<sup>13,35</sup> Salanova and coworkers<sup>53</sup> reported a long-term complete or nearly complete cessation of seizures in 56% of their patients in a summary of the Montreal experience. In 2005, Tellez-Zenteno and coworkers<sup>66</sup> reported freedom from seizures in 46% (CI 35–57%) of patients with parietal and occipital lobe epilepsy.

In our study the long-term seizure-free outcome in patients with frontal resections was 47.8%, and an additional 30.5% had a favorable improvement. In those with posterior resections, the seizure-free outcome was 56.7%. In view of similar findings in other studies we attribute our better results to more precise imaging and seizure mapping techniques.<sup>66</sup> Tellez-Zenteno and coworkers<sup>66</sup> observed an improvement of long-term outcome after 1980 in a group of patients with temporal and extratemporal lobe epilepsy, in

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comparison with the temporal subgroup alone. In temporal lobe epilepsy the epileptogenic region might be more restricted.

### *Histopathological Aspects*

In patients with a well-defined lesion, for example a neoplasm or a cavernoma, seizure-free outcome is in the range of 35.1–80%.<sup>37,52,53,78–80</sup> In contrast, patients with less well-circumscribed lesions, such as MCD, the seizure-free outcome is in the range of 33–47%.<sup>11,15,17,27,59,62</sup>

In our study, long-term seizure-free outcome after 10 years was 52.6% in patients with cortical dysplasia, 56% in those with neoplasms, 50% in those with vascular malformation, and 33.3% in patients with MCDs. Our results were better in less circumscribed lesions but worse in neoplasms. This may be due to the fact that 25 of 53 patients (47.2%) with neoplastic lesions had malignant tumors (Grades 3 and 4), 13.2% had failed epilepsy surgery, 24.5% had previous surgery at other institutions, 5.6% had dual pathological entities, and 7.5% had MCD associated with tumor tissue. All of these factors, in addition to longer follow-up periods and the fact that all patients were adults with extratemporal epilepsy lesions that were not discussed in previous studies, contribute to the discrepancy of findings between our group and others.

### *Criteria for Repeated Operation*

Repeated operation was offered to patients who fit the following criteria: 1) medically intractable epilepsy before and after a resective epilepsy surgery; 2) resective reoperation at the Bethel Epilepsy Centre (that is, patients who underwent palliative procedures such as vagal nerve stimulator, multiple subpial transection, or corpus callosotomy were not included); 3) no evidence of malignant brain tumor; and 4) second time monitoring with evidence of a remnant epileptogenic area. Patients who did not fulfill these criteria were considered to be general neurosurgical patients. Published reports documented that 20–63% of patients achieved freedom from seizures after the second operation.<sup>2,23,29,52,55,56,58,77</sup> Most of the published series consisted of patients with temporal and extratemporal lesions in different age groups and short periods of follow-up after the second operation. Our study has the advantage that the long-term follow-up after the second operation was  $5.0 \pm 2.5$  years (range 0.6–12 years), which was performed only for adult patients with extratemporal lesions. In 42% of our patients who underwent repeated operation, seizure freedom was achieved for > 5 years after the second operation. The fact that our results are better than in previous reports is possibly due to the selection of patients.

### *Antiepileptic Drugs*

Long-term follow-up results in some series with predominantly temporal resections demonstrate that up to one third of the patients remain seizure free after AEDs are discontinued.<sup>3,5,9,14,19,33,40,42,70</sup> This is in accordance with our study of extratemporal resections in which AEDs could be withdrawn in 31.1% of the patients without seizure relapses.

Recurrence of seizures after the discontinuation of AEDs in medically treated patients has been described in previous studies,<sup>4,21,31,32,38,39,44,60,74</sup> the relapse rates were 25% after 1 year and 29% after 2 years. Relapses occurred in 20% of our patients, but all regained seizure freedom after treatment with AEDs was recommenced. This probably proves a therapeutic effect of resective epilepsy surgery, even in those patients who still need AEDs after surgery, thereby confirming that epilepsy surgery can transform pharmacoresistant epilepsy to pharmacosensitive disease.

### *Late Seizure Recurrence*

Previous studies showed a stable course of the Class I seizure outcome among patients who have undergone temporal lobe surgery.<sup>12,30,47,51,60,72,76</sup> The recurrence rate among patients who were initially seizure free for 2 years was 10–15%.<sup>16,22</sup> For patients with extratemporal lesions, previous studies showed a recurrence rate of 15%,<sup>44</sup> which is similar to our study, indicating a recurrence rate of 13% after being seizure free for 2 years. Our results not only support the stability and low recurrence rate after 2 years of freedom from seizures, but also confirm previous studies showing no significant difference in the risk of long-term seizure relapse between temporal and extratemporal resections.<sup>12,38,78</sup>

### *Prognostic Factors*

In our study there is a strong relationship between short duration of epilepsy and good outcome. The relationship between the good outcome and duration of epilepsy is a controversial subject. Some authors observed that duration of epilepsy was not a prognostic factor and had no relationship to the outcome.<sup>1,20,41,64</sup> Other authors showed significant correlations between shorter duration of preoperative epilepsy and improved outcomes.<sup>7,15,61,67</sup> Some authors reported the relationship between short duration of epilepsy and good outcome in certain lesions, such as among patients with focal cortical dysplasia.<sup>34,57</sup> Most of the previous studies established this relationship in the short-term outcome. Our results strongly support the relationship between a good outcome and the duration of epilepsy in the long-term outcome of extratemporal lobe epilepsy surgery.

In our analysis, tonic-clonic seizures were a bad prognostic factor. This is a result that has already been published in temporal lobe studies and in studies containing patients with temporal and extratemporal lobe epilepsy.<sup>28,64</sup>

### *Postoperative Complications*

Van Ness et al.<sup>68,69</sup> found postoperative complications in 88% of their 57 consecutive patients who underwent neocortical resections at the Cleveland Clinic between 1979 and 1992; 37% of them had unexpected morbidity, including a single death. The persistent deficits were of minor clinical relevance in the majority of patients. In another study, 44.8% of patients experienced transient complications after cortical resections, compared with only 14.8% after lesionectomies.<sup>10,68,69</sup> Recent studies of temporal and extratemporal resections<sup>3,49</sup> report persistent complications related to surgery in only 4% of patients.<sup>12</sup> Our study shows comparable figures of transient (11%) and persistent



(3.2%) complication rates. This decline of postoperative complications is most likely due to improvements in the surgical techniques and procedures.

#### Limitations of This Study

Using Engel classifications for seizure outcome, we did not differentiate among patients in terms of the severity of seizures. In addition, different surgical techniques were applied. Moreover, this is a retrospective study, with corresponding limitations.

#### Conclusions

Our study demonstrates that resective epilepsy surgery is effective in controlling seizures in patients with both lesional and nonlesional focal epilepsies, and the outcome after surgery exceeds the results of pure AED treatment. The best outcome could be achieved in patients with detectable lesions, including neoplasms, and when the resection was confined to posterior cortical areas. Conversely, patients with MCD and gliosis had the worst outcome.

Another finding in our study is that the outcomes within the first 2 years after surgery provide a basis to estimate the future outcome for up to 14 years. This information is crucial in counseling patients about whether to continue or omit their anticonvulsant medication postoperatively.

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