PAPER

Long term follow-up of the first 70 operated adults in the Göteborg Epilepsy Surgery Series with respect to seizures, psychosocial outcome and use of antiepileptic drugs

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Objective: To compare long term (10 years) seizure outcome, psychosocial outcome and use of antiepileptic drugs (AED) with the 2 year follow-up in adults after resective epilepsy surgery.

Methods: All adults (n=70) who underwent resective epilepsy surgery from 1987 to 1995 in the Göteborg Epilepsy Surgery Series were included. Fifty-four had undergone temporal lobe resections and 16 extratemporal resections (12 frontal). A cross-sectional follow-up in the form of a semistructured interview was performed in late 2003.

Results: Mean follow-up was 12.4 years (range 8.6–16.2). Of the 70 patients (51% males), five (7%) were dead (three as a result of non-epilepsy related causes). Of the 65 patients interviewed, 38 (58%) were seizure-free at the long term follow-up: 65% of the patients with temporal lobe resections and 36% of the patients with extratemporal resections. Of the 35 patients who were seizure-free at the 2 year follow-up, 3 (9%) had seizures at the long term follow-up. Of the 30 patients who had seizures at the 2 year follow-up, 6 (20%) were seizure-free at the long term follow-up. Of all 65 patients, 45 (69%) had the same seizure status as the 2 year follow-up. Sixteen (25%) had an improved seizure status and 4 (6%) had a worsened status. Of the seizure-free patients, 11 (29%) had ceased taking AED, 28 (74%) were working and 25 (66%) had a driving license.

Conclusions: Adult patients who are seizure-free 2 years after resective epilepsy surgery are most likely to still be seizure-free 10 years later. Most are working and have obtained a driving license.

Epilepsy surgery is a well established treatment for medically intractable epilepsy.^{1,2} The ultimate aims of epilepsy surgery are to reduce the frequency and intensity of seizures and thereby to improve quality of life. Most studies of the effectiveness of epilepsy surgery have focused on seizure outcome of anterior temporal lobe resections 1–2 years after surgery. One randomised controlled study² and multiple clinical series have shown that approximately two thirds of patients become free of seizures with impairment of awareness. It has also been shown that quality of life scores improve after temporal lobe resection, especially in seizure-free patients who also have a trend towards better social function (see Engel *et al*,³ Jones *et al*⁴ and Malmgren *et al*⁵).

Concern has been raised about the long term seizure outcome of epilepsy surgery. Several studies have described late seizure recurrences after initial success, sometimes but not always related to discontinuation of antiepileptic drugs (AED).^{6–8} On the other hand, it has been suggested that seizure outcome at 2 years after surgery in patients subjected to temporal lobectomy predicts the long term outcome.^{6,9–12}

However, there are only a few studies concerning long term outcome beyond 5 years (ie, presenting data with 10 years of follow-up).¹³ Most have only included patients subjected to temporal lobectomy and very little is known about the long term seizure outcome for patients who have undergone other resection types.

Patients' aims for epilepsy surgery are, however, not limited to seizure relief. The five commonest aims for patients during presurgical evaluation cited in the study by Taylor *et al*¹⁴ were: desire for work, driving of motor vehicles, independence, socialising and freedom from drugs (see also Gilliam *et al*¹⁵). Psychosocial outcomes (eg, employment status, educational status and driving a vehicle) are seldom reported in long term

studies. Of the few studies reporting psychosocial aspects, the average follow-up time is no more than 5 years and most of them have only included patients subjected to temporal lobectomy^{4,16–18} (see Guldvog *et al*¹⁹).

The Göteborg Epilepsy Surgery Series is a multidisciplinary prospective follow-up of all patients subjected to epilepsy surgery in Göteborg since its start in 1987. We have previously described the 2 year outcome regarding alterations in seizure frequency,²⁰ general cognitive function, and memory²¹ and psychiatric morbidity²² in the first 70 consecutive operated adults. The aim of this study was to compare the long term (>10 years) outcome concerning seizure status, psychosocial issues and use of AED with the 2 year follow-up in these well characterised 70 adults.

METHODS

Description of the cohort

The cohort in this study comprised the first 70 consecutively recruited adult patients (51% male) who underwent resective epilepsy surgery in the Göteborg Epilepsy Surgery Programme between October 1987 and May 1995. Fifty-four patients had undergone temporal lobe resection and 16 had extratemporal resections (12 of these were frontal and one each was a parietal, an occipital, a temporoparietal and a frontotemporal resection). Of the 70 patients, 5 (7%) had died at the long term follow-up, two as a result of epilepsy related causes (status epilepticus) and three as a result of non-epilepsy related causes (lung carcinoma, astrocytoma and surgical complication). Of the 5 deceased patients, 2 were seizure-free at the 2 year follow-up. Of the remaining 65 patients, none was lost to follow-up.

Abbreviation: AED, antiepileptic drugs

Table 1 Patient data

Characteristic	Number	Mean	Range
Age at epilepsy onset (y)	70	16.7	1–58
Duration of preoperative epilepsy (y)	70	19.4	2–43
Age at follow-up (y)	65	47	32–68
Follow-up duration (y)	65	12.4	8.6–16.2
Localisation of surgery			
Temporal	54		3†
Extratemporal	16		
Frontal	12		2†
Other	4		
Side of surgery			
Left	39		2†
Right	31		3†

†Deceased patients.

The patients were prospectively followed and the mean follow-up of the 65 patients was 12.4 years (range 8.6–16.2). A total of 82% had a minimum follow-up duration of 10 years. Additional patient data are summarised in table 1.

Data collection

Every epilepsy surgery procedure in Sweden is reported to the Swedish National Epilepsy Surgery register which includes data on patient history and on all investigative and therapeutic procedures.²³ The register also has information on seizure situation, use of AED, and working and living situation before and 2 years after operation. Before operation, mean seizure frequency during the year preceding the presurgical investigation was reported. At the 2 year follow-up, seizure freedom was defined as no seizures (or auras only) since surgery which, in the ILAE proposal for a new classification of surgical outcome, corresponds to classes 1 and 2.²⁴ For the patients with continuing seizures postoperatively, mean seizure frequency during the year preceding the follow-up was reported and the change (reduction or, in a few cases, increase) from before to after operation was reported in per cent. The following seizure outcome categories were used: (1) seizure-free (with or without aura); (2) $\geq 75\%$ reduction of seizure frequency; (3) 50–75% reduction of seizure frequency; (4) $< 50\%$ reduction of seizure frequency and (5) worsened seizure situation.

For the present study, preoperative and postoperative register data on the first 70 patients in our surgical series were used, and for the long term follow-up, a cross-sectional semistructured telephone interview was undertaken in November–December 2003 by one of the authors (GE). The telephone interview contained the same items as the 2 year follow-up concerning seizure status, use of AED, and working and living situation. Seizure status was assessed both for the last year of follow-up (the year preceding the interview) and for the whole time period between the 2 year follow-up and the long term follow-up period. Questions on the use of AED, and working and living circumstances focused on the situation at the time of

the interview. One item on driving license and driving was added as well as one global assessment of quality of life, on a 1–7 point scale,²⁵ which had also been used at the 2 year follow-up as part of a separate assessment.^{5–26} During the interview, patients were also asked if they had experienced any significant period of depression since the 2 year follow-up, and in that case if they had consulted a physician, had received medication and whether they had been hospitalised because of depression. Detailed data on the psychiatric morbidity in this patient cohort during the first 2 postoperative years have been published previously.²²

Apart from the structured telephone interview follow-up, patient files were available from routine clinical controls between the 2 year and long term follow-up. The information given in the interview on seizure status over time could therefore be compared with the clinical notes.

Statistical analysis

Comparisons of the groups were made using the Mann–Whitney test. A *p* value < 0.05 was taken as significant.

RESULTS

Seizure outcome

Table 2 shows the distribution of patients by seizure frequency score and by time of follow-up. Only patients alive at the long term follow-up are included in both assessments (*n* = 65). At the 2 year follow-up, 35 (54%) of the 65 patients included in the study were seizure-free. Fifty-nine per cent of patients who underwent temporal resections (30 of 51 patients) were seizure-free and 36% (5 of 14 patients) who underwent extratemporal resections were seizure-free. At the long term follow-up, 38 patients (58%) were seizure-free: 65% of those who underwent temporal resections (33 of 51 patients) and 36% (5 of 14 patients) of those who underwent extratemporal resections. Of the 35 patients who were seizure-free at the 2 year follow-up, 32 (91%) continued to be seizure-free at the long term follow-up. Three (9%) had seizures at the long term follow-up (all 3 being assigned to group 3). The recurrence of seizures in these 3 patients was not caused by taper or discontinuation of AED. Of the 30 patients who had seizures at the 2 year follow-up, 6 (20%) were seizure-free at the long term follow-up: 1 of these had undergone a reoperation after which he has remained free from seizures, 2 patients had changes in AED medication while 3 patients had no change in medication. Of all 65 patients interviewed, 45 (69%) had the same seizure status as the 2 year follow-up. Sixteen (25%) had an improved seizure situation and 4 (6%) had a worsened status. Of the 14 patients subjected to extratemporal resections, 8 (57%) had the same seizure status as the 2 year follow-up. Five (36%) had an improved seizure status and 1 (7%) had a worsened status.

Medication outcome

Prior to surgery, 47 (72%) of the patients were taking two or more AED, 18 (28%) were taking one AED and no one was drug-free. At the long term follow-up, 11 (17%) had ceased AED therapy. Twenty-four (37%) were receiving AED monotherapy and 30 (46%) were receiving two or more AED (fig 1A). At the 2 year follow-up, the corresponding values were 1 (3%), 20 (53%) and 17 (45%), respectively.

Of the 38 patients who were seizure-free at the long term follow-up, 11 (29%) had ceased AED therapy. Nineteen (50%) were receiving AED monotherapy and 8 (21%) had two or more AED. At the 2 year follow-up, the corresponding values were 1 (3%), 20 (53%) and 17 (45%), respectively (fig 1B).

Of the 27 patients who were not seizure-free at the long term follow-up, none had ceased AED therapy. Five (19%) were receiving AED monotherapy and 22 (81%) were receiving two or more AED. The same values were found at the 2 year follow-up (fig 1C). At the long term follow-up, 11 (22%) of the

Table 2 Comparison between long term seizure outcome and the 2 year follow-up (*n* = 65)

Seizure outcome	Two year follow-up	Long term follow-up
Seizure-free (with or without aura)	35 (54%)	38 (58%)
$\geq 75\%$ reduction in seizure frequency	6 (9%)	8 (12%)
50–75% reduction	7 (11%)	9 (14%)
0–50% reduction	15 (23%)	9 (14%)
Worsened seizure situation (compared with preoperative situation)	2 (3%)	1 (2%)

Figure 1 Proportions of patients taking no antiepileptic drugs (AED), one drug and two or more drugs. (A) All patients. (B) Patients seizure-free at the long term follow-up. (C) Patients with seizures at the long term follow-up.

patients subjected to temporal lobe resections ($n = 51$) had ceased medication, 18 (35%) were receiving AED monotherapy and 22 (43%) were receiving two or more AED. Corresponding values for patients subjected to extratemporal resections ($n = 14$) were 0 (0%), 6 (43%) and 8 (57%), respectively.

Global assessment of quality of life and depressive state

Of the 65 patients interviewed, 59 (91%) responded to the item regarding an overall assessment of quality of life. The averaged score on a 1–7-point scale for all responders was 4.9 at the 2 year follow-up and 5.6 at the long term follow-up. There was a significant difference between the patients with no seizures at the long term follow-up and patients with seizures at both the 2 year follow-up (mean score for the seizure-free 5.5 vs 4.3 for those with seizures) and the long term follow-up (mean score for the seizure-free 6.1 vs 4.8 for those with seizures).

When asked if they had experienced any significant period of depression and/or anxiety during the whole length of the follow-up, 17 patients (29%) answered yes (11 of the seizure-free and 6 of those with seizures). Of these 17 patients, 10 had consulted a physician and/or received a pharmacological treatment for their problems.

Sociodemographic data

Of the 65 patients all had completed the Swedish 9 year compulsory school prior to surgery, 44 (68%) had completed upper secondary school and 7 (11%) had a university degree. At

the 2 year follow-up, 47 (72%) had completed upper secondary school and 8 (12%) had a university degree. At the long term follow-up, the corresponding values were 48 (74%) and 9 (14%), respectively. Before surgery, 48 (74%) of the patients were working full or part-time, 3 (5%) were studying and 14 (22%) were receiving sick pay or part-time or full-time pensions. At the 2 year follow-up, 41 (63%) were working full or part-time, 2 (3%) were studying and 21 (32%) were receiving sick pay or part-time or full-time pensions. At the long term follow-up, the corresponding values were 36 (55%), 0 and 28 (43%), respectively. However, as can be seen in table 3, there was a significant difference between the patients with no seizures at the long term follow-up and patients with seizures at both the 2 year and long term follow-up. The seizure-free patients in general continued to work over time, and a few had also progressed from part-time to full-time employment. In contrast, less than half of the patients with continuing seizures and who were working preoperatively still worked at the long term follow-up, and a larger proportion worked part-time.

The patients were also asked if they had obtained a driving license prior to or following surgery and were they driving a vehicle. The Swedish Road Administration requires a 2 year period of freedom from seizures before granting or renewing a driving license. Thirteen patients had obtained a driving license prior to surgery. However, these patients had obtained their license well before the time of surgery at a time when they were seizure-free and had not been permitted to drive a vehicle for at

Table 3 Sociodemographic data ($n = 65$)

	Presurgical No (%)	Two years follow-up No (%)	Long term follow-up No (%)
Seizure-free ($n = 38$)			
Working	31 (82)	29 (76)	28 (74)
Full-time	20	22	22
Part-time	11	7	6
Studying	1 (3)	2 (5)	0
Sick pay or pension	6 (16)	6 (16)	10 (26)*
Parental leave	0	1 (3)	0
Seizures ($n = 27$)			
Working	17 (63)	12 (44)	8 (30)
Full-time	14	7	4
Part-time	3	5	4
Studying	2 (7)	0	0
Sick pay or pension	8 (30)	15 (56)	18 (67)†
Parental leave	0	0	1 (4)

*Two receiving old-age pension.

†One receiving old-age pension.

least 2 years prior to surgery (because of seizures). Sixteen had obtained a driving license following surgery. A total of 25 (66%) of the 38 patients with no seizures at the long term follow-up had a valid driving license and of these 23 were driving.

DISCUSSION

In this study, we have reported the long term outcome of adults who underwent resective epilepsy surgery in the Göteborg Epilepsy Surgery Series between October 1987 and May 1995, a mean follow-up of 12.4 years. The proportion of seizure-free patients in our series (58%) and the difference in seizure freedom between patients subjected to temporal lobectomy (65%) and extratemporal resections (38%) is in accordance with other long term studies (59%, 66% and 34%, respectively).¹³ However, in the majority of long term follow-up studies after epilepsy surgery, only the overall proportion of seizure-free patients at various time points was reported. In this study, we have reported the actual proportion of patients with sustained seizure freedom from the time of surgery. We found that 91% of patients who were seizure-free at the 2 year follow-up were still seizure-free at the long term follow-up. This is in contrast with the results of the meta-analysis by Tellez-Zenteno *et al* who found an association between the duration of follow-up and seizure outcome (ie, the longer the follow-up, the poorer the seizure outcome). The proportion of patients found to be seizure-free in studies with more than 10 years of follow up was only 45% (pooled data, $n = 5$ studies).¹³ We do not have an explanation for the discrepancy between our results and the pooled data reported by Tellez-Zenteno *et al*. However, it is tempting to speculate that the difference is because their analysis was based on chronologically earlier studies, a factor suggested to be of importance for the outcome.¹³

Our results lend support to the notion that seizure outcome at 2 years after surgery predicts long term outcome.^{6, 9–12} Indeed, from our data this holds true not only at the group level but at the individual level, which is far more interesting for the patient. Also, it has been proposed that one of the major causes of long term seizure relapse is tapering or discontinuation of AED.^{27, 28} This notion is not supported by our results. In our study, the proportion of seizure-free patients who had stopped AED medication (29%) at the long term follow-up was similar to that reported in other studies.^{28–30} None of our patients who discontinued with AED had any relapse. However, the decision to discontinue AED following epilepsy surgery was influenced by several variables (eg, doctor and patient preferences) and has not been prospectively investigated, making it difficult to interpret differences between series.

It has been suggested that epilepsy surgery does not make a significant contribution to actual employment functioning, except for patients already in part-time employment or in those who are underemployed.³¹ On the other hand, a few studies have indicated that patients who become seizure-free may improve or at least maintain their socioeconomic situation.^{4, 5, 32} This is supported by the results of our study showing that the same proportion of patients who became seizure-free were working preoperatively and at the long term follow-up, and that some patients had progressed from part-time to full-time employment. In contrast, patients who continued to have seizures postoperatively had a very poor occupational outcome: only 30% were employed at the long term follow-up and a larger proportion than before operation worked part-time. Employment is known to be compromised by a diagnosis of epilepsy and in a recent survey to employers, Jacoby *et al* found that seizure severity, frequency and controllability were considered important features in the context of employment.³³ Employers' opinions, need for professional driving, psychological and cognitive problems may be negative factors at play in

the poor occupational outcome of those patients who had continuing seizures.

In our study, we also found that 66% of patients who were seizure-free at the long term follow-up had a driving license and drove a vehicle, and there was also a correlation between working status and possession of a driving license (ie, 83% of the patients with a driving license were working).

This patient cohort has been prospectively followed during the first 2 years after operation, not only with regard to seizure outcome but also in relation to cognitive and psychiatric outcome.^{5, 22}

In the psychiatric follow-up of this cohort, 36% of patients had a diagnosis of anxiety and/or depressive disorder in the first 2 years after operation. The presence of postoperative psychiatric morbidity was significantly related to a preoperative history of anxiety and/or depressive disorder, but not to seizure outcome.²² In the present follow-up, 29% of patients reported having had problems with depression and/or anxiety since the 2 year follow-up, again without any clear relation with seizure status. In a recent large prospective study, Devinsky *et al* found that seizure control was associated with a lower frequency of depression and anxiety disorders 2 years after resective epilepsy surgery.³⁴ The smaller sample size in our study might be one explanation for this discrepancy.

The limitations of this investigation should be considered. Our sample size was modest and the results were not compared with those of a control (or a reference) group. However, as indicated previously, only a few studies have carried out long term follow-up¹³ and in these studies there were limitations. In many prospective follow-up studies there was considerable loss of patients over time, resulting in less than 25% of patients at the long term follow-up compared with the 2 year follow-up.^{9–12} In other long term follow-up studies, data from all patients were grouped together for analysis, despite the fact there was a considerable range of follow-up times for individual patients (ie, several years to several decades). The report by Foldvary *et al*⁶ and our report are the only two long term follow-up studies where the majority of patients were followed for a long period (75% >8.5 years and 82% >10 years, respectively), and in both studies seizure outcome 2 year after surgery was found to be a good predictor of long term seizure outcome.

Although there are some studies on psychosocial outcome,^{4, 16–18, 32} none has had the same long term follow-up and/or investigated both seizure frequency and psychosocial outcome. To our knowledge, our report is the only long term follow-up (approximately 10 years) that has analysed both seizure frequency and psychosocial outcome. Since 2005, the prospective follow-up of seizure status, use of AED, and working and living situation reported to the Swedish National Epilepsy Surgery register has been extended from 2 years to 5 and 10 years after surgery for all patients undergoing surgical treatment for epilepsy in Sweden. This will enable us to provide comprehensive long term outcome data on a national level.

Taken together, the value of our study lies in the comprehensive prospective follow-up of a patient cohort over a long time period (approximately 10 years) after epilepsy surgery with no patients lost to follow-up. Seizure outcome in this cohort was similar to that reported in short term controlled studies. Also, there are no indications that this patient cohort had more cognitive or psychiatric morbidity than can be expected in patients who have had epilepsy for more than half of their lives (see table 1) before being referred for surgical evaluation.³⁵ Also, for the majority of seizure-free patients, some of the commonest aims for epilepsy surgery^{14, 15} were still fulfilled 10 years after surgery: they were working, driving and had reduced their AED load.

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