PAPER

Long term outcome of temporal lobe epilepsy surgery: analyses of 140 consecutive patients

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See editorial commentary, page 470

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Objective: To analyse the long term results of temporal lobe epilepsy surgery in a national epilepsy surgery centre for adults, and to evaluate preoperative factors predicting a good postoperative outcome on long term follow up.
Methods: Longitudinal follow up of 140 consecutive adult patients operated on for drug resistant temporal lobe epilepsy.
Results: 46% of patients with unilateral temporal lobe epilepsy became seizure-free, 10% had only postoperative auras, and 15% had rare seizures on follow up for (mean (SD)) 5.4 (2.6) years, range 0.25 to 10.5 years. The best outcome was after introduction of a standardised magnetic resonance (MR) imaging protocol (1993–99): in unilateral temporal lobe epilepsy, 52% of patients became seizure-free, 7% had only postoperative auras, and 17% had rare seizures (median follow up 3.8 years, range 0.25 to 6.5 years); in palliative cases (incomplete removal of focus), a reduction in seizures of at least 80% was achieved in 71% of cases (median follow up 3.1 years, range 1.1 to 6.8 years). Most seizure relapses (86%) occurred within one year of the operation, and outcome at one year did not differ from the long term outcome. Unilateral hippocampal atrophy with or without temporal cortical atrophy on qualitative MR imaging ($p < 0.001$, odds ratio (OR) 5.2, 95% confidence interval (CI) 2.0 to 13.7), other unitemporal structural lesions on qualitative MR imaging ($p \leq 0.001$, OR 6.9, 95% CI 2.2 to 21.5), onset of epilepsy before the age of five years ($p < 0.05$, OR 2.9, 95% CI 1.2 to 7.2), and focal seizures with ictal impairment of consciousness and focal ictal EEG as a predominant seizure type ($p < 0.05$, OR 3.4, 95% CI 1.2 to 9.1) predicted Engel I–II outcome. Hippocampal volume reduction of at least 1 SD from the mean of controls on the side of the seizure onset ($p < 0.05$, OR 3.1, 95% CI 1.1 to 9.2) also predicted Engel I–II outcome.
Conclusions: Outcome at one year postoperatively is highly predictive of long term outcome after temporal lobe epilepsy surgery. Unitemporal MR imaging abnormalities, early onset of epilepsy, and seizure type predominance are factors associated with good postoperative outcome.

Temporal lobe epilepsy is the common form of focal epilepsy. As many patients with this condition do not achieve good seizure control with the available antiepileptic drugs,[1] surgery has gradually become a basic modern treatment for drug refractory temporal lobe epilepsy worldwide. Following the pioneering work of Penfield and Flanigin,[2] Bailey and Gibbs,[3] and Falconer and Serafetinides,[4] the outcome of surgery for temporal lobe epilepsy has been evaluated in large international series.[5 6] Most recently, the first randomised controlled study comparing surgical with medical treatment clearly showed that surgery is superior to prolonged medical treatment in drug refractory temporal lobe epilepsy.[7]

Magnetic resonance (MR) imaging provides a sensitive and specific technique for detecting various abnormalities of the medial temporal lobe structures in vivo. Hippocampal sclerosis is the most common pathological finding in temporal lobe epilepsy, and about 65% of cases of temporal lobe epilepsy may be attributed to lesions arising exclusively in the hippocampus.[8] A correlation between MR imaging based qualitative or quantitative hippocampal volume and histopathologically confirmed hippocampal sclerosis has been demonstrated in numerous studies.[9 10 11 12] Currently, signs of unilateral hippocampal damage or unilateral foreign tissue lesions on MR imaging probably best predict successful postoperative outcome in patients undergoing surgery for drug refractory temporal lobe epilepsy.[13 14 15] In addition to the nature of the underlying epileptogenic lesion, age at the initial precipitating injury has been reported to be one of the major determinants of outcome.[16]

The aims of this study were first, to analyse the long term outcome of temporal lobe epilepsy surgery with respect to seizures in a national epilepsy surgery centre for adults; and second, to evaluate the preoperative factors that predict a good postoperative outcome on long term follow up.

METHODS

Patients

Kuopio University Hospital is the only comprehensive epilepsy surgery centre for adults in Finland. We analysed all adult patients operated on for drug resistant temporal lobe epilepsy at our hospital since the beginning of the epilepsy surgery programme, between 1988 and 1999. Altogether 140 patients (67 women and 73 men) were included in the study. We excluded patients with temporal lesionectomies (without amygdalohippocampectomy) and those in whom any extratemporal cortical excision had been carried out in addition to the temporal resection.

The data were collected retrospectively (by LJ) from the medical records of Kuopio University Hospital and the former

Abbreviations: ILAE, International League against Epilepsy; FOV, field of view; TE, time of echo; TR, time of repetition

Vaajasalo Hospital. The clinical aetiology of the epilepsy was classified preoperatively as probable symptomatic or symptomatic (including patients with hippocampal atrophy in the MR imaging and no other obvious aetiology). Seizure classification followed the ILAE task force on classification and terminology guidelines.[17] Preoperative seizure frequency was calculated for the year preceding the operation, excluding seizures occurring during the video-EEG recording (for seizure calculation, see "postoperative follow up" below). Typical temporal lobe auras were not included in the seizure frequency; however, unclassified seizures (possibly including auras) were included.

The presurgical evaluation

The presurgical evaluation included a neurological examination, MR imaging, ictal video-EEG recording (136 recordings with scalp and sphenoidal electrodes, 50 recordings with subdural strip electrodes), neuropsychological evaluation (n = 135), a sodium amobarbital (WADA) test (n = 140), and psychiatric evaluation (n = 118).

The surgical procedure was classified as "curative" if preoperative assessment indicated unilateral temporal lobe epilepsy. However, if the patient had bitemporal or multifocal epilepsy, or if the epileptic focus could not otherwise be completely removed, the surgery was classified as "palliative." Some patients with dual pathology (hippocampal atrophy in combination with an extrahippocampal structural lesion in the MR imaging), combined temporal and extratemporal abnormality (other temporal lobe lesion than hippocampal atrophy in association with an extratemporal lesion in the MR imaging), bitemporal MR imaging abnormality, or temporal foreign tissue lesion without ictal EEG, were also classified as palliative. In palliative patients only considerable postoperative seizure reduction, rather than freedom from seizures, was probable.

MR imaging

Between 1988 and 1993 the preoperative MR imaging was performed with various kinds of imagers and imaging protocols. High resolution MR imaging with a standardised protocol became available for presurgical evaluation at Kuopio University Hospital in 1993. Since then all candidates for epilepsy surgery have been systematically scanned with a 1.5 T Magnetom (Siemens; Erlangen, Germany). In particular, the temporal lobes were imaged with a tilted coronal 3D magnetisation prepared, rapid acquisition gradient echo (MP-RAGE) sequence with parameters 10/4/1 (TR/TE/excitations), inversion time 250 ms, flip angle 12°; FOV 250 mm, matrix 256 × 192. Experienced neuroradiologists (KP, MP) blinded to the epileptic focus evaluated the images qualitatively. Hippocampal and amygdaloid volumes were measured (KP) for investigational purposes in 67 patients.

The control group for volumetry consisted of 20 healthy individuals (10 women, 10 men), mean (SD) age, 32 (10) years (range 21 to 52 years). The protocol for hippocampal and amygdaloid volumetry has been described previously.[18]

Ictal video-EEG

The video-EEG recordings were initially done with a 32 channel Glonner Biomes 2000 system (Glonner Electronic GmbH, Munich, Germany). In 1993, a new 64 channel telemetry system was introduced (Telefactor Corporation, West Conshohoken, Pennsylvania, USA). In 1997 the video-EEG systems were completely updated (the first Telefactor system was totally modernised and a second 128 channel Telefactor system was obtained). All recordings were carried out with special emphasis on the structural clinical documentation of a given seizure. To obtain the maximum number of proven habitual seizures, antiepileptic drug treatment was individually tapered if necessary. Experienced clinical neurophysiologists (EM, JP) undertook the EEG analyses.

Neuropsychological evaluation

Neuropsychological assessment was done (by HH) using a comprehensive test battery, following clinical diagnostic requirements. Measures of verbal memory included delayed recall of paired associates, delayed story recall, and the combined scores of delayed recall of stories and paired associates (c score).[19] Assessment of visual memory included delayed recall of figures[19] and delayed recall of the Rey-Osterrieth complex figure.[20 21]

Surgical procedure

Controlled respiration with NO_2-oxygen anaesthesia was used during the surgical procedure (MV). The anterior temporal area was exposed from a large frontotemporal skin flap, removing temporal bone lambeau. After the dura was opened, electrocorticography with neocortical and acute deep mesial electrodes was undertaken (EM, JP) to tailor the possible neocortical resection and to measure epileptic activity in the hippocampus and the amygdala. Intravenous methohexitone (methohexital) (40 mg) was used to enhance the occurrence of focal epileptiform EEG abnormalities on electrocorticography. Depending on the earlier video-EEG findings and the acute electrocorticographic information, the anterior hippocampus and the amygdala, with or without the neocortical area, were removed using a microneurosurgical technique.

Postoperative follow up

Patients from the primary Kuopio University Hospital district have been followed up as outpatients since the operation. The patients referred from other parts of Finland were followed up as outpatients for three years. Routine visits were scheduled for all patients at three months, one year, and three years after the operation. In addition, each patient was contacted by telephone for further historical details and an up to date follow up. In problematic cases, medical records from other hospitals or community health centres were obtained. The original prospectively recorded seizure calendars were obtained whenever possible. Postoperative outcome was assessed according to a classification adapted from Engel.[5] However, seizure-free patients and patients with postoperative auras only are displayed as two distinct groups following the suggestions of the new ILAE classification.[22] Neighbourhood seizures (seizures occurring one month postoperatively) were excluded from the analyses.

A complication was classified as major if it affected activities of daily living, lasted more than three months, or included any significant neurological deficit. Minor complications resolved within three months.[23] Information on causes of death was acquired from the Finnish National Registry of Mortality (Statistics Finland). All specimens for pathological examination were evaluated by one experienced neuropathologist (IA).

Statistics

The data were analysed using SPSS WIN 9.0 software (SPSS Inc, Chicago, Illinois, USA). The postoperative outcome was analysed with the χ^2 test for comparisons between patient groups, and with life tables. The predictive value of different preoperative factors with respect to outcome was assessed by logistic regression analysis. The demographic variables included history of (complex) febrile seizures, age at onset of epilepsy, duration of epilepsy, clinical aetiology of epilepsy, preoperative seizure frequency (divided into subgroups by quartiles), seizure type predominance, and type of operation. Subgroups of qualitative MR imaging consisted of: hippocampal atrophy with or without temporal cortical atrophy; other unilateral structural abnormality in the temporal lobe; and other. All volumetric data for regression analyses were normalised as previously described.[24] The preoperative ictal EEG was reclassified (by EM) for regression analyses into two

subgroups consisting of unilateral mesial or temporal ictal onset, and other. A subset of neuropsychological tests evaluating the delayed visual or verbal memory (see above) was also chosen for analyses. A probability (p) value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics of operated patients

The median age of the patients at the time of the operation was 32 years (range 14 to 54). The median age at onset of epilepsy was 12 years (range 0.1 to 43) and median duration of epilepsy at the time of operation 19 years (range 2 to 47). Preoperative seizure frequency varied from 10 to 1655 seizures a year (median 78) during the year preceding the operation. In the majority of patients (82%, n = 115), most of the seizures were focal, with ictal impairment of consciousness and focal ictal EEG (median 75, range 7 to 916).

The preoperative clinical aetiology of the epilepsy was probable symptomatic in 36% of the patients (n = 50) and symptomatic in 64% (n = 90). The symptomatic aetiologies included hippocampal atrophy with no other aetiology (28), asphyxia (15), central nervous system infection (13), tumour or cystic lesion (12), focal cortical dysplasia (9), brain contusion (5), and miscellaneous aetiologies (8). In 10% of the patients (n = 14), first degree relatives had a history of epilepsy. Febrile seizures were identified in 21% of the patients (n = 30), and especially complex febrile seizures in 9% (n = 12).

On the basis of the preoperative assessment, 103 patients (74%) had unilateral temporal lobe epilepsy. Forty five patients had seizure onset on the left and 58 on the right. Thirty seven patients were operated on palliatively. These patients had bitemporal seizure onset (18), unitemporal but extratemporally extending seizure focus (6), multifocal epilepsy (2), dual pathology (2), combined temporal and extratemporal abnormality (2), bitemporal MR imaging abnormality (2), or posterior neocortical seizure onset in the dominant temporal lobe together with ipsilateral speech dominance (2). Three patients with temporal foreign tissue lesions without ictal EEG were also classified in the palliative group.

The operative procedures included anterior temporal resection and amygdalohippocampectomy alone (113) or combined with lesionectomy (9), and selective amygdalohippocampectomy (18).

Preoperative qualitative MR imaging

Qualitative MR imaging showed a unilateral structural abnormality in the temporal lobe in 53% of the patients with unilateral temporal lobe epilepsy (n = 55) (table 1). This included hippocampal atrophy with (n = 9) or without (n = 24) temporal cortical atrophy, and other unilateral structural lesions of the temporal lobe (n = 22). MR imaging was normal in 34% of patients with unilateral temporal lobe epilepsy (n = 35). The MR imaging data were also evaluated in subgroups of patients imaged before or after the introduction of a standardised MR imaging protocol (operated on between 1988 and 1993 or between 1993 and 1999, respectively). Between 1988 and 1993, a unilateral structural abnormality of the temporal lobe was found in 35% of patients (n = 17) and MR imaging was normal in 53% (n = 26). After the introduction of a standardised MR imaging protocol, the proportion of patients with a unitemporal structural abnormality increased to 70% (n = 38, $p < 0.001$), and those with normal MR imaging decreased to 17% (n = 9).

The largest subgroup among the palliatively operated patients comprised those with normal qualitative MR imaging (n = 13) (table 1). When we evaluated the MR imaging data in subgroups of patients imaged before or after the introduction of a standardised MR imaging protocol, the changes were identical to those observed in unilateral temporal lobe epilepsy ($p < 0.05$). Between 1988 and 1993, a unilateral structural abnormality of the temporal lobe was found in one patient, dual pathology or concomitant temporal and extratemporal abnormality in four, and normal MR imaging in eight. Between 1993 and 1999, there was an increase in the number of unitemporal structural abnormalities identified (to nine) and a decrease in cases with normal MR imaging (to five); six patients had dual pathology, concomitant temporal and extratemporal abnormality, or extratemporal pathology, and four had other aetiologies.

Table 1 Results of preoperative qualitative magnetic resonance imaging

Imaging findings	n
Patients with unilateral TLE	103
Normal	35
Unilateral hippocampal atrophy	24
Unilateral hippocampal and temporal cortical atrophy	9
Other unitemporal structural lesion	22
Bilateral temporal cortical abnormality	2
Dual pathology*	2
Extratemporal abnormality	3
General brain atrophy, cerebellar atrophy, or minor vascular lesions in the watershed area	6
Patients with palliative operations for TLE	37
Normal	13
Unilateral hippocampal atrophy	6
Unilateral hippocampal and temporal cortical atrophy	1
Other unitemporal structural lesion	3
Bilateral hippocampal atrophy	1
Dual pathology*	3
Combined temporal and extratemporal abnormality	6
Extratemporal abnormality	1
General brain atrophy or cerebellar atrophy,	3
Total	140

*Dual pathology other than unilateral hippocampal and temporal cortical atrophy.
TLE, temporal lobe epilepsy.

Outcome with respect to seizures

Figure 1 shows the long term outcome of surgery with respect to postoperative seizures in the different patient groups. All patients were followed up for a minimum of one year, except for one patient who died of a prolonged epileptic seizure three months after the operation.

Unilateral temporal lobe epilepsy

One year after the operation, 45% of the patients (n = 46) were completely seizure-free and 12% (n = 12) had only postoperative auras. Rare seizures (Engel II, fewer than three seizures a year) were identified in 12% of the patients (n = 12). An Engel I–II outcome was thus observed in 68% of the patients. In addition, 13% of the patients (n = 13) had a worthwhile seizure reduction (Engel III—at least an 80% seizure reduction), while 19% (n = 19) did not benefit from surgery (Engel IV). The results of the long term follow up did not differ from the results of the one year follow up ($p > 0.05$ between groups, fig 1A). On the most recent follow up date available (mean (SD) follow up, 5.4 (2.6) years; range three months to 10.5 years), 46% (n = 47) of the patients were seizure-free, 10% (n=10) had only postoperative auras, and 15% (n = 15) had rare seizures. In addition, 14% of patients (n = 14) achieved a worthwhile seizure reduction and 17% (n = 17) did not benefit from surgery (Engel IV).

We then evaluated the surgical results independently in patients operated on with or without a standardised preoperative MR imaging protocol. There was a significant difference in the postoperative outcome between these two

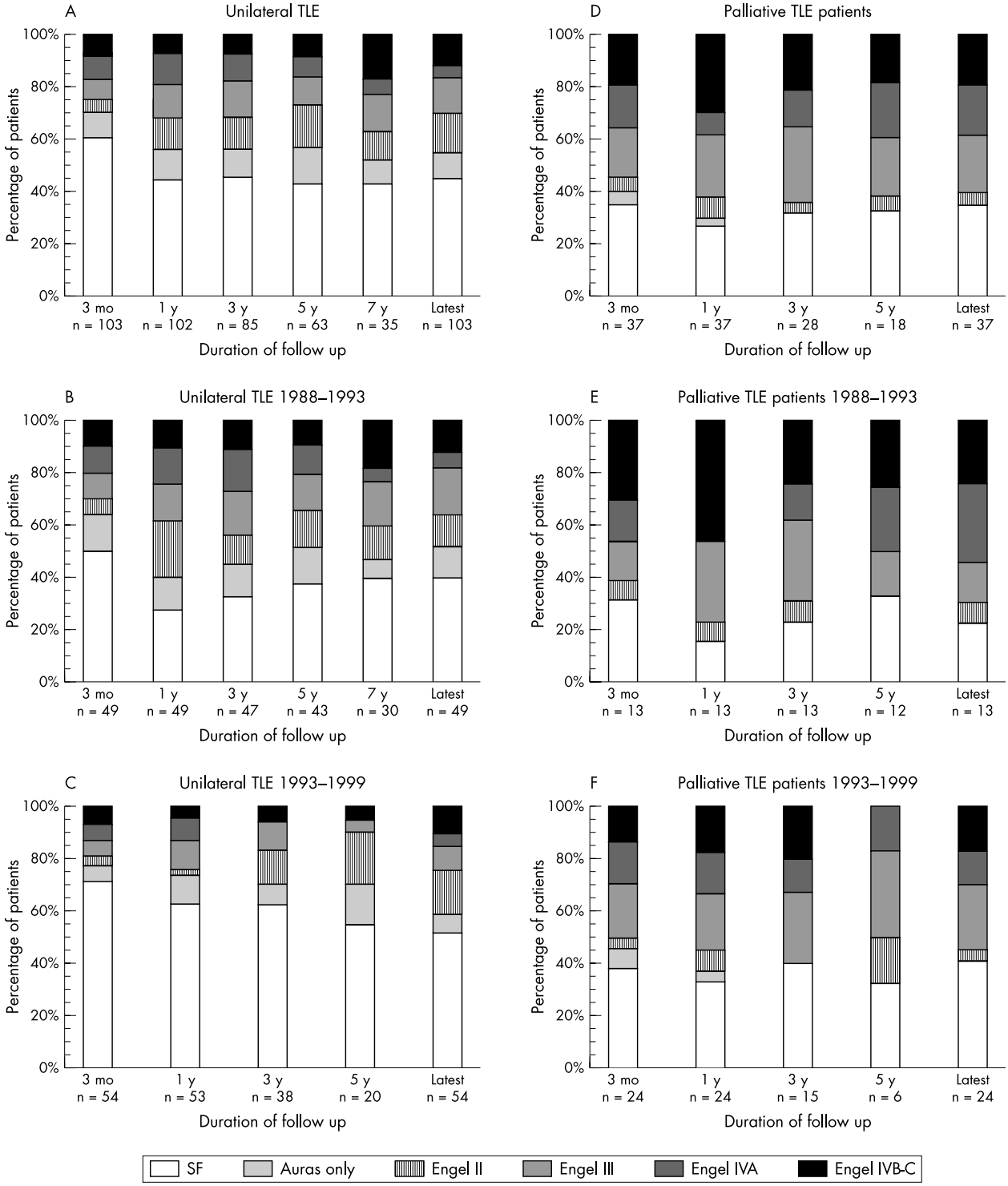

Figure 1 Outcome with respect to seizures as a percentage of patients in different Engel's classes at different time intervals. (A) All patients with unilateral temporal lobe epilepsy (mean follow up 5.4 years). (B) Patients with unilateral temporal lobe epilepsy imaged without a specified magnetic resonance (MR) imaging protocol (1988–1993; median follow up 7.7 years). (C) Patients with unilateral temporal lobe epilepsy imaged with a standardised MR imaging protocol (1993–1999; median follow up 3.8 years). (D) All palliatively operated temporal lobe epilepsy patients (mean follow up 4.4 years). (E) Palliatively operated temporal lobe epilepsy patients imaged without a specified MR imaging protocol (1988–1993; median follow up 5.9 years). (F) Palliatively operated temporal lobe epilepsy patients imaged with a standardised MR imaging protocol (1993–1999; median follow up 3.1 years). Auras only, seizure-free patients with postoperative auras only; Engel II, rare seizures (fewer than three seizures a year); Engel III, worthwhile seizure reduction (a reduction in seizure frequency of at least 80%); Engel IVA, patients with a seizure reduction of at least 50%; Engel IVB-C, no change in seizure frequency, or more frequent seizures (n = 1); latest, latest available follow up data; mo, months; SF, completely seizure-free patients; y, years.

groups ($p \leqslant 0.001$ for one year outcome). Altogether, 49 patients with unilateral temporal lobe epilepsy were operated on before the introduction of a standardised MR imaging protocol (between 1988 and 1993). One year after the operation 61% (n = 30) of the patients achieved Engel I–II outcome, with only 27% (n = 13) being seizure-free. In the long term

Table 2 Postoperative follow up of initially seizure-free patients

Findings	3 m	1 y	2 y	3 y	4 y	5 y	7 y	9 y	Latest*
Seizure-free	76 (86)	56 (64)	44 (58)	40 (54)	31 (50)	26 (50)	13 (45)	6 (50)	51 (58)
Originally seizure-free	76 (86)	56 (64)	44 (58)	38 (51)	30 (48)	23 (44)	12 (41)	5 (42)	47 (53)
Became seizure-free†		0 (0)	0 (0)	2 (3)	1 (2)	3 (6)	1 (3)	1 (8)	4 (5)
Auras only	12 (14)	13 (15)	9 (12)	9 (12)	8 (13)	9 (17)	3 (10)	2 (17)	10 (11)
Engel II‡		13 (15)	10 (13)	9 (12)	11 (18)	10 (19)	5 (17)	2 (17)	13 (15)
Engel III‡		4 (5)	9 (12)	12 (16)	7 (11)	2 (4)	3 (10)	1 (8)	7 (8)
Engel IV‡		2 (3)	4(5)	4(5)	5 (8)	5(10)	5 (17)	1 (8)	7 (8)
Total	88 (100)	88 (100)	76 (100)	74 (100)	62 (100)	52 (100)	29 (100)	12 (100)	88 (100)

Values are n (%) of patients.
*Latest: latest available follow up data.
†Some seizures after surgery but now seizure-free for at least two years.
‡Engel II: fewer than three seizures a year; Engel III: worthwhile seizure reduction (at least an 80% seizure reduction); Engel IV: no worthwhile seizure reduction (less than 80% seizure reduction).
m, months; y, years.

follow up (at the most recent follow up date available, median 7.7 years, range 1.0 to 10.5 years), 39% (n = 19) of the patients were seizure-free, 12% (n = 6) had only postoperative auras, and 12% (n = 6) had rare seizures. Additionally, 18% (n = 9) of the patients achieved a worthwhile seizure reduction, while 18% (n = 9) had no worthwhile seizure reduction (fig 1B).

A total of 54 patients with unilateral temporal lobe epilepsy were operated on after the introduction of the standardised MR imaging protocol (between 1993 and 1999). One year after the operation, 61% (n = 33) of these were free of seizures, 11% (n = 6) had only postoperative auras, and 2% (n = 1) had rare seizures. Eleven per cent (n = 6) achieved a worthwhile seizure reduction. On the most recent follow up date (median follow up 3.8 years, range three months to 6.5 years) 52% (n = 28) of the patients were seizure-free, 7% (n = 4) had only postoperative auras, and 17% (n = 9) had rare seizures. Nine per cent of the patients (n = 5) achieved a worthwhile seizure reduction. Altogether, after the introduction of the standardised MR imaging protocol 74% of patients with unilateral temporal lobe epilepsy achieved Engel I–II outcome at the one year follow up and 76% at the long term follow up (fig 1C).

Palliative group

As expected, the outcome was better in patients with unilateral temporal lobe epilepsy than in the palliative group ($p < 0.05$). One year after the operation 27% (n = 10) of palliative patients were free of seizures, 3% (n = 1) had only postoperative auras, and 8% (n = 3) had rare seizures. Additionally, 24% (n = 9) achieved a worthwhile seizure reduction. A minimum of 80% seizure reduction was therefore achieved by 62%. On the most recent follow up date available, 35% of these patients (n = 13) became seizure-free, 5% (n = 2) had rare seizures, and 22% (n = 8) achieved a worthwhile seizure reduction. The mean (SD) follow up was 4.4 (2.2) years (range 1.0 to 9.0). The results of long term follow up in the palliative group also did not differ from the results at the one year follow up ($p > 0.05$ between groups (fig 1D)).

When the outcome of palliative surgery was analysed in the subgroups operated on before or after the introduction of the standardised preoperative MR imaging protocol, similar trends of improved outcome were seen as in unilateral temporal lobe epilepsy ($p > 0.05$) (fig 1E–F). Twenty four patients were operated on after the introduction of the standardised MR imaging protocol (between 1993 and 1999). On the most recent follow up date available (median follow up 3.1 years, range 1.1 to 6.8), 42% (n = 10) of these patients were free of seizures, 4% (n = 1) had rare seizures, and 25% (n = 6) achieved a worthwhile seizure reduction. A seizure reduction of at least 80% (Engel I–III outcome) was therefore achieved on long term follow up by 71% (n = 17) of the patients who had palliative surgery after the introduction of the standardised MR imaging protocol.

Long term outcome in patients with initial successful outcome

We first analysed the long term outcome in all patients (n = 140) using life tables. Eighty six per cent of all seizure relapses (71 of 83) occurred within one year of the operation. Late seizure relapses (> 2 years after the operation) were observed in only 5% of all patients (n = 7), and 8% of all relapses were late relapses. The majority of patients with late relapses had unilateral temporal lobe epilepsy with a symptomatic aetiology (n = 6), and pathological examination showed hippocampal sclerosis (n = 5) or cortical microdysgenesis (n = 1). Late relapses were often preceded by a specific explanatory factor such as withdrawal of antiepileptic drug treatment (n = 3) or hyponatraemia (n = 1), and they did not lead to subsequent intractable seizures in any of the patients.

Initially 63% (n = 88) of all patients were seizure-free or had only postoperative auras at the first postoperative controls visit (three months postoperatively) (table 2). Fifty three per cent of these remained completely free of seizures on long term follow up (mean (SD), 5.2 (2.6) years, range 1.0 to 10.5), whereas 5% experienced some seizures but again became seizure-free (for at least two years). In addition, 11% had only postoperative auras and 15% had rare seizures. Seventeen per cent (n = 9) of patients with initial Engel II–IV outcome became free of seizures, and 8% (n = 4) had rare seizures on long term follow up (mean (SD), 4.9 (2.5) years, range three months to 10.0 years).

Analyses of different preoperative factors with respect to outcome

Hippocampal atrophy with or without temporal cortical atrophy ($p < 0.001$, odds ratio (OR) 5.2, 95% confidence interval (CI) 2.0 to 13.7) and other unilateral structural lesions of the temporal lobe ($p \leqslant 0.001$, OR 6.9, 95% CI 2.2 to 21.5) on qualitative MRI predicted Engel I–II outcome on long term follow up (using the latest available follow up data). Additional predictive factors were onset of epilepsy before the age of five years ($p < 0.05$, OR 2.9, 95% CI 1.2 to 7.2; n = 43) and focal seizures with ictal impairment of consciousness and focal ictal EEG as a predominant seizure type ($p < 0.05$, OR 3.4, 95% CI 1.2 to 9.1; n = 115). When patients with quantitative MR imaging data were analysed separately (n = 67), a volume reduction of at least 1 SD (10% for both left temporal lobe epilepsy and right temporal lobe epilepsy) from the mean of controls on the side of the seizure onset was also a predictor of Engel I–II outcome ($p < 0.05$, OR 3.1, 95% CI 1.1 to 9.2). A history of febrile seizures ($p = 0.069$, OR 2.4, 95% CI 0.9 to 6.0) or complex febrile seizures, the clinical aetiology of the epilepsy, the duration of the epilepsy, seizure frequency, localisation of ictal onset by video-EEG, neuropsychological data, and the type of operation did not predict Engel I–II postoperative outcome in this study.

Table 3 Complications in 140 patients operated on for temporal lobe epilepsy

Complication	Minor	Major
Surgical		
Haematoma or haemorrhage	4*	1
Hydrocephalus	1	
Aseptic meningitis	5†	
Infection	1	
Deep vein thrombosis	1†	
Neurological		
Homonymous hemianopia		1
Dysphasia	3†	1
Total number of complications	15	3
Total number of patients with complications	13	3

*Three chronic subdural haematomas and one subdural effusion.
†One patient with transient dysphasia also had aseptic meningitis; one patient with transient dysphasia also had deep venous thrombosis.

Complications and mortality

Altogether three major complications (2.1%) and 15 minor complications (10.7%) were identified (table 3). Major complications included prolonged aphasia, homonymous hemianopia, and subarachnoid haemorrhage caused by an intraoperative depth electrode. The most important minor complications included chronic subdural haematoma (n = 3), subdural effusion (resolved without operative treatment), hydrocephalus, and bone lambeau infection.

Information on the causes of death was acquired from the Finnish National Registry of Mortality in order to determine whether the death was related to epilepsy. Altogether six patients died during the follow up. Two of these patients had been completely free of seizures postoperatively (14 and 27 months), and four had an unfavourable surgical outcome. No mortality was attributable to surgery. The causes of death related to epilepsy (four of the six) were sudden unexpected death in epilepsy, suicide (depression related to poor seizure control), and prolonged epileptic seizure (n = 2). Epilepsy related deaths were prominent among patients with recurrent postoperative seizures (n = 3).

Pathological examination of resected tissue

Pathological examination of resected tissue showed three different entities: patients with hippocampal sclerosis or gliosis (n = 60); patients with tumours or cystic lesions (n = 18); and patients with cortical microdysgenesis (n = 17) (table 4). Altogether hippocampal sclerosis was confirmed in 41 of 46 symptomatic patients with hippocampal atrophy on the preoperative MR imaging. Focal cortical dysplasia was observed in one patient, and a benign or low grade tumour (dysplastic neuroepithelial tumour, ganglioglioma, hamartoma, or oligodendroglioma) in six patients who were preoperatively evaluated as probable symptomatic. Hippocampal sclerosis (n = 10), hippocampal gliosis (n = 3), or hippocampal microdysgenesis (n = 7) were identified in 40% of patients with a preoperative probable symptomatic aetiology of their epilepsy (n=20).

Table 4 Pathology of resected tissue

	n
No diagnostic lesions	13
Sclerosis/gliosis or numerous corpora amylacea	69
Hippocampus	60
Hippocampal sclerosis	55
Hippocampal gliosis	5
Amygdala	4
Temporal lobe	5
Microdysgenesis	24
Hippocampus	7
Temporal lobe	17
Dysplasia	3
Temporal lobe	3
Tumour or cystic lesion	18
Oligodendroglioma (low grade)	4
Astrocytoma (low grade)	1
Ganglioglioma	3
Hamartoma	3
Dysplastic neuroepithelial tumour	3
Cavernous haemangioma	3
Cysta epidermoides	1
Other	
Perivascular haemosiderin laden macrophages	1
Sample not available or not evaluable	12
Total	140

DISCUSSION

The purpose of this longitudinal follow up study was to analyse the long term results of temporal lobe epilepsy surgery in adults, and to identify the preoperative factors that predict a good postoperative outcome on long term follow up. Altogether 140 consecutive adult patients operated on for drug resistant temporal lobe epilepsy were included. Predictive factors for Engel I–II postoperative outcome were unilateral hippocampal atrophy with or without temporal cortical atrophy on qualitative MR imaging, other unitemporal structural lesions on qualitative MR imaging, small quantitative hippocampal volume on the side of the seizure onset, onset of epilepsy before the age of five years, and focal seizures with ictal impairment of consciousness and a focal ictal EEG as a predominant seizure type. The best outcome was observed after the introduction of a standardised MR imaging protocol (between 1993 and 1999): 52% of patients with unilateral temporal lobe epilepsy were seizure-free and 7% had only postoperative auras on long term follow up. A reduction in seizure frequency of at least 80% on long term follow up was achieved by 71% of patients who received palliative surgery, indicating that palliative surgical treatment can be beneficial for selected patients with temporal lobe epilepsy without a restricted unilateral seizure focus. Most seizure relapses (86%) occurred within the first postoperative year, and outcome at one year postoperatively was highly predictive of long term outcome after both "curative" (unilateral) and palliative surgery.

Outcome with respect to seizures

Previous studies have usually classed patients with postoperative auras as seizure-free, as defined in the original Engel's classification (Engel IB).[5] However, we have classified seizure-free patients (ILAE 1) and patients with postoperative auras only (ILAE 2) as two distinct entities following the suggestions of the new ILAE classification.[22] The ILAE classification counts seizure days instead of the number of seizures and therefore we were unable to use if fully in our study.

In the long term follow up, 46% of the patients with unilateral temporal lobe epilepsy became completely free of seizures and 10% had only postoperative auras. An Engel I–II outcome was achieved by 70% of patients. However, an improved outcome was observed after the introduction of the 1.5 T imager.

Assessments of surgical series show that 37–71% of patients operated on for drug refractory temporal lobe epilepsy become seizure-free,[4 7 25 26 27 28 29 30 31 32 33] and comparable outcomes can also be expected in the elderly.[34] A meticulous analyses of 126

studies published between 1991 and 2000 showed that a median of 70% of patients became seizure-free (range 33% to 93%), suggesting an improvement in the outcome in more recent studies.[35] Furthermore, selected patient populations—such as patients with hippocampal sclerosis,[36 37] patients with complex febrile seizures,[38] or patients with foreign tissue lesions[39 40]—have significantly higher success rates, with 80–94% of patients becoming seizure-free. Outcome at one year postoperatively was highly predictive of long term outcome, both in unilateral temporal lobe epilepsy and in the palliative group. This is in line with previous observations.[26 41] Moreover, 86% of the seizure relapses occurred within the first postoperative year. Late relapses were observed in 5% of patients, but these did not lead to subsequent seizure intractability. Late recurrences were associated with a symptomatic aetiology of epilepsy, hippocampal sclerosis, and specific explanatory factors such as withdrawal of antiepileptic drug treatment. In the extensive study of Foldvary and coworkers (mean follow up 14 years), 86% of recurrences took place within two years of surgery, and seizure-free status at two years was predictive of long term remission. Later recurrences tended not to lead to medical intractability.[33] In another recent study,[32] 66% of patients with temporal lobe epilepsy were seizure-free at one year after surgery, 63% at two years, 60% at five years, and 55% at 10 years. Follow up both at one and two years was highly predictive of the long term outcome, and most late recurrences were associated with hippocampal sclerosis or temporal lobe gliosis. In conclusion, most seizure relapses occur within two years of operation, and the outcome at one year[14 28 42] or two years postoperatively[31 33 43] is highly predictive of the long term outcome.

Prognostic factors for successful postoperative outcome

Unilateral hippocampal atrophy with or without temporal cortical atrophy on qualitative MR imaging, other unitemporal structural lesions on qualitative MR imaging, and a hippocampal volume reduction of at least 1 SD from the mean of controls on the side of seizure onset predicted Engel I–II outcome in a logistic regression analyses. Qualitative MR imaging reveals lateralising abnormalities in 74%, and hippocampal atrophy in 52–63% of patients undergoing epilepsy surgery for temporal lobe epilepsy.[13 39 44] Volumetric MR imaging studies have shown that up to 88% of patients with drug resistant temporal lobe epilepsy have hippocampal damage on quantitative MR imaging.[45] Both ipsilateral hippocampal damage and ipsilateral foreign tissue lesions on MR imaging are important predictors of successful postoperative outcome in patients undergoing surgery for drug refractory temporal lobe epilepsy.[13 14 15] In various different studies, 62–96% of patients with hippocampal damage on MR imaging became seizure-free.[36 39 44] On the other hand, only 16–56% of patients with normal MR imaging achieve seizure-free status.[13 15 39 44] The value of MR imaging is increased when the imaging data are coanalysed with interictal or ictal EEG recordings.[14 46 47]

Most studies investigating the prognostic value of MR imaging, including our own, have failed to include patients in whom surgery was rejected because an epileptogenic lesion was not identified. Thus the predictive value of hippocampal damage seen on MR imaging may be overestimated by small retrospective studies of outcome in highly selected patients.[48] In a recent study of consecutive patients evaluated for surgical treatment of temporal lobe epilepsy it was found that quantitative MR imaging had a sensitivity of 55% and specificity of 86% for detecting mesial temporal sclerosis in comparison with ictal foramen ovale recordings. Conventional diagnostic MR imaging had a sensitivity of 42% and a specificity of 80% for detecting mesial temporal sclerosis.[49] Thus the prognostic value of ictal EEG is probably underestimated in postoperative series compared with studies that include all evaluated surgical candidates. This might explain why localisation of ictal onset by video-EEG did not predict surgical success in our study.

Onset of epilepsy before the age of five years and focal seizures with ictal impairment of consciousness and a focal ictal EEG as a predominant seizure type were also independent predictive factors for Engel I–II outcome. Preoperative convulsive seizures have been associated with a poor surgical outcome before, but most previous studies have not identified an association between age of onset of epilepsy and postoperative outcome.[35] However, hippocampal sclerosis, early onset of epilepsy, and focal seizures with ictal impairment of consciousness and a focal ictal EEG are common and well described features of mesial temporal lobe epilepsy.[50 51] An early onset of epilepsy has also been recognised as a significant risk factor for hippocampal volume loss in several studies.[52 53 54]

An unexpectedly small proportion of patients with a history of febrile seizures (21%) or complex febrile seizures (9%) were identified. Retrospective studies from tertiary epilepsy centres suggest that many patients with drug resistant temporal lobe epilepsy have a history of complex febrile seizures.[55] There is also an association between prolonged febrile seizures in early childhood and mesial temporal sclerosis,[56] as well as between complex febrile seizures and a successful postoperative outcome.[35] Retrospective estimation of febrile seizures is difficult and prone to error. The details of early childhood seizures are not often clearly recalled. There are also different definitions of febrile seizures. Highly selected cross sectional studies with a small number of patients from a single centre also limit the interpretation of the available data.[57]

Palliative surgery

Altogether, 26% of the patients in our study received palliative opertions. These were mainly based on independent bitemporal seizure onset in subdural video-EEG recordings. A cut off point of 80% for patients with a strong unilateral predominance was used as a guideline.[58] However, the finding that fewer than 80% of seizures originate from one temporal lobe should not be an absolute contraindication to temporal lobectomy.[59] A satisfactory outcome is possible in patients with bilaterally symmetrical mesial temporal sclerosis by MR imaging criteria.[60] As the expected outcome in patients having palliative operations clearly differs from that in patients with unilateral temporal lobe epilepsy, different outcome measures should be used. We suggest that at least 70% of patients with palliative operations should achieve a minimum of 80% seizure reduction postoperatively.

Complications and mortality

The percentage of complications in the present study was comparable with a recently published Swedish survey.[23] No mortality was attributable to the surgery itself. However, four of the six deaths in our consecutive follow up series were related to epilepsy. Although deaths directly related to epilepsy surgery are very rare, it remains uncertain to what extent a reduced seizure frequency and an improved quality of life can reduce mortality in patients operated on for temporal lobe epilepsy. Mortality is reduced in seizure-free patients compared with patients with recurrent postoperative seizures.[61] Surgery for temporal lobe epilepsy surgery does not, however, reduce the overall mortality associated with chronic epilepsy.[62]

Pathological examination of resected tissue

In addition to hippocampal sclerosis, tumours, or cystic lesions, a large proportion of patients had isolated cortical microdysgenesis in the temporal cortex. Amygdalar pathology, on the other hand, was rare. Cortical microdysgenesis is characterised by grey matter heterotopias, increased cellularity of the white matter and neuronal clustering, satellitosis, and rows of perivascular glia.[63] The significance of these microscopic findings in epilepsy is controversial. Certain characteristics of cortical microdysgenesis have been associated with

the epileptic process, while others appear to be normal variants.[64] Although classified as a malformation, it has been suggested that cortical microdysgenesis could develop as a result of epilepsy.[63] We did not assess the impact of pathological analyses on the outcome of surgery in this study, but different features of cortical microdysgenesis have been associated both with good[65] and with poor[64] surgical outcome.

Conclusions

Surgery is better than prolonged medical treatment in adult patients with drug refractory temporal lobe epilepsy. In this longitudinal follow up study we analysed the long term results of temporal lobe epilepsy surgery in a national epilepsy surgery centre for adults, and identified the prognostic factors for postoperative outcome. In addition to temporal lobe abnormalities on qualitative MR imaging, an early onset of epilepsy, seizure type predominance, and quantitative hippocampal volume reduction on the side of the seizure onset also predicted Engel I–II postoperative outcome in the long term follow up. Postoperatively, 86% of the seizure relapses occurred within the first year, and the outcome at one year did not differ from the long term outcome in patients having either surgery for unilateral temporal lobe epilepsy or palliative surgery. Furthermore, palliative surgical treatment was beneficial in a selected group of patients with temporal lobe epilepsy who did not have a restricted unilateral seizure focus. As many patients were referred for surgical evaluation long after the drug resistant seizure disorder had developed, we should now be considering the optimal timing of surgery.

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