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Survival Analysis of the Surgical Outcome of Temporal Lobe Epilepsy Due to Hippocampal Sclerosis

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Summary: *Purpose:* Surgical results in patients with mesial temporal lobe epilepsy due to hippocampal sclerosis (MTLE/HS) are often reported in conjunction with other etiologies of TLE.

Methods: We prospectively collected surgical outcome data for 2 to 11 years for 134 consecutive patients who specifically had MTLE and unilateral HS, according to magnetic resonance imaging (MRI) and confirmed by histopathology. Sixty-five had postoperative neuropsychological testing. Outcome was analyzed by using Engel's classification (a) through Kaplan–Meier estimated survival curves (as a function of the time to seizure recurrence), (b) as percentage of patients in each outcome class on a yearly basis, and (c) at the last updated follow-up.

Results: Kaplan–Meier estimates of complete seizure freedom (Engel's class IA) for years 1, 2, 5, and 10 were 85%, 77%, 74%, and 66%, and of Engel's class I were 89%, 86%, 83%, and 81%. Only nine (6.7%) patients had outcome classes III or IV at any point during follow-up. Of the patients tested, 26% of those operated on the left side and 22% of those operated on the right had postoperative decline of >1 SD in verbal or visual memory, respectively.

Conclusions: High rates of seizure freedom can be obtained and remain stable over the years in patients operated on for unilateral MTLE/HS, even in countries with limited resources. **Key Words:** Temporal Lobe epilepsy—Hippocampal sclerosis—Epilepsy surgery—Long-term outcome.

Surgical treatment is usually indicated for patients with medically refractory mesial temporal lobe epilepsy due to unilateral hippocampal sclerosis (MTLE/HS) (1). Nonetheless, debate still exists on the actual rates of postoperative seizure control, the stability of surgical results over time (2,3), and frequency of surgical complications. Most outcome studies include a small number of patients, data regarding complications are limited, and postoperative follow-up periods are usually short (4).

Most outcome studies of temporal resections include patients with different etiologies, and this precludes preoperative prognostication based on specific etiologic substrates. In particular, only a few reports exist of long-term surgical outcome of patients in whom TLE is specifically due to unilateral HS: the more recent ones have reported favorable results sustained over time (5,6), whereas a previous report suggested significant rates of seizure recurrence (7). Other potentially relevant issues are that outcome studies are usually cross-sectional, Kaplan–Meier survival curves reflecting the probability of remaining seizure free over time are seldom presented, and the consequences of achieving an entirely seizure-free outcome, as compared with persistence of auras, occasional breakthrough seizures, or recurrence of attacks on reduction or discontinuation of antiepileptic drugs (AEDs) are not considered separately (4,7–10). These more detailed, yet clinically significant, aspects of surgical outcome demand recognition of specific subclasses within accepted outcome classification scales (11). Because most of these issues ultimately affect postoperative quality of life, these uncertainties still hamper surgical referrals (6,12,13).

Assuming a conservative prevalence of seven per 1,000 inhabitants, Brazil has >1 million persons with epilepsy. In the mid-1990s, the Brazilian government included preoperative evaluation and surgical treatment of patients with medically refractory epilepsies in the select group of "high-complexity procedures" officially funded by the National Health System (Sistema Unico de Saude; SUS). Seven tertiary university hospitals with multidisciplinary teams have been accredited and are periodically monitored. Each Center performs 80 to 100 operations per year, and public funding and monitoring crafted a model in which the usual socioeconomic pyramid is reversed: the

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poorest patients are the ones with the easiest access to the system. This governmental policy of allocating significant resources into surgical treatment for epilepsy is unique for a developing country. In Porto Alegre, one of these Centers, we have been following a homogeneous cohort of patients evaluated and operated on over the last 11 years with the specific syndrome of MTLE/HS. Here, we report the longitudinal evolution of these patients according to the clinically relevant subclasses of Engel's outcome classification system (11) and show that restricting the analysis to a specific etiologic subgroup of TLE may allow a better prediction of long-term surgical outcome.

PATIENTS AND METHODS

Surgical outcome in relation to seizure control and postoperative motor and language complications was analyzed yearly for all 135 consecutive patients operated on for MTLE/HS, from January 1992 to December 2000. These were drawn from a total of 437 patients operated on for intractable epilepsy in the same period, 226 of whom had surgery for TLE. In addition to the 135 with HS (60%), 49 patients with TLE had low-grade gliomas**,** nine had nonspecific gliosis, seven had cavernomas, five had dysgenetic lesions, and in the remaining 21, magnetic resonance imaging (MRI) and pathology were normal. Patients were followed up for a minimum of 2 to 11 years, with a mean of 5.47. One (0.7%) was lost to follow-up. The number of patients whose outcome was analyzed on a yearly basis is shown in Table 1.

Patients had (a) clinical features of MTLE (14–16); (b) interictal scalp/sphenoidal EEGs displaying unilateral or bilateral independent anteromesial temporal epileptic discharges; (c) at least one electroclinical seizure on scalp/sphenoidal video-EEG monitoring; and (d) MRI or histopathologic findings characteristic of HS (7,17). MRIs were assessed independently by the radiologists and the epilepsy team, and the diagnosis of HS demanded the presence of at least two of the following: hippocampal atrophy, decreased intrahippocampal signal on T_1-weighted images, or increased intrahippocampal signal on T_2-weighted and fluid-attenuated inversion recovery (FLAIR) images. In this series, volumetric studies of the hippocampi were not used for diagnosis. Histopathology was based on qualitative evidence of significant neuronal loss (17,18), in hippocampal subfields CA1, CA3, and dentate gyrus, associated with a relative preservation of CA2 neurons. All patients had ≥2 years of postoperative follow-up. The presence of dual pathology was an exclusion criterion.

TABLE 1. *Year-to-year cross-sectional analysis of the surgical outcome using Engel's Classification*

	Number of patients per duration of follow up										
Outcome class *	1 year	2 years	3 years	4 years	5 years	6 years	7 years	8 years	9 years	10 years	11 years
IA	114	103	93	72	52	42	28	18	10	4	2
IB	3	6	3	3	3	4	3	2	1	1	1
IC	0	5	11	8	6	3	2	1	1	1	0
ID	3	6	4	2	2	4	2	2	1	0	0
Class I (%)	**88.8%**	**88.8%**	**91.0%**	**91.4%**	**91.3%**	**91.4%**	**87.5%**	**85.2%**	**92.9%**	**85.7%**	**100.0%**
IIA	3	2	0	0	0	0	0	0	0	0	0
IIB	1	1	1	0	0	0	0	0	0	0	0
IIC	0	1	0	0	1	0	0	0	0	0	0
IID	4	3	3	3	2	2	1	1	0	0	0
Class II (%)	**5.9%**	**5.2%**	**3.3%**	**3.2%**	**4.3%**	**3.4%**	**2.5%**	**3.7%**	**0.0%**	**0.0%**	**0.0%**
IIIA	4	5	4	4	2	2	3	2	0	0	0
IIIB	0	0	0	0	0	0	0	0	0	0	0
Class III (%)	**3.0%**	**3.7%**	**3.3%**	**4.3%**	**2.9%**	**3.4%**	**7.5%**	**7.4%**	**0.0%**	**0.0%**	**0.0%**
IVA	0	0	0	0	0	0	0	0	0	0	0
IVB	2	2	2	0	0	0	0	0	0	0	0
IVC	0	0	0	0	0	0	0	0	0	0	0
Class IV (%)	**1.5%**	**1.5%**	**1.6%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**
Total operated	**135**	**135**	**122**	**93**	**69**	**58**	**40**	**27**	**14**	**7**	**3**
Lost to follow up	1	1	1	1	1	1	1	1	1	1	0
Followed (%)	99.3%	99.3%	99.2%	98.9%	98.6%	98.3%	97.5%	96.3%	92.8%	85.7%	100.0%

*According to Engel (11);

Class I: Free of disabling seizures. IA, completely seizure free since surgery; IB, nondisabling simple partial seizures only since surgery; IC, some disabling seizures after surgery, but free of disabling seizures for ≥2 years; ID, generalized convulsion with antiepileptic drug withdrawal only. Class II: Rare disabling seizures ("almost seizure-free"). IIA, initially free of disabling seizures but has rare seizures now; IIB, rare disabling seizures since surgery; IIC, more than rare disabling seizures after surgery, but rare seizures for ≥2 years; IID, nocturnal seizures only. Class III: Worthwhile improvement. IIIA, worthwhile seizure reduction; IIIB, prolonged seizure-free intervals amounting to more than half the follow-up period, but <2 years. Class IV: No worthwhile improvement. IVA, significant seizure reduction; IVB, no appreciable change; IVC, seizures worse.

Prolonged video-EEG recordings with scalp/sphenoidal electrodes in the 10-20 and 10-10 systems were performed to record seizures and to characterize the profile of interictal spikes in wakefulness and sleep, under usual and reduced AED dosages. The last 24 h of video-EEG monitoring were analyzed to quantify interictal epileptiform discharges. We defined specific subgroups of electrical abnormalities, according to the side-to-side ratio of the anterobasal temporal interictal epileptiform discharges. Thus discharges were classified as (a) being exclusively unilateral, (b) having a >90% predominance of one side, (c) having a 70 to 90% unilateral predominance, or (d) showing a <70% unilateral predominance. With the exception of three patients, extratemporal interictal epileptiform discharges were not present in the EEG samples taken for analysis. The ictal scalp/sphenoidal EEG findings were classified as (a) being unequivocally localized to one temporal lobe, (b) lateralized to one hemisphere, or (c) with uncertain lateralization. In addition, patients were evaluated with a standardized neuropsychological test battery, focusing on verbal and nonverbal memory domains, consisting of the Wechsler Memory Scale–Revised, the Rey Auditory Verbal Learning Test, and the Rey Visual Design Learning Test (19,20). Results were considered abnormal when <1 standard deviation (SD) to the mean. Neuropsychology assessment was not used in the lateralization of the epileptogenic zone. However, in the vast majority of patients, tests for memory function were not discordant from the side of MRI and ictal EEG abnormalities. When discordant, an intracarotid amobarbital test was performed. Interestingly, all patients thus evaluated showed adequate functional reserve contralateral to the proposed surgical side (21). Postoperative neuropsychological testing of memory function was performed in 65 patients randomly selected, between 9 and 24 months after surgery, by using parallel versions of the preoperative test battery. Twenty-seven had been operated on, on the right, and 38, on the left temporal lobe. The difference between post- and preoperative memory scores was used to define changes in memory function. Significant memory decline was defined as –1 SD from the preoperative status. The presence of overt amnestic syndrome was evaluated through neurologic examination assessing the patients' general recollection of recent events.

One or more MRI studies were performed for each patient. From 1992 to 1995, patients (n = 32) were studied with a 0.5-T, and since 1996, with a 1.5-T Siemens Magnetom. The neuroradiologists and the epilepsy surgery team independently evaluated the presence of hippocampal atrophy, abnormal signal, and of any other temporal or extratemporal abnormalities. Imaging findings indicative of HS were identified preoperatively in 126 (93%) of the 135 patients. All nine with a normal MRI were studied with the 0.5-T scanner and were included based on pathologic confirmation of HS. Finally, 28 patients were evaluated with subdural electrodes when lateralization of the epileptogenic zone was challenged by apparent incongruence between the side of the MRI abnormality and either the semiologic features or the ictal scalp EEG findings. One of these patients was not operated on because of subdural electrode seizure onset contralateral to the side of the HS. The remaining 27 had seizure onset concordant to the side of the MRI abnormality. All had bilateral temporal eight-contact subdural strips (Ad-Tech, Medical Instrument Corporation, Racine, WI, U.S.A.) inserted through temporal burr holes.

Age at seizure onset ranged from 1 to 35 years (mean, 7.6 years). Mean age at operation was 31.6 years (range, 8–62 years), and epilepsy duration, 24.2 years (range, 3–60 years). Only five patients were younger than 15 years, and four were older than 50 years at operation. Seventy-nine patients had an anterior temporal lobectomy (ATL) (22), in which the anterior 3 to 4 cm of the anterior temporal neocortex were resected. Mesial structures were then removed, beginning with aspiration of the amygdala, followed by en bloc resection of the anterior 2 to 3 cm of the hippocampus and of the parahippocampal gyrus, extending posteriorly to the midmesencephalic level. The other 56 patients had a selective amygdalohippocampectomy (SAH), in which mesial structures were removed according to the technique originally described by Niemeyer (23). Access to the ventricle was obtained through a 1.5- to 2.5-cm incision in the second temporal gyrus, and excision of the amygdala, hippocampus, and parahippocampal gyrus proceeded in the same fashion as performed for ATL (Fig. 1). The choice of surgical approach paralleled the advancements in the understanding of the epileptogenic bases of MTLE/HS. In the beginning, all patients had an ATL. This was followed by a period when we performed both techniques without any specific attempts at randomization, the decision to perform ATL or SAH being taken during the operation, based on the anatomic presentation of the superficial temporal veins and the orientation of the second temporal gyrus. Because we realized that surgical results with the selective approach were similar to those obtained with ATL, we then always favored the neocortex-sparing technique. Hippocampal tissue sufficient for histopathologic examination was obtained in 116 (86%) of the 135 patients. The diagnosis of HS was based on the qualitative assessment of the pattern of cell loss and gliosis in hippocampal subfields CA1, CA3, endfolium, and in the dentate gyrus, and followed published guidelines (7,24,25). All operations were performed by the same neurosurgeon (E.P.).

Patients were discharged on therapeutic dosages of at least one first-line AED. Follow-up was obtained every 6 months in the first year, and yearly thereafter, through either outpatient visits or personal telephone contacts. Outcome was assessed independently by the neurology and neurosurgical teams, which alternated the contact

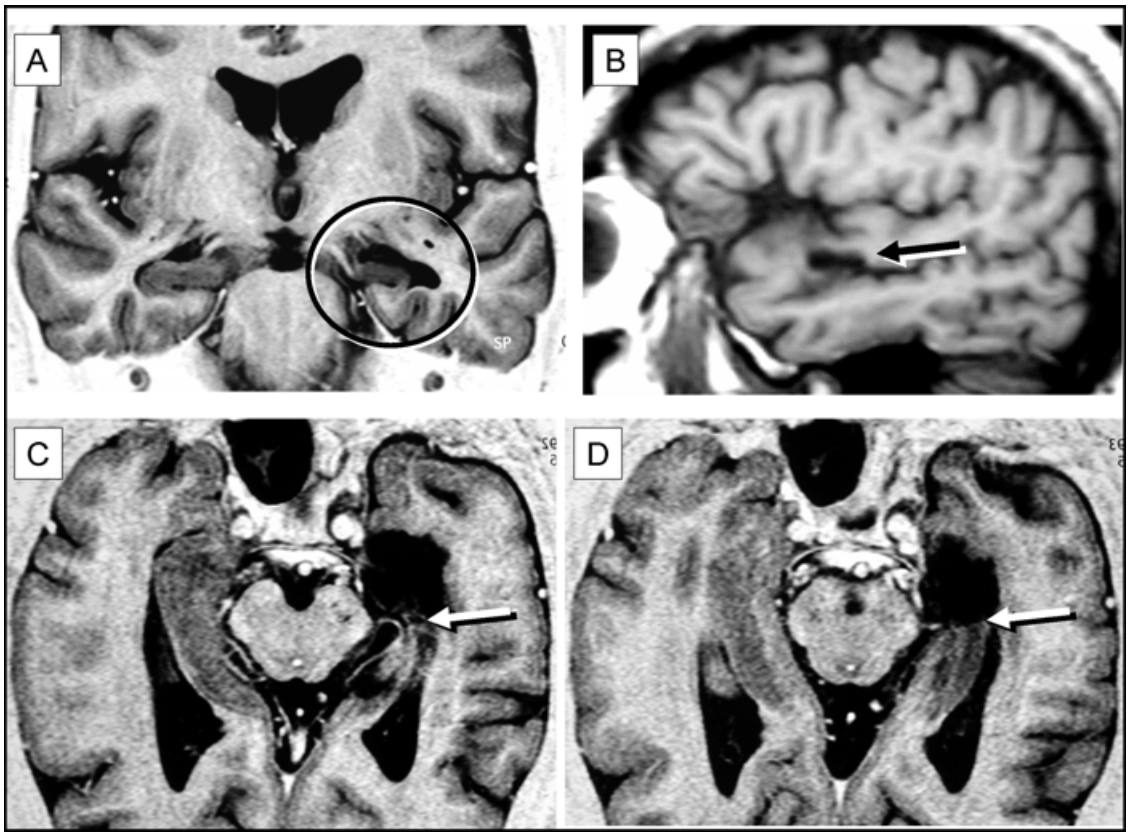

Fig. 1. A: Preoperative coronal magnetic resonance imaging (IR) showing the hippocampal sclerosis. **B:** Postresection sagittal slice (T_1) in a patient undergoing a selective amygdalohippocampectomy (*black arrow* points to the small cortical incision). **C, D:** Postresection axial slices (IR). *White arrows*, The posterior extension of the hippocampal resection, to the midmesencephalic plane.

with patients and relatives. A dedicated telephone line is available at the neurology outpatient clinic, and thus most seizure recurrences have been reported between scheduled outpatient visits and entered into a structured outcome data sheet. Interviews for follow-up purposes consisted of questioning patients or relatives for recurrence of symptoms previously associated with auras, episodes of transient alteration of consciousness, and signs suggestive of complex partial, partial motor, or generalized tonic–clonic seizures. This information was complemented by data regarding dosages of AEDs and any modifications thereof between each visit or telephone contact. The temporal relation of recurrent auras or other types of seizures to reductions or modifications in the AED dosages or regimen was specifically noted. Attempts were made to keep therapeutic dosages of a first-line AED for $\geq$2 years after surgery, when slow discontinuation began in those patients who were seizure free. The temporal relation of recurrent auras or other types of seizures to reductions in the AED dosages was specifically noted. We considered as seizures related to withdrawal or reduction in medication only those occurring within 1 week of such modifications and that were afterward fully controlled by resumption of the previous AED regimen. Of 86 seizure-free patients with >36 months of follow up, 42 (49%) have discontinued their AEDs, 12 (14%) are using <50% of the preoperative dosage of a first-line AED, and the remaining 32 (37%) still take between 50% and 100% of the preoperative dosages of a first-line AED.

Outcome in relation to seizure control was based on Engel's classification, using all 13 subclasses (11). Class I describes patients who are free of disabling seizures; class II, those who have rare disabling seizures; class III, patients with worthwhile improvement; and class IV, those in whom surgery did not result in a worthwhile improvement in seizure frequency. The subclass IA specifically describes patients who are completely seizure free since surgery, including complete control of simple partial seizures (auras). The yearly proportion of patients in each outcome class at years 1 through 11 (see Table 1) and the outcome at the last follow-up (Table 2) were obtained. Survival analyses were performed, and Kaplan–Meier curves delineated to examine the probability of patient retention over the years in Engel's outcome classes IA, I (A, B or D), and I and II combined (Fig. 2), and to estimate retention in each of these outcome classes when comparing the two surgical techniques. Dropped from class I survival curves were all patients who had any postoperative complex partial or generalized seizure, except when these occurred within 1 week of reduction

TABLE 2. *Last surgical outcome*

Outcome class *	%
IA	71.1
IB	3.0
IC	11.9
ID	3.7
Class I	89.6
IIA	0.7
IIB	0.0
IIC	0.7
IID	3.0
Class II	4.4
IIIA	3.7
IIIB	0.0
Class III	3.7
IVA	0.0
IVB	1.5
IVC	0.0
Class IV	1.5
Total operated	135
Lost to follow up	1
Followed (%)	99.3%

According to Engel (11); see Methods.

or discontinuation of AED; Engel's outcome class ID (11).

Mean survival time in each outcome class and 95% confidence intervals (CIs) were calculated. In addition, *t* test, contingency tables, and Fisher's exact test were used to correlate seizure control with clinical, neurophysiologic, preoperative neuropsychological, imaging, and histopathologic variables, as well as to compare results obtained with each surgical technique. Significance was established as $p < 0.05$. Updated versions of SSPS and Statview statistical packages were used. Acute postoperative complications in regard to hematomas, infections, motor or language deficits, global amnesia, and psychosis were noted. Finally, occupational status before surgery and at the last follow-up was obtained for all patients, according to whether they were fully employed, studying regularly, or unemployed.

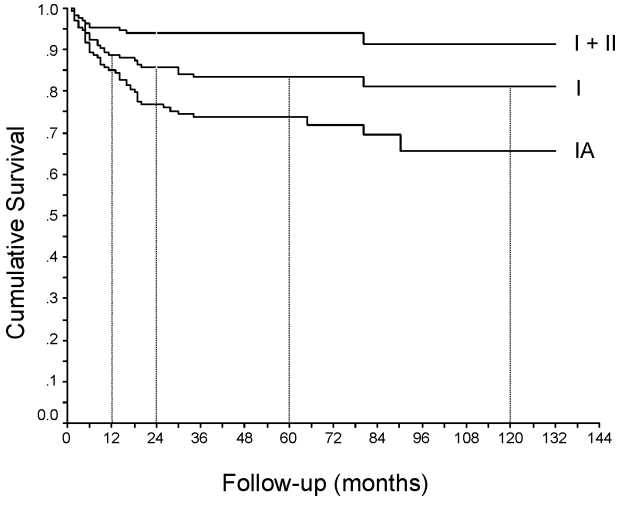

Fig. 2. Kaplan–Meier cumulative survival in Engel's outcome classes I or II, I, and IA.

RESULTS

All 108 patients operated on after noninvasive presurgical evaluation had concordant ictal EEG and MRI findings, in addition to nondiscordant semiologic features. Interictal scalp EEG spiking ratios between both temporal lobes were not taken into account for this decision, but most often had a >70% predominance in the side from where seizures were recorded, and MRI showed signs of HS. The two patients with seizure onset on scalp EEG apparently contralateral to the side of the HS were later proven by intracranial studies to have seizure onset concordant with the HS lateralization. None of the 27 patients operated after evaluation with subdural strips had seizure onset contralateral to the MRI abnormality.

Cross-sectional outcome analyses

Absolute numbers of patients followed for one to 11 years were 134, 134, 121, 92, 68, 57, 39, 26, 13, six, and three. One patient undergoing an SAH was lost to follow-up. The proportion of patients in each outcome class per duration of follow-up is shown in Table 1, and outcome at recently updated (last) follow-up is shown in Table 2. Thirteen (9%) patients had seizure recurrences while reducing medications (Engel's class ID) and resumed seizure control on reinstitution of the previous regimen.

Survival analysis of outcome classes IA, I, and I or II

The probability of a given patient to remain in outcome class IA after 1, 2, 5, and 10 years after surgery was 85%, 77%, 74%, and 66% (Fig. 2). Mean survival time in this outcome class was 8.03 years (95% CI, 7.22–8.84). Furthermore, the probability of survival in outcome class I (A, B, or D) at the same postoperative points in time was 89%, 86%, 83%, and 81% (vertical lines showed in Fig. 2), with a mean survival time of 9.23 years (95% CI, 8.57–9.89). Finally, probability of survival in either outcome class I or II at years 1, 2, 5, and 10 after operation was 96%, 94%, 94%, and 91% (mean survival time, 10.26 years; 95% CI, 9.80–10.73).

Patients in outcome classes III or IV

Seven (5.2%) of the 134 patients had outcome class III, and two (1.5%) were in class IV at any point during follow-up. All had recurrent seizures during the first postoperative year and have remained in these less-favorable outcome classes over the years.

Surgical technique and degree of seizure control

At last follow-up, no significant difference in the achievement of Engel's outcome classes IA, I, and I or II was seen when comparing the 79 patients who had an

TABLE 3. *Correlations of clinical and surgical variables with outcome classes IA and I*

		IA	Other	p	I	Other	p
Mean age onset (SD)		6.7 (6.3)	9.9 (9.2)	0.02*	7.01 (6.8)	11.6 (9.5)	0.01*
Mean age op (SD)		31 (9.3)	34.2 (9.4)	0.09*	31.8 (9.5)	31.8 (8.2)	0.97*
Mean duration (SD)		24.4 (9.9)	24.2 (11)	0.91*	24.9 (10.3)	20.13 (7.3)	0.08*
Side				0.2**			1.0**
	Left	60	15		67	8	
	Right	40	19		52	7	
Technique				1.0**			1.0**
	ATL	60	19		71	8	
	SAH	40	15		48	7	
Pathology				0.78***			0.69***
	HS +	85	30		101	14	
	Unavailable	15	4		18	1	
MRI				1.0***			1.0***
	HS	93	32		111	14	
	Normal #	7	2		8	1	
Subdural strips				0.64**			1.0***
	Yes	19	9		25	3	
	No	81	25		94	12	
Interictal EEG				0.01**			0.2**
	a/b	83	20		94	9	
	c/d	17	14		25	6	
Ictal EEG				0.2**			0.2**
	a	79	23		93	9	
	b/c	21	11		26	6	

Ages and duration of epilepsy in years; # all with 0.5 Tesla machines.
Interictal EEG findings: a/b, 90–100% lateralization of discharges; c/d, <90% lateralization (see Methods); Ictal EEG findings: a, localized to a temporal lobe; b, lateralized to one hemisphere; c, uncertain localization; *Student's *t* test; **Contingency table (χ^2) analysis; ***Fisher's exact test;
ATL, anterior temporal lobectomy; HS, hippocampal sclerosis; SAH, selective amygdalohippocampectomy.

ATL versus those 55 who had an SAH (the single patient lost to follow-up was operated on with this technique). As shown in Table 3, 76% and 90% of those undergoing an ATL were in outcome class IA and I (mean follow-up, 6.65 years), as compared with 73% and 87% of those receiving an SAH (mean follow up, 3.88 years). Furthermore, tests for equality of survival distributions comparing both techniques in outcome classes IA, I, and I or II were not significantly different.

MRI and histopathologic data

In accordance with inclusion criteria, all 135 patients had either MRI features *or* a histopathologic diagnosis of HS. Histopathology was available for 116 (86%) patients, and a diagnosis of HS was confirmed in all, including the only nine patients in whom MRI did not show HS. Thus, of 135 patients, 107 (79%) had both MRI and histopathologic evidence of HS, 19 had HS on MRI but tissue was not available for examination, and nine had HS on pathology in the context of a normal 0.5-T MRI.

Correlates of surgical outcome

An earlier age at onset of recurrent seizures significantly correlated with achievement of both class IA and class I outcomes. In addition, a completely seizure-free outcome since operation (class IA) was significantly more likely in those patients whose interictal EEGs showed ≥90% predominance on the operated-on side. Such outcome was obtained by 83 (80%) of the 103 patients with that ratio, but in only 17 (54%) of the 31 with lesser degrees of lateralization of interictal epileptogenic discharges ($p = 0.01$; Table 3).

Conversely, Table 3 shows that no significant correlations were noted between age at surgery, epilepsy duration, side operated on, and ictal EEG findings, with the outcome achieved at the latest follow-up visit.

Surgical complications and postoperative neuropsychological evaluation

Mortality, intracranial hematomas, and motor deficits did not occur in this series. In addition, no infectious complications affected the central nervous system (CNS) or the surgical wound. A few patients had transient fever in the postoperative period. Whenever a suspicion of a CNS infection was present, lumbar puncture was performed, but a diagnosis of bacterial meningitis was never confirmed. Finally, no instances of overt dysphasia or amnestic syndrome could be clinically detected through the neurologic examination, although mild naming difficulties, not formally quantified, were reported by three of the 39 patients undergoing a left anterior temporal lobectomy. Subsequent outcome visits of these patients showed significant recovery. Of the 38 patients operated on the left side who had postoperative neuropsychological assessment, five (13%) had a reduction of >1 SD from preoperative logical memory scores, whereas 10 (26%) had a similar decline in verbal learning tests. In contrast, only

one (4%) of the 27 patients operated on, on the right temporal lobe had a >1 SD reduction in scores of logical memory, and three (11%) worsened on verbal learning. However, six (23%) had a significant decline in tests of visual memory. Two patients had postoperative transient psychosis.

Occupational status

Before operation, 39 (29%) patients were unemployed, 23 (17%) were studying regularly, and the remaining 72 (54%) were fully employed. At the last follow-up, the percentage of those fully employed increased to 76% (n = 102), whereas that of students and unemployed decreased to 4% (n = 5) and 20% (n = 27), respectively.

DISCUSSION

The systematic review of publications on seizure outcome after temporal lobectomy recently published by McIntosh et al. (4) has set a new standard regarding future reports on this subject. The authors showed that contrasting results in different series are likely due to variable ways to collect outcome data (2,7,10,26–34), to inconsistent approaches to missing values (e.g., patients lost to follow-up), and also to variations in the number of patients and duration of postoperative follow-up. The data reported here benefit from this critical appraisal of the literature in that it addresses underreported aspects of the surgery for TLE.

The present series includes all patients consecutively operated on for a very specific epilepsy syndrome, defined by a homogeneous pathology (HS). We have shown high rates of seizure freedom on a yearly basis and also at the last follow-up, irrespective of the type of surgical technique used. In addition, survival analyses show that the probability of these patients to remain completely seizure free (outcome class IA) varied from 85% at the end of the first year to 74% at 5 and to 66% at 10 years after operation. The same pattern of outcome (89%, 83%, and 81% at years 1, 5, and 10) was seen when we analyzed overall outcome in class I, which is considered a major outcome goal in epilepsy surgery (4,11). This demonstrates that favorable and stable results can be anticipated for patients remaining seizure free after the first postoperative year. It should be realized that patients dropped off from the class IA survival curve whenever they had a single seizure, even a simple partial seizure. Because patients and doctors often try to reduce or stop medication over the years, this reduction in "completely seizure free since surgery" status is to be expected. This approach allows a realistic appraisal of the need for long-term AED treatment after successful surgery for TLE/HS. Attempting to retain patients in class IA without reasonable trials of AED dosage reduction or discontinuation would certainly lead to overtreatment of a significant proportion of them.

Only a few reports specifically address the surgical outcome of patients with the syndrome of MTLE/HS (4,5,7). However, data on this *specific* syndrome can be singled out from tables and subanalyses of results contained in several other publications on the surgical outcome of TLE (6,35–40; Table 4). With the exception of a few studies that used different inclusion criteria (18,39), seizure-free rates of 79 to 86% have been reported (5,6,35–38,40). The results we present confirm that MTLE/HS has a very favorable surgical outcome, and the survival analyses show that such results can be predicted to be largely stable over time.

Seizure-free rates in patients with MTLE/HS are considerably higher than those reported when patients with different etiologies of TLE are pooled as a group. For instance, the single randomized study comparing surgical versus medical treatment of TLE reported that 64% of operated-on patients achieved outcome class I (41).

TABLE 4. *Proportion of Engel's outcome class I in major surgical series for TLE: impact of a separate analysis of patients with HS*

First author (ref)	year	All patients		HS patients only		non-HS patients		Years of follow up mean (range)
		n	Class I (%)	n	Class I (%)	n	Class I (%)	
Berkovic SF (7)	1995	135	55%	85	58%	50	50%	3.7 (1-7)
Fried I (37)	1995	73	84%	43	86%	30	80%	n/a (1-5)
Arruda F (35)	1996	74	72%	47	85%	27	48%	2.8 (n/a)
Sperling MR (31)	1996	89	70%	n/a	n/a	n/a	n/a	5.0
Berg AT (36)	1998	214	71%	86	84%	128	63%	n/a
Radhakrishnan K (40)	1998	175	77%	74	85%	101	71%	3.6 (2-6)
Kilpatrick C (38)	1999	56	86%	56	86%	0	n/a	3.1 (1-5)
Wiebe S (41)	2001	36	64%	25	n/a	11	n/a	1.0
Mohamed A (5)	2001	34	79%	34	79%	0	n/a	2.6 (1-7)
McIntosh AM (4)*	2001	126 studies	70%	n/a	n/a	n/a	n/a	2.9 (0-30)
Wieser HG (6)	2003	369	67%	94	83%	275	61%	7.2 (1-24)
Paglioli E**	2004	135	88%	135	88%	0	n/a	5.2 (2-11)

*extensive review of 126 outcome studies, without individual analysis of patients with HS.
**current series.
n/a: not available.

However, only 70% of these patients had MTLE/HS, and it is possible that within this subgroup, the rate of seizure freedom may have been higher. In addition, the very same studies we abstract in Table 4 report less favorable results when data from *all etiologies* of TLE are pooled (6,7,35–40). Finally, the initial results of a multicenter prospective cohort of patients operated on for refractory seizures do not take into account the underlying etiology when reporting higher relapse rates of patients operated on in the medial temporal lobe regions (42). It is likely that the analysis of the surgical outcome of TLE as merely a topographic entity will not further the understanding of the surgical treatment of specific epileptic *diseases* involving the temporal lobes. The different epileptogenic lesions vary both in degree of epileptogenicity and in specific localization *within* the temporal lobe (43). This duo "pathological substrate–specific topography" defines discrete subsyndromes, and this construct not only enhances the biologic relevance of surgical results, but also probably explains discrepancies in outcome reports for TLE in the literature.

Our results differ from those previously reported for operated-on patients with MTLE/HS in two major points. One relates to the demonstration that high rates of seizure freedom can be stable over the years (7,34), and the other concerns the achievement of such results through a partial resection of the hippocampus (up to the midmesencephalic plane) (34). Seizure recurrence can be assessed both early and late during follow-up, and our results in this regard can be analyzed from Figure 2. The possibility of late recurrences (after the second postoperative year) has been considered an even more important issue in the appraisal of the overall prognosis of the surgery for TLE (7,12,13,44,45). Our Kaplan–Meier estimated survival in class I between years 2 and 10 went from 86% to 81%, whereas another series analyzed in the same fashion reported rates from 63% to 50% between years 2 and 5 after operation (7). It is possible that variable inclusion criteria, methods of outcome assessment, or surgical technique may account for the differences in long-term results. The fact that the patients reported here had a low rate of late seizure recurrence, even though a significant proportion of them had an SAH, suggests that less-favorable surgical outcomes over the years in MTLE/HS should not be systematically attributed to the remaining temporal neocortex nor to the preservation of the posterior portion of the hippocampus.

We found that when the resected TL structures had $\geq$90% of the interictal epileptiform discharges, a significantly higher probability of complete postoperative seizure control existed (outcome class IA). Nevertheless, some patients with lesser degrees of lateralization of bitemporal epileptiform discharges achieved class IA outcome. Moreover, the side-to-side ratio of anterobasal temporal discharges did not correlate with achievement of outcome class I (Table 3). In agreement with other series (4), ours also did not find a significant correlation between other clinical, neurophysiologic, and neuropsychological variables and surgical outcome (Table 3). It is possible that the presence of unilateral HS takes precedence over other potential factors in predicting a favorable surgical outcome for patients with the specific syndrome of MTLE/HS.

In the present series, no unexpected postoperative complications occurred. More specifically, no patient had motor deficits, overt dysphasia, or amnestic syndrome. In a recently reported large series, major complications occurred in only four (0.8%) of 453 patients undergoing SAH, three of whom had mesial temporal tumors (6). Thus, current evidence supports an optimistic view, in that the good results obtained with the surgical treatment of MTLE/HS are associated with a low risk of unexpected complications. Conversely, a decline of >1 SD in memory function occurred in one fourth of our patients retested after surgery, and this complication, as well as mild dysnomic problems in patients operated on, on the dominant temporal lobe, was previously reported in series of patients operated on for TLE (19). The extent to which these changes negatively affect quality of life in patients who become seizure free is not known.

Limitations existed in our study, particularly the fact that we obtained phone follow-up data for some patients and in-person history for other patients, without validation and proof that the phone follow-up methods are as sensitive for detecting seizure recurrence. However, telephone interviews to complement outcome data are an almost universal method used in outcome studies of large series of patients (6,18,26). Also, postoperative naming difficulties referred to by some patients were not objectively probed. We believe these limitations do not interfere with the main conclusions we draw from our results.

We have reported on the surgical treatment of young adults whose recurrent seizures started around the end of the first decade of life. It is well known that 10 to 20 years usually elapse before these patients are referred for surgical consideration. Part of this is due to the usual evolution of MTLE/HS, which may have a silent period between the first few seizures and midadolescence, when the full-blown picture of refractory complex partial seizures emerges. Nevertheless, the combination of very favorable results sustained over the years with a low rate of surgical complications adds to the current debate on whether surgery in these patients should be considered earlier. This may be even more relevant in the light of recent studies showing that AED management is not very effective after two or three medication trials fail to bring seizures under control (46). The positive occupational gains reported here and in other series (47) would also favor earlier surgical consideration in medically refractory patients with unilateral MTLE/HS.

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