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Surgical Outcome of Epilepsy Patients Evaluated with a Noninvasive Protocol

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Summary: Surgery is now an accepted treatment for some medically intractable epilepsies. Presurgical evaluation is particularly important for the localization of the epileptogenic zone, which may necessitate sophisticated imaging techniques and intracranial electroencephalogram (EEG) recordings. If patients are carefully selected, however, successful results can be achieved with noninvasive evaluation methods. Seventy-seven patients were operated on for intractable seizures. All patients underwent EEG, neuropsychological, psychiatric, and magnetic resonance imaging investigations. Ictal EEG-video recording was performed in all nonlesional and in some lesional cases that had discordant data. Selective amygdalo-hippocampectomy was performed on patients with mesial temporal lobe epilepsy (MTLE), an extended or a limited lesionectomy was performed on patients with structural lesions, and a lesionectomy with deafferentation was performed on two patients with West syndrome. Electrocorticography was not used. Temporal lobe directed surgery was performed in 63.6% of the cases. The pathological examinations of all cases showed hippocampal sclerosis (HS) in 43%, tumor or tumor-like lesions in 36%, and cortical dysplasia in 5% of patients. After a mean follow-up of 17 months (range, 2–53), 75% of the patients were seizure-free with or without aura and 15% had a marked improvement, whereas 10% did not benefit from surgery. Neuropsychological outcome of patients with MTLE and HS also showed worthwhile results. Our patients, who were evaluated without pre- and perioperative intracranial recordings and other sophisticated techniques, had an outcome comparable to those in other series from more experienced centers. Our experience indicates that successful results, especially for patients with MTLE-HS and lesion-related epilepsies, can be obtained at centers with limited resources if the diagnoses and evaluation procedures are performed carefully. **Key Words:** Epilepsy surgery—Hippocampal sclerosis—Amygdalo-hippocampectomy.

Although surgery has been used for the treatment of epilepsy patients throughout history, the modern era is said to have begun with V. Horsley (1) at the end of 19th century. On the other hand, we found the procedure of cauterization for epilepsy in one of the oldest Ottoman medical texts from the 15th century, which was written by a Turkish surgeon Dr. Serafettin Sabuncuoglu (2). Turkey has an epilepsy prevalence rate of 8.8 to 10.2 per 1,000 (3), corresponding to approximately 650,000 epilepsy patients and almost 60,000 candidates for surgery. However, epilepsy surgery is a relatively new concept in our country, generally functioning with restricted resources. Despite these limitations, our center set up to improve the quality and increase the quantity of the patients evaluated according to a noninvasive presurgical protocol.

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METHODS

Of the 140 patients admitted to the epilepsy surgery program at the University of Istanbul, Cerrahpasa Medical Faculty, between May 1995 and August 1999, 77 underwent surgery. Additionally, 25 patients have concluded the preoperative evaluation and are ready for surgery. Twelve patients (0.9%) needed further investigations; some were rescheduled for monitoring, and the remaining patients either demonstrated pseudoseizures or did not accept surgery. The epilepsy patients were considered surgical candidates if they were medically intractable or if they had a lesion related to their seizures. Our evaluation is carried out without invasive recordings, with two beds for long-term video-electroencephalogram (EEG) monitoring at the child neurology and neurosurgery wards. Our preoperative evaluation proto-

col includes physical, neurological, psychiatric, and neuropsychological examinations.

All patients have had 1.5 T magnetic resonance imaging (MRI) scans in axial, coronal, and sagittal planes, 4-mm slices at T1, T2, spinecho T1, 3D spoiled gradient recalled acquisition in steady state (SPGR), and fluid-attenuated inversion recovery (FLAIR) sequences. Single-voxel magnetic resonance spectroscopy was performed on the patients with nonlesional temporal lobe epilepsy as an additional procedure. Patients had EEGs while awake and asleep. Closed-circuit television and 32-channel scalp EEG recordings were run to capture ictal events in nonlesional and some lesional patients. All cases with temporal lobe involvement had sphenoidal electrodes inserted free hand for long-term monitoring. Antiepileptic drugs (AEDs) were decreased in a stepwise manner, at least 3 days before monitoring. Standard neuropsychological tests used were the Wechsler Adult Intelligence Scale, Edinburg handedness inventory, Stroop color interference test, Wisconsin Card Sorting test, Verbal fluency test, Ray Auditory Verbal Learning test, Wechsler Memory Scale, Boston naming test, Token test, Benton facial recognition test, and Benton judgment line orientation test. The tests were standardized for Turkish patients (4,5). The Wada test, or intracarotid amobarbital procedure, was the only invasive test and was performed only on selected cases because of difficulties in getting the drug. Psychiatric evaluation consisted of a psychiatric interview, Hamilton's depression test, Beck's anxiety scales, Symptoms Checklist–90, and a recently started quality-of-life scale, Epilepsy Surgery Inventory-55 (ESI-55).

If all preoperative investigations revealed concordant data, the patients were referred for surgery; otherwise, they were either scheduled for reevaluation or other alternative treatments were recommended. Transsylvian Selective amygdalo-hippocampectomy (SAH) as described by Yasargil et al. (6) was performed when the preoperative evaluation was consistent with a unilateral mesial temporal lobe seizure focus. An extended resection of a lesion with or without SAH was preferred according to the localization of the lesion, and a limited (gross total) resection was applied if the lesion was in an eloquent area. Electrocorticogram (ECoG) recording was not used, but functional cortical mapping has recently been instituted. Routine pathology studies were performed on resected specimens with some additional studies on the hippocampus. AED medication was maintained in all patients postoperatively for 1 to 2 years and thereafter was decreased in agreement with the patient. MRI was performed within 24 hours after surgery whenever possible, and patients were reevaluated after 6 months and every year thereafter with wake and sleep video-EEG recordings, MRI, neuropsychology, and psychiatry.

RESULTS

The characteristics of the operated patients are shown in Table 1. Forty-nine (63.6%) patients had temporal, 23 (29.8%) had extratemporal, and 5 (6.4%) had multilobe resections. There were 19 frontal approaches, 3 parietal, and 1 occipital approach in the extratemporal group, which revealed cortical dysplasia (5 patients), arteriovenous malformation (1 patient), tumor and tumor-like lesions (9 patients), and nonspecific gliosis (4 patients) at microscopic evaluation.

Extended resections with or without SAH were performed on 12 and 8 patients, respectively. SAH was performed on 35 patients. There were 11 patients with limited resections. Multilobe resection was accomplished in three patients, a lobectomy in five, and a modified hemispherectomy in a single patient. In two patients with West syndrome, resection and deafferentation was done to prevent the discharges from spreading to other regions of the brain.

Pathology revealed mesial temporal sclerosis in 33 patients, tumoral lesions in 20, dysembryoplastic neuroepithelial tumor (7) in 4, vascular lesions in 2, hamartoma in 2, gliosis in 11, and cortical dysplasia (CD) in 5 patients.

None of the patients with SAH had major postsurgical complications except transient third nerve palsy in three (8.6%) patients. Both the patient with a modified hemispherectomy and the patient with a frontal lobectomy developed hydrocephalus. Hemipareses that were preoperatively detected in three children with frontal lobe lesions showed some progress, and a patient with a histologically unspecified large multilobar vascular lesion developed hemiplegia that later regressed to paresis. The youngest patient (3 months old) with a large CD and suffering from status epilepticus died of infection 1 week after surgery. The outcome is summarized in Table 2 according to the classification of Engel (8).

The mean follow-up was 17 months (range, 2–53); 75% of patients were either seizure-free (Ia: 66%) or only had rare auras (Ib: 9%). Almost half of this group had HS; the longest follow-up was 41 months. MTLE-HS cases had the best outcome; 85% of these patients were in class I. Three of the four class IV patients (one had a temporal dysembryoplastic neuroepithelial tumor, another had a frontal ganglioma, and a third had a frontal CD) had subtotal resections because of adjacent eloquent cortices.

TABLE 1. *Characteristics of 77 operated epilepsy patients*

No. of patients	77
Mean age at surgery (y)	22.3 ± 11.3 (3 mo–56 y)
<18 yrs (No.)	24
>18 yrs (No.)	53
Mean age at onset (y)	10.3 ± 9.52 (1 day–55 y)
Sex (F/M)	37/40
Mean duration (y)	11.9 ± 8.54 (3 mo–37 y)

TABLE 2. *Postoperative outcome by pathology*

	All		HS		T&TL		CD		Gliosis	
	No.	%	No.	%	No.	%	No.	%	No.	%
Class I	57	75	28	85	23	82	1	25	4	36.3
Class II	12	15	4	12	3	10.7	1	25	4	36.3
Class III	3	5	1	3	—	—	1	25	2	27.2
Class IV	4	5	—	—	2	7	1	25	1	
Exitus	1						1			
Total	77	100	33	100	28	100	5	100	11	100

T&TL: tumor and tumor-like lesion.

The fourth patient with hemiconvulsion, hemiplegia, epilepsy syndrome developed hydrocephalus and cranial bone infection after a modified hemispherectomy. Four patients had reoperations: two for cranial bone infection and two for the remnant lesions; their outcome was classified after the reoperation.

Assessment of neuropsychological test results in patients with HS postoperatively revealed mild improvement in nonverbal memory scores in 24%, mild impairment in 14%, and no change in 62% of patients. Verbal memory evaluation showed no change in 43%, mild improvement in 33.3%, and mild impairment in 24% of patients. All 24 patients who had the Wada test passed, and 19 were operated on without any complication. Both language and memory were tested during Wada, but memory lateralization was taken into account because SAH was the preferred surgical procedure, which often results in no language complications. Almost 50% of patients who took the Wada test had memory lateralized on one side with an excellent outcome postoperatively both at seizure control and memory performance.

Patients had a psychiatric interview before surgery and during the follow-up period. Three patients had serious postoperative depression (all had MTLE-HS) that was resolved with antidepressant therapy. The results of other tests have not yet been analyzed.

DISCUSSION

Epilepsy surgery may be beneficial and without complications for most patients. Selection basically depends on diagnosis of surgically remediable cases, especially MTLE-HS (9), which may be recognized from patient history and will usually not need invasive evaluation. A high proportion of our patient population consisted of this type of epilepsy, mostly fulfilling the criteria of the clinical picture in the literature (10) described to get the best outcome. However, because a risk of seizure relapse over time was previously reported by different authors, our preliminary successful seizure control needs to be interpreted cautiously because of the relatively short follow-up period (range, 2–53 months) (11,12).

Patients with class III and IV outcomes had either sequel lesions (infection, trauma, or cerebrovascular accident) or tumors that were incompletely removed. Although this group comprises only 18% of the total, we may still need to reanalyze the patients for a better approach. The more difficult situations such as nonlesional extratemporal or diffuse lesional cases that needed further evaluation consisted of 0.9% of all evaluated patients. The surgical outcome for this group even in the most experienced centers is not as good as for temporal and lesional cases (13). The limitation in our technical facilities is a handicap for invasive recordings and ECoG at the moment, but studies questioning the significance of spikes recorded during ECoG for both nonlesional (14) and lesional (15) cases indicate the difficulty in arriving at a consensus on this issue. On the other hand, studies suggesting the efficacy of scalp EEG (16–18) correlated with other findings and with the impact of neuropsychological tests, as well as with high-resolution appropriate MRI images (19) during the preoperative evaluation period, support the use of noninvasive methods. Even performing long-term EEG monitoring to capture ictal events has been disputed in patients whose interictal EEG findings were localized and lateralized and concordant with the other data (20). On the other hand, we are well aware that an MRI lesion may not be indicative of the site of seizure origin (21), and there may be the possibility of false lateralization by surface EEG in patients with lesions (22). Such facts may constitute difficulties for the decision-making process of the clinician during the preoperative evaluation.

Among our patients, 24 were children; 3 of them had MTS, 19 had cerebral tumors, and 2 had West syndrome. Surgery for West syndrome has been reported in the last decade especially for lesional cases with localized ictal EEG (23); our infants improved after resective surgery performed with deafferentation technique (24). MTLE-HS usually does not comprise the majority of cases in childhood, and our children have remained seizure-free after surgery. But the time of the surgery in young patients may still be debatable because good seizure control may be achieved with medication in 25% of patients (25), and there may be remissions during the natural course of the disease (10).

Neuropsychological tests were performed in all patients, but only the patients with MTLE-HS were analyzed to evaluate the changes after SAH. Although there seems to be no difference in seizure outcome between anterior temporal lobectomy and SAH (26), memory is reported to be better after SAH (27,28). Our results were concordant with the literature (29), providing further evidence for the argument. The Wada test is a useful tool for predicting seizure laterality and control (30), as well as postoperative memory changes and outcome in MTLE (31). We were able to perform this test in only 24 pa-

tients because the drug is not available in our country. The analysis of the results will be a subject of another paper.

Because human tissue should not be wasted, research studies on hippocampus with pathological, immunocytochemical, and microdialysis methods have recently been initiated by our basic scientists using the limited resources of their laboratories. We hope this expansion will provide further insight into the understanding of the underlying mechanisms of hippocampal epileptogenesis.

In conclusion, the decision for epilepsy surgery needs a multidisciplinary approach; like a puzzle with many pieces, different investigations work in conjunction to create an integrated picture of epileptic events. Experiences accumulated in developed centers may enable us to bypass some of the natural trial and error faced when dealing with the unknown, and we may achieve good standards in epilepsy surgery by searching for rational ways of utilizing the tools available in our developing country settings.

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