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Clinical Article

Comparison between Initial and Recent Surgical Outcome of 15-Year Series of Surgically Remediable Epilepsy

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Objective : The aim of this study is to compare the surgical outcome of the initial and recent surgical cases, during our 15-years experience, in terms of the surgical strategies and the prognostic factors for surgically remediable epilepsy.
Methods : We retrospectively reviewed and compared the surgical outcomes between the initial 256 (Group I) and recent 139 (Group II) patients according to the time period of operation for a total of 518 consecutive epilepsy surgeries at our institution since 1992. The patients of the middle intermediate period, which were subjected to changed surgical strategies, were excluded.
Results : The surgical outcome data from the initial and recent groups showed a much improved outcome for patients who underwent temporal lobe epilepsy (TLE) surgery over time. The number of patients with a good outcome (Engel class I-II) was much increased from 87.7% (178 TLE cases of Group I) to 94.8% (79 TLE cases of Group II) and this was statistically significant ($p = 0.0324$) on univariate analysis. Other remarkable changes were the decreased performance of intracranial invasive studies from 43.5% in Group I to 30.9% in Group II due to the advanced neuroimaging tools. The strip/grid ratio was reduced from 131/32 in Group I to 17/25 in Group II, because of a markedly reduced mesial TLE surgery and an increased extratemporal epilepsy surgery.
Conclusion : Our results show that surgical outcome of epilepsy surgery has improved over time and it has shown to be efficient to control medically intractable epilepsy. Appropriate patient selection, comprehensive preoperative assessments and more extensive resection are associated with good postoperative outcomes.

KEY WORDS : Epilepsy · Surgery · Treatment · Outcome.

INTRODUCTION

The reported annual incidence rates of epilepsy have varied between 40 and 200/100,000 depending on the geographic location[26]. The average lifetime prevalence rate is 0.4-0.8% of the general population[21]. Epilepsy is classified according to the guidelines of the International League against Epilepsy[5,9]. Fifty-two percent of the patients have partial or secondarily generalized seizures, 39% have generalized seizures from the outset and the rest have nonconvulsive seizures (e.g., absence or myoclonic)[19]. Between 60 and 70% of individuals with epilepsy are successfully treated with antiepileptic drugs (AED)[17]. However, 30 to 40% of patients with epilepsy have either intractable or uncontrolled seizures despite the use of multiple AED regimens[16,28].

Medically intractable epilepsy can be defined as seizures that are frequent and disabling, and as seizures that occur in patients who are drug refractory to at least two or three AEDs of first choice[18]. Epilepsy surgery has developed into a safe and effective treatment for the patients with drug resistant epilepsy. Patients with medial temporal lobe epilepsy (MTLE) and lesional epilepsy may be favorable candidates for epilepsy surgery[6]. It had been proven that surgery is superior to prolonged medical treatment for drug refractory TLE through a randomized controlled study[32]. After TLE surgery, 60% to 70% of patients were reported to have become seizure free and another 20% had a significant reduction of seizures[12]. After extratemporal epilepsy (ETE) surgery, 32-45% of the patients became seizure free and 27-35% improved[22,29].

However, the seizure outcome after surgery may be quite

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variable and this is influenced by numerous factors despite many studies on the predictors of the postoperative seizure outcome[31].

The aims of this study are to compare the surgical outcome of the initial and recent surgical cases, during our 15-years of experience, and to analyze the factors that are associated with improve the postoperative outcome in terms of the surgical strategies.

MATERIALS AND METHODS

We reviewed the hospital records of the epilepsy patients out of a total 726 surgical cases since the epilepsy surgery program was commenced in November 1992. A total of 518 consecutive patients underwent epilepsy surgery for drug resistant epilepsy between November 1992 and December 2009. The patients were divided into three groups according to the time period of the operation : 1) the initial period from 1992 to 1996, 2) the middle period from 1997 to 2000, and 3) the recent period from 2001 to 2009. We excluded 123 patients who were operated on during the middle period. It was the transition period of much trial and change to establish the current epilepsy surgery program. Our study included 395 patients in the initial and recent periods. Two-hundred-and-fifty-six patients were operated on during the initial period (Group I) and 139 patients were operated on in the recent period (Group II).

The presurgical evaluation included the patient's medical history, neurological examination, neuroimaging to identify any substrate-related lesion, non-invasive 24 hr video-electroencephalography (EEG) recording (scalp and sphenoidal recording), neuropsychological evaluation and a WADA test. Invasive monitoring in the form of a subdural grid or strip was also performed in some patients. Intraoperative electrocorticography (ECoG) was used in the majority of cases and the somatosensory evoked potentials or awake evaluation were used intraoperatively in some cases.

Magnetic resonance imaging (MRI) was performed for all the patients using 1.5T or 3.0T scanners. MRI demonstrated structural abnormalities such as hippocampal sclerosis, cortical dysplasia and tumor. In addition, fluorodeoxyglucose-positron emission tomopraphy (FDG-PET), single photon emission computerized tomography (SPECT) and functional MRI (fMRI) were also used.

All the patients underwent surgical treatment. Most of the surgical procedures were to excise the epileptic zone, which was identified via preoperative evaluation. The resection area was planned based on the preoperative MRI and EEG findings. We were able to get additional information from the intraoperative ECoG. Various brain resections were done for each individual patient according to the preoperative evaluation and intraoperative monitoring. The type of resective surgery was classified as TLE surgery and ETE surgery. All TLE surgery was performed based on standard anterior temporal lobectomy with amygdalohippocampectomy and this was tailored case by case. The ETE patients received corresponding lesionectomy or cortisectomy. Other surgery such as corpus callosotomy, hemispherectomy and vagal nerve stimulation (VNS) was performed in selected patients. We recorded the details of each surgery and the surgical complications. After surgery, all the patients were maintained on the same AED regimens as before surgery and we tapered the medicine according to the patient's condition.

We retrospectively reviewed the following data from the hospital records : age, gender, a febrile convulsion history, a family history of epilepsy, age at the onset of epilepsy, the preoperative seizure frequency, age at surgery, type of surgery and surgical complications. The outcome data were obtained from the follow up clinic program, outpatient reports and telephone calls and we identified each patient's post-operative seizure status.

They were followed at least until 2 years and surgical outcome was compared at 2 year follow up. The surgical outcome was accessed according Engel's classification. Class I patients were those who showed the absence of seizures or the presence of auras only or the presence of seizures only during drug withdrawal, Class II patients had rare seizures or nocturnal seizures only, Class III patients showed worthwhile improvement and Class IV patients showed no improvement. The patients were categorized as having a good outcome (Engel's class I-II) or a poor outcome (Engel's class III-IV). For comparing patients with good to poor outcomes, we used Student's independent t-test or chi square test.

RESULTS

The clinical characteristics of these patients, with detailed differences between the two groups, are summarized in Table 1. The values are given as the mean ± standard deviation. Group I was composed of 256 patients who were operated on during the initial period from 1992 to 1996. There were 147 males (57.5%) and 109 females (42.5%). The mean age of the patients at seizure onset was 12.3 ± 6.5 years (range : 6-49 years). The mean age at surgery was 25.7 ± 8.1 years (range : 21-63 years) and the mean duration of epilepsy was 13.4 ± 8.1 years (range : 5-25 years). The mean duration of follow up was 9.9 ± 6.4 years (range : 2-15 years).

Group II consisted of 139 patients who were operated on during the recent period from 2001 to 2009. Seventy three patients were male (52.5%) and 66 patients were female

(47.5%). The mean age at the onset of epilepsy was 13.8 ± 8.3 years (range : 0-34 years). The mean age at surgery was 28.8 ± 10.7 years (range : 7-58 years) and the mean duration of epilepsy was 14.9 ± 9.4 years (range : 1-50 years). The mean duration of follow up was 3.7 ± 2.4 years (range : 2-8.7 years).

A total of 205 patients (51.8%) underwent invasive monitoring in the form of a subdural grid or strip. In Group I, 168 patients (63.6%) needed invasive monitoring. A subdural strip was inserted in 131 cases (51.1%) and a subdural grid was inserted in 32 cases (12.5%). In Group II, 42 patients (30.1%) underwent invasive monitoring. A subdural strip was inserted in 17 patients (12.2%) and a subdural grid was inserted in 25 patients (17.9%). Although the overall use invasive monitoring decreased, the strip/grid ratio was reversed from 131/32 in Group I to 17/25 in Group II.

Table 2 shows the results of univariate analysis of significant variables between the good (Engel's Class I-II) and poor (Engel's Class III-IV) outcomes in Group I and Group II. There was no significant correlation of good or poor outcome with each variables except identifiable lesions in MRI.

The outcome of each surgical cases based on Engel class are summarized in Tables 3 and 4. In Group I, 178 patients (69.5%) received temporal lobe resections. An Engel class I-II outcome was noted in 156 patients (87.7%) and 22 patients (12.3%) had a poor outcome (Class III-IV). Of the 40 patients (15.6%) who underwent extratemporal resections, an Engel class I-II outcome was noted in 31 patients (77.5%) and a class III-IV outcome was noted in 9 patients (22.5%). Corpus callosotomy was performed in 7 patients (2.7%) and all of them had poor outcome. Two patients received functional hemispherectomy and they had class I outcomes. Multilobar resection was carried out in 29 patients, and an Engel class I-II outcome was noted in 18 patients (62.1%) and a class III-IV outcome was noted in 11 patients (37.9%).

In Group II, there were 79 patients (56.8%) with temporal lobe resections. Seventy five patients (94.8%) were in Engel class I-II and 4 patients (5%) had a poor outcome (Class III-IV). Forty four patients (31.6%) underwent extratemporal resections. An Engel class I-II outcome was noted in 37 patients (84.1%) and a class III-IV

Table 1. Clinical characteristics of 256 initial and 139 recent patients

	Group I (%)	Group II (%)	Total (%)
Mean age at onset (yr)	12.3 ± 6.5	13.8 ± 8.3	12 ± 7.3
Mean age at surgery (yr)	25.7 ± 8.1	28.8 ± 10.7	26 ± 9.3
Mean duration of epilepsy (yr)	13.4 ± 8.1	14.9 ± 9.4	14.0 ± 8.7
Mean duration of follow up (yr)	9.9 ± 6.4	3.7 ± 2.4	7.4 ± 6.0
Febrile convulsion	66 (25.9)	22 (12.9)	88 (22.2)
Head trauma	19 (7.4)	18 (12.9)	37 (9.3)
Birth injury	6 (2.3)	2 (1.4)	8 (2.0)
Identifiable lesions on MRI	159 (62.2)	98 (70.5)	228 (65.0)

Plus-minus values are means ± SD

Table 2. Results of univariate analysis of significant variables

	p-value	
	Group I	Group II
Mean age at onset (yr)	0.411	0.139
Mean age at surgery (yr)	0.403	0.058
Mean duration of epilepsy (yr)	0.220	0.336
Febrile convulsion	0.286	0.979
Head trauma	0.574	0.246
Prenatal infarction	0.777	0.235
Identifiable lesions on MRI	0.179	0.000*

*$p < 0.0001$

Table 3. Outcomes of each surgical series based on Engel classification in Group I patients

Surgical series (n = 256)	Engel class			
	Class I (%)	Class II (%)	Class III (%)	Class IV (%)
Temporal lobe resection (n = 178)	109 (61.3)	47 (26.4)	18 (10.1)	4 (2.2)
Extratemporal resection (n = 40)	23 (57.5)	8 (20.0)	7 (17.5)	2 (5.0)
Corpus callosotomy (n = 7)	-	-	4 (57.1)	3 (42.9)
Functional hemispherectomy (n = 2)	2 (100)	-	-	-
Multilobar resection (n = 29)	8 (27.6)	10 (34.5)	9 (31.0)	2 (6.9)

Table 4. Outcomes of each surgical series based on Engel classification in Group II patients

Surgical series (n = 139)	Engel class			
	Class I (%)	Class II (%)	Calss III (%)	Class IV (%)
Temporal lobe resection (n = 79)	63 (79.7)	12 (15.1)	2 (2.5)	2 (2.5)
Extratemporal resection (n = 44)	26 (59.1)	11 (25.0)	2 (4.5)	5 (11.4)
Corpus callosotomy (n = 3)	-	1 (33.3)	2 (66.7)	-
Vagal Nerve Stimulation (n = 13)	1 (7.6)	-	6 (46.2)	6 (46.2)

Table 5. Univariate analysis for outcome of epilepsy surgery

Surgical series	Engel class, Group I		Engel class, Group II		*p*-value
	Class I-II (%)	Class III-IV (%)	Class I-II (%)	Class III-IV (%)	
Temporal lobe resection	156 (87.7)	22 (12.3)	75 (94.8)	4 (5.2)	0.0324
Extratemporal resection	31 (77.5)	9 (22.5)	37 (84.1)	7 (15.9)	0.1168

outcome was noted in 7 patients (15.9%). Corpus callosotomy was performed in 3 patients (2.1%). Vagal nerve stimulation (VNS) emerged as an adjuvant option and this was performed in 13 patients (9.3%). Only 1 (7.6%) of them had a good outcome and 12 patients (92.4%) had a poor outcome.

Table 5 shows the results of the univariate analyses of the good (Engel's Class I-II) and poor (Engel's Class III-IV) outcomes between Group I and Group II. There were significant improvements of outcomes for TLE surgery (p = 0.0324). For the ETE surgery, the patients with a good outcome increased from 77.5% in Group I to 84.1% in Group II but there was no significant difference.

There were complications in 9 patients (2.2%). Four of them (44.4%) had post-operative wound infection. We removed the infected bone flaps and these were followed by cranioplasty. Two patients (22.2%) suffered post operative meningitis. There was one patient who underwent repeated craniotomy to evacuate epidural hematoma. One patient (11.1%) who had venous infarction needed craniectomy and one (11.1%) patient had transient sensory aphasia.

DISCUSSION

Epilepsy surgery is considered to be effective according to the findings on long-term follow-up. In a reported series, 60-70% of the patients who received temporal lobe epilepsy surgery have become seizure free and 32-45% of the patients who underwent extratemporal lobe epilepsy surgery have become seizure free[8,20,24,25,34]. There are numerous factors that influence the postoperative seizure outcomes. The predictive factors for the seizure outcomes after epilepsy surgery have been widely studied in many reports. Patients with temporal lobe and hippocampal abnormalities seen on qualitative MRI, complex febrile seizures and foreign tissue lesions can expect a higher success rate[1-3,14]. Patients with an early onset of epilepsy and a shorter history of seizures are also expected to have a good postoperative outcome on the long-term follow up[13,30,33].

We focused on the improvement of the epilepsy surgery outcomes over time and the factors that might influence these changes in conjunction with the surgical strategy. The patients were divided into two groups on the basis of the time of surgery to compare the changes of outcomes over time. The surgical outcomes were compared between the initial and recent patients with medically intractable epilepsy. Our protocol for the management of medically intractable epilepsy first included standard comprehensive preoperative evaluations such as patient's history, physical examination, neuropsychological evaluation as well as various imaging studies such as CT, MRI, fMRI, SPECT and FDG-PET, 24 hr-EEG monitoring and a WADA test. The selected patients sometimes underwent invasive monitoring in terms of a strip or grid. After all of these evaluations, we performed resective surgery that corresponded to the identified epileptic focus. Intraoperative ECoG was used to aid in delineating the epileptogenic zone.

In our study, intracranial monitoring decreased from 43.5% in Group I to 30.9% in Group II and the strip/grid ratio was reversed as 17/25 in Group II compared with 131/32 in Group I. As advanced diagnostic tools (fMRI, FDG-PET, SPECT, etc.) and high field (3.0T) MRI became available, diagnosis of the seizure focus became possible without invasive monitoring[15].

In some cases of bitemporal interictal epileptic form discharge and nonlateralized ictal surface recordings, we performed bilateral strip electrode implantation to lateralize the ictal focus. Although the efficacy of bilateral invasive monitoring for identifying an epileptogenic focus has been proven, it has also been shown that the patients who have bitemporal epileptogenicity have a worse surgical outcome[23,27]. Accordingly, strip-based bitemporal epilepsy was gradually excluded from our surgical indications. In contrast, number of grid based lateral TLEs or ETEs was increased. As a result, the grid cases exceeded the strip cases.

In our study, we found a statistically significant correlation between good outcome and identifiable lesions in MRI. We found 62.2% of the MRI lesions in Group I and 70.5% in Group II. There were more MR lesions in Group II and the patients who had MR abnormalities showed better outcomes as compared with that of the patients without them. The association of well circumscribed lesion and good post operative outcome has been demonstrated in many literatures[4,7,10].

We compared surgical outcome according each surgical series. A good outcome of TLE was much increased from 87.7% in Group I to 94.8% in group II. There were advancements of the surgical procedures both methodologically and technically over time. There were some modifications, after the initial period, when performing tailored resection that corresponded with the intraoperative ECoG findings. In recent period, more extended resection has been performed and the resection exceeded the areas that revealed epileptic discharge on the intraoperative ECoG. Consequently, this has all improved the overall outcome of TLE surgery, as well as the proportion of Engel class II outcomes was decreased and the proportion of Engel class I outcome was increased among the patients with a good outcome.

There has been a change that less early invasive multilobar surgery (11.3%) is now being performed and VNS (9.3%) has emerged as an adjuvant option for treating medically intractable epilepsy. Multilobar epilepsy surgery has been shown to have a poor outcome in many studies[11,32]. Our study showed agreement with literature as only 27.6% of the patients had a Class I outcome in Group I. Multilobar surgery is not being performed at our hospital any more. Instead, we applied VNS as a recent adjuvant surgical option. VNS is an alternative treatment for patients with medically refractory epilepsy and who are unsuitable candidates for conventional epilepsy surgery, or who have had such surgery without an optimal outcome. However, the outcome of VNS was not satisfactory. Only 1 patient (7.6%) had good outcome.

The improvement of the outcomes of the Group II patients can be attributed to advancements in selecting patients and the progress in surgical technique through a multidisciplinary approach. Group II patients had less invasive monitorings and more circumscribed MRI lesions. By changing our strategies, such as less invasiveness with advanced facilities, more strict selection of surgical candidate by ruling out uncertain cases and more extended resection for TLE, we were able to improve the outcomes of epilepsy surgery over the time.

CONCLUSION

This study shows that epilepsy surgery has become more effective over the years for treating medically intractable epilepsy patients and there has been continuous improvement of the outcomes. This development is attributed to well-suited patient selection, accurately identifying the epileptic focus through various presurgical evaluations and a more extended resection by an experienced surgical team. Studying the prognostic factors and the evolution of surgical strategies for surgically remediable epilepsy can surely lead to better surgical outcomes.

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