

Imprints of Seizure Rate and Epilepsy Duration on Temporal Lobe Epilepsy Outcome

Research Article

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Abstract

HS associated TLE is the common cause of PRE. Surgery is generally used to control seizures for these patients but most often seizure recurrence observed, reasons are not known. The aim of the study is to evaluate the effects of seizure rate and epilepsy duration on the long term post-surgical outcome of AEDs and onset age matched 153 HS associated PR-TLE patients. All the patients invariably associated with HS. Clinical data recorded during 2011 and 2023 obtained from outpatient at the department of Neurology, Krishna Institute of Medical Sciences, Secunderabad, India. EEG, MRI and FluoroJade stain used to diagnose the TLE-HS in patients. All patients undergone medial temporal lobectomy for HS and assessed for seizure free outcome after first, third and fifth years using Engel's and ILAE outcome system of classification. Overall 70.8% patients had very good post-surgical outcome (Engel's-I & II or ILAE-I) in first year, it was reduced to 59.3% in third year and 47.6% in fifth year. The mean seizure rate was 6 per month (range 0.3 – 258 per month). Patients belong to daily and yearly seizure classes had good post-surgical outcome after first year of the surgery ($p = 0.43$), however mean drop of Engel's-I or ILAE-I & II outcome after 5th year of the surgery was more in patients with weekly seizures ($p = 0.63$). Likely the mean epilepsy duration was 13.57 years (range 01 M – 42 years). Patients with less epilepsy duration had good post-surgical outcome than higher duration ($p = 0.41$). Besides unreliability of Engel's-I or ILAE-I & II outcome during post-surgical period observed in patients with less epilepsy duration ($p = 0.58$) and less surgery age ($p = 0.32$). Through this study we observed that high seizure rate reduced the consistency of the seizure freeness after surgery. On the other side higher duration of epilepsy and surgery ages lessen the immediate seizure freeness as well as consistency in outcome. However we did not find any statistical significance ($p < 0.05$) while analyzing these data. This study suggests the valuation of Histology, Biochemical and Molecular factors with long term post-surgical outcome.

Keywords: Seizure Rate; Epilepsy Duration; Hippocampal Sclerosis; Temporal Lobe Epilepsy; Pharmaco Resistant Epilepsy; Engel's Outcome; ILAE Outcome

Abbreviations

AEDs: Antiepileptic drugs; DN-KIMS: Department of Neurology, Krishna Institute of Medical Sciences; EEG: Electro Encephalo Gram; HS: Hippocampal Sclerosis; ILAE: International League Against Epilepsy; MRI: Magnetic Resonance Imaging; PR-TLE: Pharmaco resistant temporal lobe epilepsy; TLE: Temporal Lobe Epilepsy.

Introduction

Temporal lobe epilepsy (TLE) is a form of focal epilepsies that is always recalcitrant to antiepileptic drugs (AEDs) known as pharmaco resistant temporal lobe epilepsy (PR-TLE) [1, 2]. Hippocampal sclerosis (HS) is the most common epileptic foci finding in PR-TLE patients where surgery is enormously used to control seizures [3-

6]. Despite the seizure freeness allied with epilepsy surgery, sizable number of post-surgical patients remains to have seizures. Also, it has been noticed that decreasing of seizure freeness over the years in patients with seizure free outcome, although AEDs used [7, 8]. The motives for surgery failure in PR-TLE patients and lack of seizure free consistency over the post-surgical period are not well acknowledged. One conceivable supposition is that an enduring seizures cause an epileptogenic fuel processes such as synaptic plasticity, cell proliferation, cell death, inflammation and immune responses [7-12], that finally triggers new epileptic foci [13, 14]. So it is presumed that higher the seizure rate and longer the epilepsy, the higher the risk of new epileptic foci, consequently lower the chance to be seizure free after epilepsy surgery. Therefore the seizure rate and duration of epilepsy should be an important prophets of outcome in epilepsy surgery. The purpose of our study was to determine whether there is a link to seizure rate and duration with long term outcome.

Methods

The study was recorded and conducted as a review at the Department of Neurology, Krishna Institute of Medical Sciences (DN-KIMS), Secunderabad, India. Our internal ethical committee was informed about the study and it has approved. Data from HS associated PR-TLE patients operated at the DN-KIMS were collected. Patients were examined and operated on between 2011 and 2023 were reviewed. A total of 153 PR-TLE patients using 3-4 AEDs with <12 years of onset age were considered for this analysis [Table-I]. Histological studies with fluorojade stain confirmed the association of HS (Neuronal cell death) in the PR-TLE tissue samples [15]. All patients underwent unvarying presurgical examination like neuropsychology, EEG and MRI including quantitative hippocampal volume measurements with T_2 relaxation time [16] and Sodium Amytal (WADA) test [17]. Post-surgical MRI studies in patients with no significant seizure free showed that the envisioned structures were resected. Post-surgical upshot data at first, third and fifth year postoperatively were classified by means of Engel's classification. (Engel's-I = seizure free with rare auras, Engel's-II = 1 or 2 seizures per year, Engel's-III = more than 90% of the seizures reduced, Engel's-IV = no significant reduction or worse [18]. Patients falling into the various subgroups of Engel's classes were pooled. The International League against Epilepsy (ILAE) lately advocated a revision of the classification [19]. In this study Engel's-I = ILAE 1 and 2, Engel's-II = ILAE 3, Engel's-III = ILAE 4, Engel's-IV = ILAE 5. The outcome of the surgery considered into ILAE classification criteria was collected individually. Student t-test was used to identify the significant variances.

Result

EEG, MRI and histological studies conformed the association of HS to PR-TLE patients [Figure 1]. Overall 70.8%, 59.3% and 47.6% HS allied PR-TLE patients were seizure free (ILAE-I outcome) in one year, three years and five years after the surgery. The number of patients with different outcome classes after 1st, 3rd and 5th years of surgery were as follows: ILAE-I = 109, 97, 73; ILAE-II = 34, 45, 56; ILAE-III = 10, 11, 24; ILAE-IV-VI = 00, 00, 00. The mean seizure rate was 6 per month (range 0.3 – 258 per month). As per the ILAE outcome chart [19] we noticed that patients be the members of daily (mean seizures 37.6 per month) and yearly (mean seizures 0.7 per

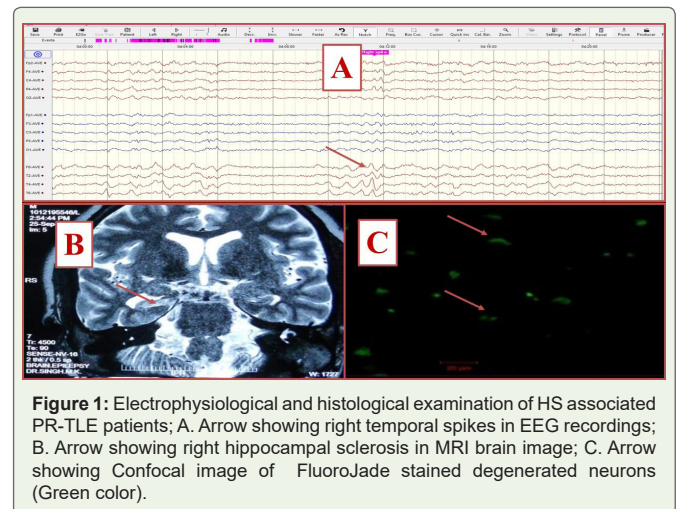


Figure 1: Electrophysiological and histological examination of HS associated PR-TLE patients; A. Arrow showing right temporal spikes in EEG recordings; B. Arrow showing right hippocampal sclerosis in MRI brain image; C. Arrow showing Confocal image of FluoroJade stained degenerated neurons (Green color).

month) seizure classes were good post-surgical outcome after first year of the surgery ($p = 0.61$). For instance post-surgical ILAE-I outcome in different seizure classes: daily = 84%, 70.8%, 64.5%; weekly = 63%, 44%, 31%; monthly = 66%, 52%, 47%; yearly = 71.8%, 62.5%, 50% after 1st, 3rd and 5th years respectively [Figure 2]. But average falling of seizure freeness after 5th year of surgery was more in patients with weekly seizures ($p = 0.63$). Mean dropping of ILAE-I outcome in various seizure classes: Daily = 10.5%, weekly = 16.2%, monthly = 7.8% and yearly = 11.5% after 5th year of surgery [Figure 3].

The mean duration of epilepsy was 13.57 years (range 01 M – 42 years). Based on the outcome chart of different epilepsy duration groups it was observed that patients be the members of less epilepsy duration groups (<1 year and 1-12 years) were exhibiting good post-surgical outcome after first year of the surgery ($p = 0.41$) than more epilepsy duration groups. For instance post-surgical ILAE-I outcome in different epilepsy duration groups after 1st, 3rd and 5th years: <1 year = 83%, 67%, 50%; 1-12 years = 92%, 79%, 71%; 13-22 years = 41%, 23.7%, 19%; 23-32 years = 36%, 26%, 13.6%; 33-42 years = 15%, 11%, 09% respectively [Figure 4]. Interestingly dipping of seizure freeness after 5th year of surgery was more in patients with lowest epilepsy duration. In this study the average falling of ILAE-I outcome in various epilepsy duration groups: <1 year = 16.5%; 1-12 years = 10.5%; 13-22 years = 10.5%; 23-32 years = 11.5%; 33-42 years = 3% after 5th year of surgery ($p = 0.58$) (Figure 5). Further we studied the association of surgery age of patients with different seizure frequency and epilepsy duration groups. We observed a positive correlation of surgery age with different epilepsy duration groups and also dropping of ILAE-I outcome after 5th year of surgery, in illustration the surgery age of 13.4 years = 8%, 20.4 years = 5.5%, 28.3 years = 7.5%, 38.12 years = 16.5% and 40.6 years = 18% reduction in seizure free outcome ($p = 0.32$). The youngest patient was 7 years old at the time of operation with ILAE-I outcome thereafter the surgery. She had suffered from epilepsy since the age of 4 years (4 years of epilepsy duration) with seizure frequency of 8 per year. Similarly the oldest patient was 50 years old at the time of operation with ILAE-III outcome afterwards the surgery. He had suffered from epilepsy since the age of 24 years (26 years of epilepsy duration) with seizure frequency of 9 per year.

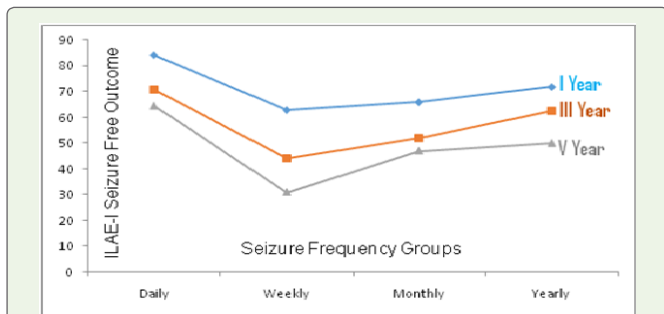


Figure 2: ILAE-I outcome in various seizure frequency groups after I, III and V years of surgery. * (Daily: > 365 seizures/year; Weekly: > 56 seizures/year; Monthly: >12 seizures/year; Yearly: < 12 seizures/year)

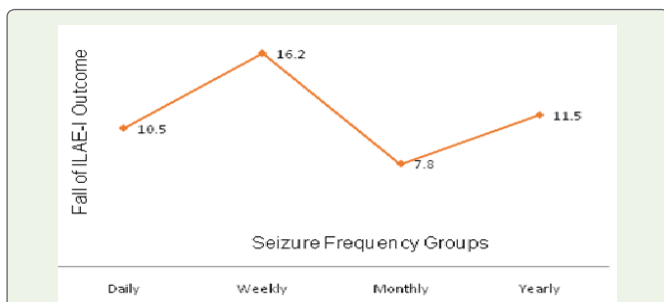


Figure 3: Mean reduction in ILAE-I outcome in various seizure frequency groups after V year of surgery. * (Daily: > 365 seizures/year; Weekly: > 56 seizures/year; Monthly: >12 seizures/year; Yearly: < 12 seizures/year)

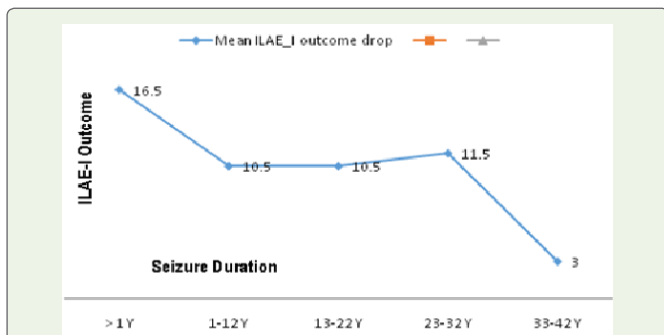


Figure 4: ILAE-I outcome in various seizure duration groups after I, III and V years of surgery

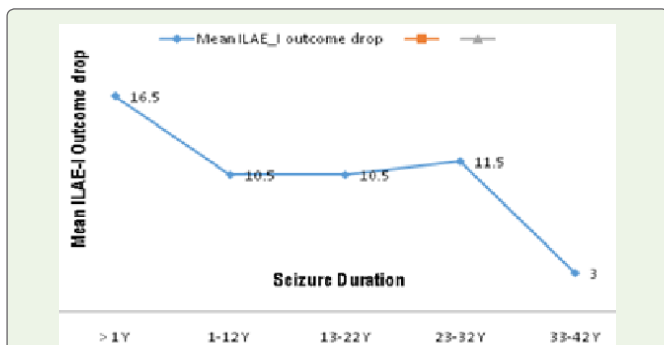


Figure 5: Mean reduction in ILAE-I outcome in various seizure duration groups after V year of surgery.

Table 1: Showing HS allied PR-TLE patient's clinical data. All patients using 3-4 AEDs and have <12 years of onset age.

S. No	Seizure Frequency per Year	Seizure Duration in Years	ILAE Outcome		
			1 st Year	3 rd Year	5 th Year
1	1250	0.8	I	II	III
2	487	28	II	III	III
3	09	11	I	I	II
4	367	3	I	I	I
5	3046	12	I	II	II
6	15	10	I	II	II
7	368	0.9	I	I	II
8	13	0.5	I	I	I
9	654	1	I	I	II
10	120	9	II	II	II
11	8	12	I	II	III
12	1678	3	I	I	I
13	9	21	II	II	III
14	14	31	II	II	II
15	7	42	III	III	III
16	567	11	I	I	I
17	368	12	I	II	III
18	16	10.5	I	I	I
19	368	27	II	II	II
20	1246	12	I	I	I
21	368	2.4	I	I	I
22	234	21	II	II	II
23	6	11	II	II	III
24	3065	12	I	I	I
25	1246	15.7	I	II	II
26	8	13	II	II	II
27	18	9	I	II	II
28	358	7.5	I	I	II
29	14	3.5	I	I	I
30	1256	35	III	III	III
31	1265	11.2	I	I	I
32	4	12	I	II	II
33	8	9.6	I	I	I
34	65	5.5	I	I	I
35	21	12.9	II	II	II
36	1245	11	I	I	II
37	56	2.5	I	II	II
38	126	4.7	I	I	I
39	126	27	II	II	II
40	8	11.6	I	I	I
41	1248	3.5	I	I	I
42	359	15.7	I	II	II
43	568	3.4	I	I	II
44	12	15.5	II	II	II
45	6	11.5	I	I	I
46	7	19	II	II	II
47	18	11	II	II	II
48	6	1.8	I	I	I
49	232	3.7	I	I	II
50	368	11.5	I	I	I
51	17	34	II	II	II
52	346	37	II	III	III
53	6	12	I	I	I
54	45	34	II	II	II

55	1256	11	I	I	I
56	87	23	II	II	II
57	656	32	II	II	II
58	6	11	I	I	I
59	789	5.6	I	I	I
60	4	3.9	I	I	I
61	234	15.3	II	II	II
62	8	2.3	I	I	I
63	121	17.3	II	II	II
64	358	11.3	I	I	I
65	465	23	II	II	II
66	7	6.4	I	I	I
67	16	41	III	III	III
68	256	12	I	II	II
69	1896	3.6	I	I	I
70	189	2.3	I	I	II
71	359	1.6	I	I	I
72	1234	12.6	I	I	II
73	6	3.5	I	III	III
74	6	3.7	I	I	I
75	21	5.3	I	I	I
76	34	11.4	I	II	II
77	867	12	I	I	I
78	58	14	II	II	II
79	390	11	I	I	II
80	24	15	II	II	II
81	56	41	II	II	II
82	389	32	I	I	II
83	4	11	I	I	I
84	192	9	I	I	I
85	9	23	II	II	II
86	9	0.9	I	I	I
87	234	27	II	II	II
88	1456	11.3	I	III	III
89	13	11.9	I	II	II
90	8	1.8	I	I	I
91	19	41	III	III	III
92	8	18.5	I	II	II
93	563	11	I	I	I
94	34	11.3	I	II	II
95	387	12	I	I	I
96	9	15.7	II	II	III
97	16	1.0	I	I	I
98	657	0.1	II	II	II
99	9	1.2	I	I	I
100	563	1.7	I	I	I
101	1236	23	II	II	II
102	7	37	I	I	II
103	12	12.7	II	II	II
104	456	5.5	I	I	I
105	15	13.5	I	I	II
106	456	1.5	I	I	I
107	376	3.9	I	I	I
108	631	4.6	I	I	I
109	46	9	II	II	II
110	8	11	I	I	I
111	122	11.5	I	II	II
112	564	7.5	I	I	I
113	9	12.5	I	III	III

114	346	14	II	II	II
115	9	3.7	I	I	I
116	6	11	I	I	I
117	896	22	II	II	II
118	7	10.5	I	I	I
119	234	11	I	II	II
120	368	23	II	II	II
121	9	12	I	I	I
122	78	11	I	I	I
123	387	12	I	I	I
124	12	23	II	II	II
125	68	15	I	I	II
126	359	3.2	I	I	I
127	156	4	I	I	I
128	12	7	I	I	I
129	87	5	I	II	II
130	415	9	I	I	I
131	4	12	I	II	II
132	8	21	III	III	III
133	7	15	II	II	II
134	18	25	II	II	II
135	675	11	I	II	II
136	124	41	III	III	III
137	680	14	II	II	II
138	8	11	I	I	II
139	357	12	I	I	I
140	568	27	II	II	II
141	1246	39	I	I	III
142	14	11	I	II	II
143	1056	11.5	I	I	I
144	224	34	I	II	III
145	1250	1.5	I	I	I
146	6	11	I	II	II
147	56	8	I	II	II
148	367	1	I	I	II
149	3096	0.2	I	I	I
150	13	3	I	II	II
151	04	0.4	I	I	I
152	78	5	I	II	II
153	712	8	I	II	II

Discussion

In this study we observed that, the seizure rate and the duration that the patients have had HS linked PR-TLE, have a profound effect on the outcome of their subsequent surgery. We found a trend for a better outcome in patients with daily and yearly seizures as well as shorter duration of epilepsy and surgery age which was not statistically significant. All the PR-TLE patients were homogeneous in terms of onset age, AEDs usage and surgery procedures [1,20-22]. Patient assortment and presurgical investigations were standardized. The upshot of the surgery considered into ILAE classification criteria was collected independently and blindly (i.e. with no submission while collecting the information as to what it was to be analysed for), to reduce information collection bias. Our study was based on the results of most other studies, which tried to link up the seizure rate and duration of epilepsy discretely with post-surgical outcome [23-26] [27-29]. Due to polemics in prediction of long term outcome [1,30-

32], we used one year, three years and five years next to the surgery for outcome prediction. Our study plainly described that the seizure rate and epilepsy duration govern the seizure predisposition later years after the surgery. The main advantage of our study was that no patient was lost throughout the follow-up assessments and all supported well. Patients who grieved from epilepsy with frequent seizures for a long time may have greater risk of depressive and cognitive side effects of epilepsy surgery [33], but some patients can have a tremendous outcome. This result is imperative when determining whether a patient should be offered surgery. Furthermore our data fairly support the existence of an ongoing epileptogenic process, triggered by frequent seizures and duration of epilepsy within certain surgery age. At least in our patient population, a kindling process can be entirely included. Kindling may be related to the seizure rate and duration of epilepsy besides, lack of statistical significance.

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