Intertechnique Agreement in Epilepsy Imaging

Epilepsi Görüntülemesinde Modaliteler Arası Uyum

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ABSTRACT

Objective: To analyze seizure semiology, scalp video-electroencephalography, magnetic resonance imaging (MRI) and 18F-fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET) findings in patients with medically refractory epilepsy, to assess the concordance rate between clinical-electroencephalography findings and neuroimaging studies for localizing epileptogenic foci.

Material and Methods: This retrospective study included 108 consecutive patients (male/female=59/49;mean age=26.6±10.5 years) who were classified according to clinical-electroencephalography findings (either temporal or extra-temporal lobe epilepsy [TLE]) between January 2011 and January 2017. Statistical analysis was performed using a t, Mann-Whitney U, McNemar, or $\chi 2$ tests.

Results: Fifty-six patients had TLE (male/female=30/26, mean age=30.1±8.9 years) and 52 had extra-TLE (male/female=29/23,mean age=22.8±10.9 years) according to clinical-electroencephalography findings. Twelve of 108 patients (male/female=6/6, mean age=28.7±10.2 years) underwent epilepsy surgery and the mean postoperative follow-up period was 32 months. The highest concordance rate between clinical-electroencephalography findings and neuroimaging studies (76%) was found in patients with non-hippocampal sclerosis abnormality in TLE group. In patients with malformations of cortical development on MRI, the concordance rate (84.2%) between clinical-electroencephalography findings and MRI was better than those between clinical-electroencephalography findings and FDG-PET (52.6%) (p=0.010).The concordance rate between clinical-electroencephalography findings and neuroimaging studies for TLE (48.2%) was better than for extra-TLE (9.6%) (p<0.001). No significant difference was found in the localization of the epileptogenic focus between MRI and FDG-PET according to the seizure outcome of patients (p=1).

Conclusion: FDG-PET may not help in revealing epileptic region in cases with abnormal MRI especially in malformations of cortical development. The highest concordance rate between clinical-electroencephalography findings and neuroimaging studies is found in TLE patients with findings inconclusive of hippocampal sclerosis. With low concordance rate between clinical-electroencephalography findings and neuroimaging studies in extra-TLE, meticulous use of multiple modalities is necessary for accurate pre-surgical evaluation.

Key Words: Epilepsy, Magnetic resonance imaging, Positron emission tomography

ÖZ

Amaç: Medikal tedaviye dirençli epilepsi hastalarında nöbet semiyolojisi, skalp-video elektroensefalografi, manyetik rezonans görüntülüme (MRG) ve 18-floro-2-deoksi-glukoz pozitron emisyon tomografi (FDG-PET) bulgularının değerlendirilmesi, epileptojenik odağı lokalize etmede klinik-elektroensefalografi bulguları ile nörogörüntüleme yöntemleri arasındaki uyumun değerlendirilmesi amaçlandı.

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Gereç ve Yöntemler: Retrospektif olan çalışmamız hastane etik kurul onayı alınarak yapıldı. Çalışmaya, Ocak 2011 ile Ocak 2017 tarihleri arasında, klinik-elektroensefalografi bulgularına göre temporal (30 erkek, 26 kız, ortalama yaş 30.1±8.9 yıl) ve ekstra-temporal lob epilepsi (29 erkek, 23 kız, ortalama yaş 22.8±10,9 yıl) gruplarına ayrılan ardışık 108 hasta (59 erkek, 49 kız, ortalama yaş 26.6±10.5 yıl) dahil edildi. Kategorik-sayısal değişkenler t, Mann-Whitney U, McNemar veya Ki-kare testi ile analiz edildi.

Bulgular: Çalışmaya dahil edilen 108 hastanın 12'si (6 erkek, 6 kız, ortalama yaş 28.7±10.2 yıl) epilepsi cerrahisi geçirdi ve bu hastaların operasyon sonrası ortalama takip süresi 32 aydı. Klinik-elektroensefalografi bulguları ile nörogörüntüleme yöntemleri arasında en yüksek uyum (%76) hippokampal skleroz dışı anormallikler sahip temporal lob epilepsili hastalarda saptandı. MRG'de kortikal gelişimsel anormalliklere sahip hastalardaki, klinik-elektroensefalografi bulguları ile MRG arasındaki uyum (%84.2), klinik-elektroensefalografi bulguları ile FDG-PET arasındaki uyumdan (%52.6) yüksekti (p=0.010). Temporal lob epilepsilerindeki klinik-elektroensefalografi bulguları ile nörogörüntüleme yöntemleri arasındaki uyum (%48.2), ekstra-temporal lob epilepsilerine (%9.6) göre daha yüksekti (p<0.001). Opere olan hastaların takiplerine göre MRG ile FDG-PET arasında epileptojenik odağı lokalize etmede anlamlı farklılık saptanmadı (p=1).

Sonuç: FDG-PET epileptojenik odağın lokalize edilmesinde, özellikle MRG'de kortikal gelişimsel anormalliklerin saptandığı hastalarda yardımcı olamayabilir. Klinik-elektroensefalografi bulguları ile nörogörüntüleme yöntemleri arasındaki en yüksek uyum hippokampal skleroz dışı anormalliklere sahip temporal lob epilepsili hastalarda saptandı. Ekstra-temporal lob epilepsilerindeki klinik-elektroensefalografi bulguları ile nörogörüntüleme yöntemleri arasındaki düşük uyum, ekstra-temporal lob epilepsilerinin cerrahi öncesi değerlendirilmesinde, farklı yöntemlerin kullanılmasını gerektirmektedir.

Anahtar Sözcükler: Epilepsi, Manyetik rezonans görüntüleme, Pozitron emisyon tomografi

INTRODUCTION

Epilepsy is a common neurological disorder with a prevalence of 0.4–0.8% (1, 2) and nearly one-third of patients with epilepsy have medically refractory epilepsy (3). Surgery has been validated as an effective treatment for selected patients with medically refractory epilepsy both in children and adults. Epilepsy surgery involves resection/destruction/disconnection of the epileptogenic region without causing neurological deficit (1, 2, 4). Diagnostic evaluation is based on the clinical and non-invasive modalities including electroencephalography (EEG), structural (magnetic resonance imaging [MRI]), and metabolic (positron emission tomography [PET], ictal single-photon-emission computed tomography) imaging (4). Scalp video-EEG monitoring is the primary method of searching for localizing ictal activity and MRI plays a crucial role in identifying the anatomic location of the epileptogenic focus. The sensitivity of MRI in identifying the epileptogenic focus has been reported as being between 80% and 90% (3), however, in some patients; MRI fails to show lesions, despite localizing features on seizure semiology and EEG (5). In this situation, multiple diagnostic modalities are usually necessary to detect the epileptogenic focus and the correlation of clinical-EEG findings with these studies is essential to localize the proper epileptogenic focus in patients who can be good candidates for surgery. In previous studies, a wide range of concordance rate between clinical-EEG findings and neuroimaging studies (MRI and PET) has been reported for temporal (13%–68%) and extra-temporal lobe epilepsy (TLE, 36%–83%) in patients with medically refractory epilepsy (6–9).

Our study was designed to analyze seizure semiology, scalp video-EEG, MRI and 18F-fluoro-2-deoxy-D-glucose (FDG) PET findings in patients with medically refractory epilepsy and to assess the concordance rates (CR) between clinical-electroencephalography findings and neuroimaging studies for localizing epileptogenic foci. Unlike most previous studies, we also evaluated the CR between clinical-electroencephalography findings and neuroimaging studies in non-hippocampal sclerosis abnormalities of the temporal lobe.

MATERIAL and METHODS

Patient population

The study was approved by the local ethics committee (ethics reference number: 36/09). This retrospective study included 108 consecutive patients with medically refractory epilepsy (male/female = 59/49; mean age = 26.6 ± 10.5 years, age ranges, 4–46 years) who underwent presurgical evaluation for epilepsy surgery between January 1, 2011 and January 1, 2017. Exclusion criteria for the patients in the study included a) having inadequate medical information (the age at epilepsy onset, duration of epilepsy, and potential risk factors for epilepsy such as family history, febrile seizures), scalp video-EEG, MRI and FDG-PET (n = 7), b) missing or inconclusive histopathological records (n = 4), c) prior cranial surgery (n = 7), and d) having brain neoplasm, vascular malformation, posttraumatic lesions, and infarction or bleeding residua (n = 19).

Scalp electroencephalography

All patients were admitted to the video-EEG monitoring unit for 3–10 days; recordings were obtained using a 32-channel EEG system (Grass-Telefactor). Electrodes were placed according to the standard 10–20 system; in addition T1 and T2 electrodes were placed. The seizure semiology and interictal-ictal EEG changes of patients were reviewed by experienced epileptologists after a consensus was reached (F.I.T., S.S. for adult patients, D.Y., C.G., G.T., and M.T. for pediatric patients). The location and frequency of interictal epileptiform discharges were assessed by visual analysis of interictal EEG samples. Patients' seizure types and epilepsy syndromes were

determined according to International League Against Epilepsy classifications (10). No patients underwent to intracranial EEG monitoring. According to clinical-EEG findings, the patients were divided into two groups: TLE (lateralizing, 100% [56/56]) and extra-TLE (lateralizing, 76.9% [40/52], non-lateralizing, 23.1% [12/52]).

Magnetic resonance imaging

All MRI was performed on 1.5T scanners (Symphony, Siemens, Germany and Achieva, Philips Healthcare, Netherlands) with a multi-channel head coil and included the following sequences: axial spin-echo T1-weighted imaging (WI) (TR/TE: 300–500/15–30 ms), axial fluid-attenuated inversion recovery (FLAIR,TR/TE: 8000–10000/100–120 ms), axial T2WI and coronal T2WI (TR/TE: 4000–5500/90–110 ms) and coronal inversion recovery (TR/TE/TI: 9000–9650;6000–7000/16;15/750;400 ms) obtained perpendicular to the long axis of the hippocampus, axial T2* weighted gradient-echo (TR/TE: 850;700/20–20 ms), coronal 3D T1-weighted gradient-echo (TR/TE: 1800–2000;19–25/3.9;4.6–5.2 ms). All sequences were obtained with 3 mm section thickness except 3D T1-weighted gradient-echo (1 mm). Images were analyzed for the hippocampal sclerosis, non-hippocampal sclerosis abnormality of the temporal lobe, and malformations of cortical development by consensus of two neuroradiologists (A.G. and K.K.O.) who were unaware of the clinical-EEG and FDG-PET findings of patients. The MRI features of hippocampal sclerosis included hippocampal atrophy, increased signal on T2WI/FLAIR, and loss of internal architecture of hippocampus (11–13). The hippocampal volume loss without T2/FLAIR signal abnormality or hippocampal T2WI/FLAIR signal abnormality without volume loss, and signal and/or morphological asymmetry of the amygdale, indistinct gray-white matter junction in the medial temporal lobe were considered to have potential epileptogenic lesions and were recorded as MRI-positive, non-hippocampal sclerosis abnormality of the temporal lobes.

Positron emission tomography

Interictally, epileptogenic zones are frequently associated with reduced regional cerebral metabolism, which can be detected with PET by using FDG (14). If more than one PET scan had been performed on a patient, the first FDG-PET scan was used in this analysis. All patients underwent FDG-PET at the Department of Nuclear Medicine and all studies were performed at least 2 days after the last seizure of patients. PET scans were interpreted by consensus of three experienced nuclear medicine physicians (B.V.S., E.L.E., and B.E.) who were unaware of the clinical histories or the results of other presurgical evaluations of the patients. For the PET images, the area of the greatest decrease in uptake of FDG was considered the epileptogenic zone based on symmetry by means of side-by side visual analysis.

Histopathology

All tissue specimens and histopathology independently evaluated by a neuropathologist with 25 years of experience (F.S.). Focal cortical dysplasia was classified according to ILAE 2011 classification (10). Hippocampal sclerosis was defined by characteristic loss of neurons and gliosis in the hippocampus, preferentially involving the dentate, CA4, CA3, and CA1 regions (15).

Evaluation of findings

All neuroimaging and electrophysiological studies were done within 6–8 weeks, and the localization of the presumed epileptogenic zone was determined by consensus during the patient management conference of the epilepsy unit (including adult and pediatric epileptologists, nuclear medicine physicians, neuroradiologists and neurosurgeon [B.B.]). 'Concordance' was accepted when the abnormal findings were consistent between clinical-electroencephalography findings and neuroimaging studies. Patients who had concordance between clinical-EEG findings and neuroimaging studies underwent surgery. The postoperative seizure outcomes of patients at final follow up were assessed by using Engel classification system (16). Patients were categorized as seizure-free (Engel's class I) or not (Engel's classes II–IV).

Statistical analysis

Continuous data that were expressed as the mean ± standard deviation or median (interquartile range) were analyzed using a t-test or Mann-Whitney U test. Categorical data that were expressed as numbers with percentages were compared using a χ^2, McNemar or Fisher's exact test. Binary logistic regression analysis was performed to identify risk factors of hippocampal sclerosis. Statistical analysis was conducted with statistical software (SPSS, version 21.0; SPSS Inc, Chicago, IL, USA). Results were considered statistically significant at $p < 0.05$.

RESULTS

Fifty-six patients had TLE (M/F = 30/26, mean age = 30.1 ± 8.9 years, age ranges, 12–45 years) and 52 had extra-TLE (M/F = 29/23, mean age = 22.8 ± 10.9 years, age ranges, 4–46 years) according to clinical-EEG findings. Twelve of 108 patients (11.1%) (M/F = 6/6, mean age = 28.7 ± 10.2 years, age ranges 12–44 years) underwent epilepsy surgery and the postoperative follow-up period ranged from 14 to 54 months (mean, 32 months). Seventy-five of 108 patients (69.4%) had possible risk factors (i.e. febrile seizure, head injury, family history of epilepsy, perinatal insult, and encephalitis) for epilepsy. No significant difference was found between age at onset of epilepsy and the presence of risk factors ($p = 0.406$) (see Table I, supplementary material).

The mean ages of patients ($p < 0.001$) and age at epilepsy onset ($p = 0.007$) of extra-TLE patients were lower than those of TLE patients. There was no significant difference in the epilepsy duration between TLE and extra-TLE groups ($p = 0.051$). Clinical characteristics of the patients, history related

Table I: Medical information, scalp video-electroencephalography (EEG), magnetic resonance imaging (MRI) and 18F-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) findings of patients categorized as temporal lobe epilepsy (TLE) and extra-TLE.

	Age*/ Sex	Age at onset of seizures	Epilepsy duration*	Risk factors	GTCS	SE	ii-EEG	i-EEG	Semiology and EEG	MRI	FDG-PET
1	32/M	13	19	1	+	+	L t	L t	TLE-L	L t,NHAS	L t
2	26/M	6	20	1	–	–	L t	L t	TLE-L	L t,FCD	L t
3	45/M	36	9	1	+	+	Blt t	R t	TLE-R	L t,FCD	n
4	25/M	5	20	1,2,4	–	–	R t	R t	TLE-R	R t,FCD	n
5	26/F	20	6	3	+	–	R t	R t	TLE-R	R t,FCD	R t
6	42/M	35	7	2,6	+	–	R t	R t	TLE-R	R t,NHAS	n
7	37/M	24	13	0	+	+	L t	L t	TLE-L	L t,NHAS	L t
8	36/F	20	16	3,4	–	–	Blt t	R t	TLE-R	n	R t
9	35/M	18	17	4	+	–	Blt t(R>L)	Blt t (L>R)	TLE-L	n	Blt t
10	39/M	25	14	4	+	+	Blt t	Blt t	TLE-L	L HS	n
11	33/M	7	26	1,4	–	–	L t	L t	TLE-L	L HS	Blt t
12	31/F	20	11	0	–	–	L t	L t	TLE-L	R t,NHAS	Blt t
13	27/M	12	15	1,4	+	–	Blt t	Blt t(R>L)	TLE-R	R t,NHAS	R t
14	25/M	17	12	1,3	–	–	R t	R t	TLE-R	R t,NHAS	R t
15	29/M	10	19	1	+	–	L t	L t	TLE-L	L t,NHAS	L t
16	25/F	3	22	4	–	–	L t	L t	TLE-L	L t,NHAS	L t
17	20/F	8	12	0	+	–	R t	R t	TLE-R	R t,NHAS	R t
18	31/F	6	25	2,4	+	–	R t	R t	TLE-R	R oc, FCD	n
19	22/F	7	15	3	–	–	L t	n	TLE-L	R t,NHAS	n
20	40/F	17	23	0	+	–	L t	L t	TLE-L	L t,NHAS	L t
21	40/M	19	21	4,5	+	+	R t	n	TLE-L	n	L t
22	23/F	12	11	0	+	+	L t	L t	TLE-L	L t,NHAS	L t
23	33/F	12	21	1,3,4	+	+	Blt t(L>R)	R t	TLE-L	L HS	Blt t
24	41/M	27	14	0	–	+	Blt t(R>L)	R t	TLE-R	n	R t
25	36/M	30	6	0	+	–	L t	L t	TLE-L	R t,NHAS	R t
26	36/F	28	8	3	+	+	L t	L t	TLE-L	n	L t
27	25/F	11	14	1,4	+	+	L t	n	TLE-L	R t,NHAS	n
28	20/M	13	7	0	+	+	L t	L t	TLE-L	L t,FCD	L t
29	19/M	1.5	17.5	2,3	–	–	L t	L t	TLE-L	L t,FCD	L t
30	20/F	10	10	3	–	–	Blt t(L>R)	n	TLE-L	R t,NHAS	R t
31	18/F	5.5	12.5	0	+	+	L t	L t	TLE-L	L t,NHAS	L t
32	31/F	15	16	3	+	–	L t	L t	TLE-L	n	n
33	34/M	14	20	1,4	+	+	L t	L Hms	TLE-L	L HS	L t
34	31/F	1.5	29.5	1,4	+	+	R t	L t	TLE-L	L HS	L t
35	43/F	15	28	3,4	–	–	Blt t(L>R)	L t	TLE-L	R HS	n
36	27/M	1	26	4	+	–	Blt t(L>R)	L t	TLE-L	L HS	L t
37	35/F	17	18	4	+	–	Blt t(L>R)	L t	TLE-L	L HS	L t
38	36/M	2.5	33.5	1,3	–	–	Blt t(R>L)	R t	TLE-R	L HS	L t
39	24/F	20	4	0	+	–	R t-p	R t-p	TLE-R	n	R t
40	38/M	30	8	4	+	–	L t	L t	TLE-L	L HS	n
41	41/F	16	25	3	+	–	R t	Blt t	TLE-R	R HS	n
42	44/F	7	37	4	–	+	L t	L t	TLE-L	L HS	L t
43	40/M	1.5	38.5	4	+	+	R t	R t	TLE-R	R HS	R t
44	33/M	12	11	1,4	+	–	Blt t(R>L)	R t	TLE-R	R HS	R t

45	27/M	3	24	4	+	+	L t	L t	TLE-L	L HS	L t
46	45/M	10	35	1,3	+	–	Blt t(L>R)	n	TLE-L	L HS	Blt t
47	37/M	5	32	3	+	–	R t	R t	TLE-R	R HS	R t
48	19/F	16	3	0	+	+	n	R t-p	TLE-R	R HS	n
49	32/F	18	14	0	+	–	R t	R t	TLE-R	R t,NHAS	R t
50	25/M	13	12	0	+	–	L t	L t	TLE-L	n	L t
51	12/M	9	3	0	–	–	R Hms	R t	TLE-R	R t,FCD	Blt t
52	12/M	9	3	0	–	–	L fr-t	L fr-t	TLE-L	n	L t
53	8/F	2.5	5.5	0	–	–	L t	L t	TLE-L	n	n
54	20/F	7	13	4	+	+	R Hms	R Hms	TLE-R	R HS	R t
55	12/F	0.75	11.25	6	–	–	L fr	L fr	TLE-L	L HS	L t
56	43/F	14	29	0	+	–	R t	R t	TLE-R	R t,FCD	n
57	20/F	8	12	0	+	+	n	n	ETLE	R fr,FCD	R fr
58	20/F	15	5	1	–	–	Blt t	n	ETLE	heterotopia	n
59	16/M	14	2	1,3	+	–	L fr	L fr	ETLE-L	L p,FCD	n
60	33/M	15	18	2	+	–	Blt t	n	ETLE-R	n	n
61	35/M	7	28	1,6	–	–	L fr	L fr	ETLE-L	L fr,FCD	n
62	40/M	31	9	0	+	+	R fr	R oc	ETLE-R	n	n
63	32/F	5	27	1	+	–	L fr	L fr	ETLE-L	L fr,FCD	L fr
64	22/M	10	12	3	–	–	L Hms	extra-t	ETLE	L t,NHAS	Blt t
65	28/M	5	23	0	+	–	R fr	n	ETLE-R	n	n
66	29/F	13	16	2	–	–	L fr	L fr	ETLE-L	L fr,FCD	L fr
67	43/M	30	13	1	+	+	L Hms	L fr	ETLE-L	n	L fr
68	26/M	11	15	1,2,3,4	–	–	R fr-t	R Hms	ETLE-R	n	R t-p
69	31/M	6	25	1,3	+	+	n	fr	ETLE	n	n
70	32/F	20	12	1,3,4	+	+	n	n	ETLE	n	n
72	34/M	16	18	2	+	+	Blt t(L>R)	extra-t	ETLE-L	n	n
72	38/F	4	34	1,3	+	–	L t	L t-p	ETLE-L	n	n
73	23/F	6	17	1,3	+	+	R p	R fr	ETLE-R	n	n
74	46/F	4	42	3,4	+	–	L Hms	n	ETLE	L HS	L t
75	19/F	16	3	0	+	–	R fr-t	R fr-t	ETLE-R	n	n
76	25/M	17	8	1,3	+	–	R fr-t	R fr-t	ETLE-R	n	n
77	18/F	3	15	1,2,3	–	–	Blt fr	generalized	ETLE	n	n
78	36/M	10	26	1,2	+	+	R fr-t	R fr	ETLE-R	n	R fr-p
79	22/F	2.5	19.5	4	+	+	Blt t(L>R)	R t	ETLE-R	n	n
80	23/F	11	12	2	+	–	L Hms	L Hms	ETLE-L	n	n
81	21/M	8	13	3,4,5	+	–	L fr	extra-t	ETLE-L	n	n
82	25/F	7	18	0	+	+	n	L Hms	ETLE-L	n	n
83	26/M	4	22	3	+	+	Blt t	n	ETLE-R	R fr,FCD	R fr
84	39/M	20	19	3,4	+	+	n	R Hms	ETLE-R	n	R fr
85	22/M	12	10	2,4,5	+	–	n	R extra-t	ETLE-R	n	n
86	30/F	4	26	0	+	–	L t	n	ETLE-L	n	n
87	19/M	8	11	3	+	+	Blt fr(L>R)	L fr	ETLE-L	n	n
88	12/M	5	7	6	–	–	Blt fr(L>R)	generalized	ETLE	n	n
89	12/F	7	5	0	–	–	n	n	ETLE	n	n
90	10/M	7	3	0	–	–	L fr	n	ETLE-L	n	n
91	14/F	11	3	6	–	–	L fr	n	ETLE-L	n	n
92	14/F	12	2	0	–	–	Blt fr	n	ETLE	n	n

93	14/F	3	11	1	–	–	R fr	R fr	ETLE-R	R schizencephaly	R fr
94	9/M	9	0	0	–	–	n	L fr	ETLE-L	n	Blt fr
95	2/M	0.25	1.75	6	–	–	L t-p-oc	n	ETLE-L	n	n
96	1/M	0.5	0.5	4	–	–	Blt fr-t(L>R)	n	ETLE-L	n	n
97	7/M	3	4	0	–	–	L fr	n	ETLE-L	n	n
98	12/M	7	5	4	–	–	R fr-t	n	ETLE-R	n	n
99	13/M	7	6	4	–	–	L Hms	n	ETLE-L	n	n
100	6/F	0.5	5.5	0	–	–	R p	R p	ETLE-R	R p,FCD	Blt p
101	15/M	7	8	0	–	–	L fr	L fr	ETLE-L	n	n
102	11/M	3.5	7.5	4	–	–	Blt fr	Blt fr	ETLE	n	L t
103	6/M	6	0	0	–	–	L t	n	ETLE	n	n
104	9/M	5	4	4	–	–	L fr	L fr	ETLE-L	n	L fr
105	14/M	0.7	13.3	4	–	–	R Hms	R Hms	ETLE-R	n	n
106	5/F	0.1	4.9	0	–	–	n	n	ETLE	n	n
107	15/F	14	1	4	–	–	n	R Hms	ETLE-R	n	n
108	12/F	12	0	0	+	–	R Hms	L Hms	ETLE	L fr, polymicrogyria	n

: years,* **t:** *temporal,* **fr:** *frontal,* ***p: *parietal,* ***oc:*** *occipital,* ***n:*** *normal,* ***GTCS:*** *generalized tonic clonic seizure,* ***SE:*** *status epilepticus,* ***ii:*** *interictal,* ***i:*** *ictal,* ***MRI:*** *magnetic resonance imaging,* ***FDG-PET:*** *18F-fluoro-2-deoxy-D-glucose positron emission tomography,* ***TLE:*** *temporal lobe epilepsy,* ***ETLE:*** *extra temporal lobe epilepsy,* ***L:*** *left,* ***R:*** *right,* ***HS:*** *hippocampal sclerosis,* ***NHAS:*** *non-hippocampal sclerosis abnormality of the temporal lobe,* ***FCD:*** *focal cortical dysplasia, Risk factors;* ***0:*** *no risk factors,* ***1:*** *head injury,* ***2:*** *perinatal insult,* ***3:*** *family history of epilepsy,* ***4:*** *febrile seizure,* ***5:*** *encephalitis,* ***6:*** *others,* ***Blt:*** *bilateral,* ***Hms:*** *hemisphere.*

to seizures, findings of scalp video-EEG monitoring, MRI and FDG-PET studies were presented in Table I, II.

In TLE group, the results were abnormal in 82.1% (46/56) of patients on MRI (hippocampal sclerosis [n = 20], non-hippocampal sclerosis abnormality [n = 17], and malformations of cortical development [n = 9]) and 75% (42/56) patients on PET. There was a significant relationship between a history of febrile seizure and hippocampal sclerosis on MRI ($p < 0.001$). When logistic regression analysis was performed between hippocampal sclerosis and febrile seizures; hippocampal sclerosis could be predictive of 23.4% of febrile seizures and the sensitivity and specificity of febrile seizures were 0% and 100%, respectively.

The clinical-electroencephalography findings were concordant with MRI and FDG-PET in 67.8% (38/56) and 62.5% (35/56) of patients with TLE, respectively (Table II). This difference in the CR (67.8% versus 62.5%) was not statistically significant ($p = 0.159$). The highest CR between clinical-electroencephalography findings and neuroimaging studies were found in patients with non-hippocampal sclerosis abnormality (76%, 13/17) and hippocampal sclerosis (50%, 10/20) in TLE group (see Figure 1, 2). The differences in the CRs between clinical-electroencephalography findings and neuroimaging studies among the hippocampal sclerosis, non-hippocampal sclerosis abnormality, and the malformations of cortical development were not statistically significant (p value range 0.094 to 1).

In extra-TLE group, the results were abnormal in 23% (12/52) of patients on MRI (hippocampal sclerosis [n = 1], non-hippocampal sclerosis abnormality [n = 1], and malformations of cortical development [n = 10]) and 26.9% (14/52) of patients on FDG-PET. The clinical-electroencephalography findings were concordant with MRI and FDG-PET in 13.4% (7/52) and 21.1% (11/52) of patients with extra-TLE. The difference in the CR (13.4% versus 21.4%) was statistically significant ($p = 0.044$) (Table III). The CR between clinical-electroencephalography findings and neuroimaging studies for TLE (48.2%, 27/56) was better than for extra-TLE (9.6%, 5/52) ($p < 0.001$). In patients with malformations of cortical development on MRI, the clinical-electroencephalography findings were concordant with MRI and FDG-PET in 84.2% (16/19) and 52.6% (10/19) of patients, respectively (see Figure 3). The difference in the CR (84.2% versus 52.6%) was statistically significant ($p = 0.010$).

Twelve of 32 patients (TLE [n = 11] and extra-TLE [n = 1]) who had concordance between clinical-electroencephalography findings underwent epilepsy surgery (Table IV). According to the seizure outcome of patients, MRI and FDG-PET were correct the localization in 100% (12/12) and 100% (12/12) of patients, respectively ($p = 1$). Surgical outcome was excellent in 83.3% of the patients (10/12) with an Engel class I outcome. Other two patients had significant improvement with an Engel class II outcome.

Table II: Clinical features, magnetic resonance imaging (MRI) and 18F-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) findings of patients categorized as temporal lobe epilepsy (TLE) and extra-TLE.

Variables	Total (n = 108)	TLE (n = 56)	Extra-TLE (n = 52)
History related to seizure			
Age at onset of seizures, years	11.1±8.1 (0.1–36)	12 (6.2–18)	7 (4–12)
Epilepsy duration, years	15.5±9.3 (0–42)	15 (9.6–22)	12 (6.1–18)
Febrile seizure, % (n)	33.3 (36)	39.3 (22)	26.9 (14)
Head injury, % (n)	26.9 (29)	26.8 (15)	26.9 (14)
Family history of epilepsy, % (n)	25 (27)	25 (14)	25 (13)
Perinatal insult, % (n)	11.1 (12)	7.1 (4)	15.4 (8)
Encephalitis, % (n)	2.8 (3)	1.8 (1)	3.4 (2)
No risk factors, % (n)	30.6 (33)	30.4 (17)	30.8 (16)
Clinical-scalp video-EEG results, % (n)			
Lateralizing	88 (96)	100 (56)	76.9 (40)
Non-lateralizing	11.1 (12)	–	23.1 (12)
FDG-PET, % (n)			
Normal	48.1 (52)	25 (14)	73.1 (38)
Abnormal	51.9 (56)	75 (42)	26.9 (14)
Unilateral temporal	48	37	11
Bilateral temporal	8	5	3
MRI, % (n)			
Normal	46.2 (50)	17.9 (10)	76.9 (40)
Abnormal	53.8 (58)	82.1 (46)	23.1 (12)
Clinical-EEG findings and MRI and FDG-PET, % (n)			
Concordant	29.6 (32)	48.2 (27)	9.6 (5)
Non-concordant	70.4 (76)	52.8 (29)	90.4 (47)

Table III: Table shows the abnormal magnetic resonance imaging findings of 58 patients with clinical-electroencephalography findings and 18F-fluoro-2-deoxy-D-glucose positron emission tomography results.

	HS (n=21)	Non-HS (n=18)	MCD (n=19)	
			FCD (n=15)	Other than FCD (n=4)
EEG				
Lateral	20	17	14	2
Non-lateral	1	1	1	2
PET				
Unilateral Hm	13	13	8	1
Bilateral Hm	3	2	2	-
No Hm	5	3	5	3

HS: *hippocampal sclerosis,* ***MCD:*** *malformations of cortical development,* ***FCD:*** *focal cortical dysplasia,* ***EEG:*** *electroencephalogram,* ***PET:*** *positron emission tomography,* ***Hm:*** *hypometabolism.*

Table IV: The histopathologic finding of 12 patients who underwent epilepsy surgery.

TLE	n	Extra-TLE	n
HS type I	4	FCD type IIb	1
HS type I and FCD type IIb	3		
HS type II and FCD type IIIa	2		
HS type III	1		
FCD type IIa	1		

TLE: *temporal lobe epilepsy,* ***HS:*** *hippocampal sclerosis,* ***FCD:*** *focal cortical dysplasia*

DISCUSSION

Many patients with mesial temporal sclerosis have febrile seizures or other cerebral insults early in life; however, it is likely to be multifactorial (17). In our study, we found a significant historical difference in between patients with and without hippocampal sclerosis for febrile seizures, as found in previous studies (17–19). The age of seizure onset was younger in our patients with focal cortical dysplasia compared to those with other etiologies, as found in previous study (20).

In our study, the CR between clinical-electroencephalography findings and neuroimaging studies for TLE was not low (48.2%) compared with the previous studies (13%–68%) (6, 7). Similar with a previous report (21), in our study, the highest CR between clinical-electroencephalography findings and neuroimaging studies was found in patients with non-hippocampal sclerosis abnormality (76%) in TLE group. This abnormality was defined on the basis of the MRI criteria rather than histopathological examination in our study because only one patient of 17 with non-hippocampal sclerosis abnormality underwent to surgery and the histopathological diagnosis of this patient was focal cortical dysplasia type IIa. Gok et al. (21) have shown that the finding of 75% of patients with non-hippocampal sclerosis abnormality showing focal lesions in histology emphasizes the importance of describing even the most subtle changes in MRI reports. Some of these patients may have hippocampal sclerosis without detectable hippocampal atrophy or T2 signal abnormality, which makes detection difficult on MRI. In our study, on MRI, hippocampal sclerosis was the most common lesion in patients with TLE, as found in previous studies (22, 23). Ten of these patients who had concordance between clinical-electroencephalography findings and neuroimaging studies underwent surgery, and MRI and FDG-PET correctly identified hippocampal sclerosis in 100% of surgical specimens. In line with this finding, MRI and FDG-PET were repeatedly found as an effective tool in diagnosis of hippocampal sclerosis with a sensitivity of 90% to 95% compared with histopathologic examination as a standard (22, 23).

In our study, the CR between clinical-electroencephalography findings and neuroimaging studies for extra-TLE was low (9%) compared with the previous studies (36%–83%) (8,9). However, the CR between clinical-electroencephalography findings and FDG-PET (21%) was better than those between clinical-electroencephalography findings and MRI (13%), as found in previous studies (24). Among our patients with extra-TLE, focal cortical dysplasia was the most common malformations of cortical development identified on MRI similar to the previous studies (25, 26). Comparing to MRI, FDG-PET was found more yielding in showing the focal cortical dysplasia, and more sensitive in localizing the epileptogenic focus in both TLE and extra-TLE in previous studies (26-29). In our study, however, MRI was better than FDG-PET to show the focal cortical dysplasia, given that one-third of patients with focal cortical dysplasia, and approximately two-thirds of patients with other malformations of cortical development had normal FDG-PET scans. Higher diagnostic yield of MRI in this series may have resulted from the fact that all MRI studies applied a dedicated epilepsy protocol and possibly longer experience of the neuroradiologists on epilepsy imaging. Nevertheless our results showed that FDG-PET may fail to localize malformations of cortical development when MRI does, MRI and FDG-PET shows the similar sensitivity to localize the epileptogenic focus in patients who underwent epilepsy surgery.

The use of FDG-PET for patients with apparently normal MRI has been discussed by several authors (8, 19). MRI fails to show lesions in some patients with medically refractory epilepsy that is often associated with malformations of cortical development, especially focal cortical dysplasia (5). In our study, 26% of patients with apparently normal MRI had positive FDG-PET results. Unfortunately, we could not obtain pathological examination findings in these patients because none of them underwent surgery due to imprecise focus determination. FDG-PET/MRI coregistration, where PET images are fused onto the structural MRI of the same patient and hybrid PET-MRI that allows for acquisition of both PET and MR in one session offer a potential improvement in the detection of cortical dysplasia and the epileptogenic zone localization (28, 30–32). FDG-PET/MRI coregistration could not be performed in our study due to retrospective study design, and this situation may have reduced the diagnostic yield of neuroimaging. We could expect different results if we used FDG-PET/MRI coregistration, especially in extra-TLE group with high non-concordance rate (90%).

Our study has limitations. Although the same imaging protocol was used on 1.5T scanners, use of two MRI scanners from different manufacturers may still have hampered technical uniformity of studies. Then, we solely evaluated hippocampus visually but did not perform quantitative volumetric analyses in the patients. MRI volumetry might reveal subtle hippocampal volume loss; however quantitative analysis is usually not performed during routine practice with high daily through put in radiology services. Besides, visual and quantitative assessment of the hippocampus showed no significant change in diagnosis of hippocampal sclerosis, thus MR volumetry was not strongly recommended for unilateral cases (33, 34). Finally, patients with negative MRI lacked a specific pathological diagnosis because surgical operation did was not offered them. Imprecise focus determination or patients' refusal of surgery was reasons why a limited number of patients had surgery.

In conclusion, our results show that FDG-PET may not help in revealing epileptic region in cases with abnormal MRI especially in malformations of cortical development. The highest CR between clinical-electroencephalography findings and neuroimaging studies is found in TLE patients with findings inconclusive of hippocampal sclerosis. With low CR between clinical-electroencephalography findings and neuroimaging studies in extra-TLE in the present study, meticulous use of

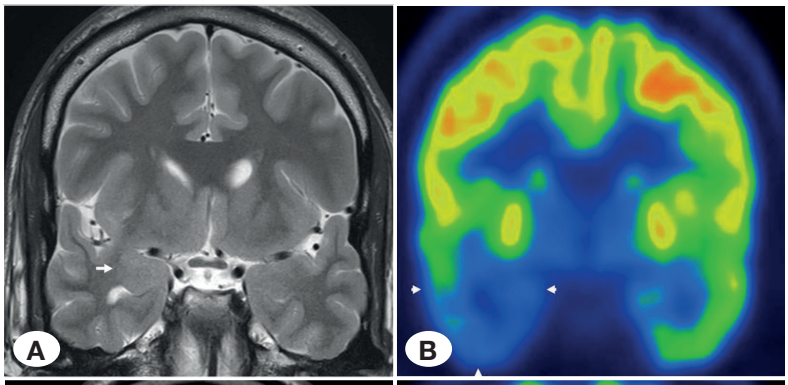

Figure 1: The concordance between MRI and FDG-PET in a 26-year-old male with non-hippocampal sclerosis abnormality. **A)** Coronal oblique fast spin-echo T2-weighted (TR/TE: 5000/120 ms) shows thickening of the right mesial temporal cortex and amygdale (arrow). **B)** Coronal oblique FDG-PET scan shows different metabolism between temporal lobes that the right side shows hypometabolism (arrowheads).

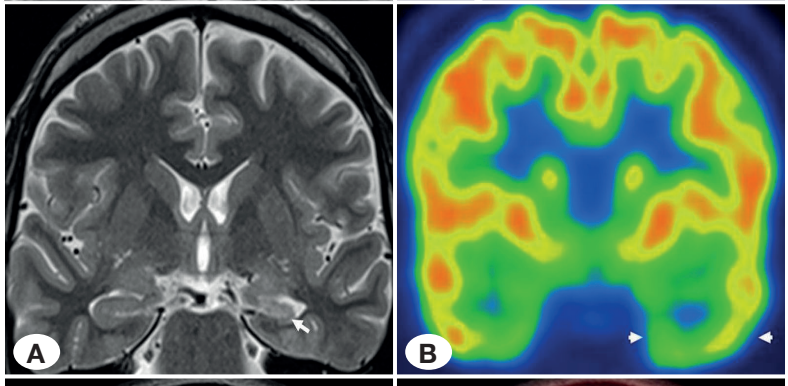

Figure 2: The concordance between MRI and FDG-PET in a 28-year-old male with hippocampal sclerosis. **A)** Coronal oblique fast spin-echo T2-weighted image (TR/TE: 4000/100 ms) shows atrophy and increased signal of the left hippocampus (arrow). **B)** Coronal oblique FDG-PET scan shows hypometabolism in the left temporal lobe (arrowheads).

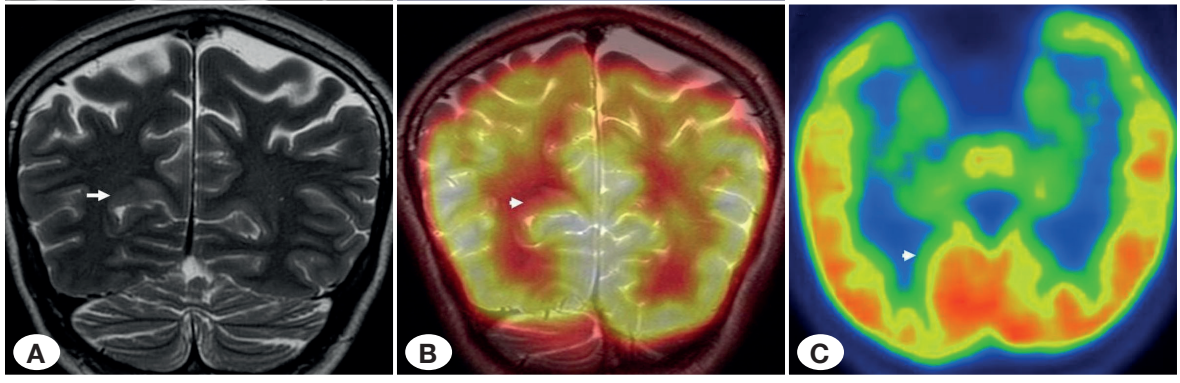

Figure 3: The non-concordance between MRI and FDG-PET in a 27-year-old female with focal cortical dysplasia. **A)** Coronal oblique fast spin-echo T2-weighted image (TR/TE: 4000/100 ms) shows thickening of the right parietal cortex at the level of the parieto-occipital sulcus (arrow). **B-C)** Oblique coronal and axial FDG-PET scans show no hypometabolism around the region of the parieto-occipital sulcus (arrowheads)

multiple modalities is necessary for accurate pre-surgical evaluation.

Compliance with Ethical Standards:

Conflict of Interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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