Focal Cortical Dysplasia and Refractory Epilepsy: Role of Multimodality Imaging and Outcome of Surgery

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ABSTRACT

BACKGROUND AND PURPOSE: Focal cortical dysplasia (FCD) is one of the most common causes of drug resistant epilepsy. Our aim was to evaluate the role of presurgical noninvasive multimodality imaging techniques in selecting patients with refractory epilepsy and focal cortical dysplasia for epilepsy surgery and the influence of the imaging modalities on long-term seizure freedom.

MATERIALS AND METHODS: We performed a retrospective analysis of data of 188 consecutive patients with FCD and refractory epilepsy with at least 2 years of postsurgery follow-up. Predictors of seizure freedom and the sensitivity of neuroimaging modalities were analyzed.

RESULTS: MR imaging showed clear-cut FCD in 136 (72.3%) patients. Interictal FDG-PET showed focal hypo-/hypermetabolism in 144 (76.6%); in 110 patients in whom ictal SPECT was performed, focal hyperperfusion was noted in 77 (70.3%). Focal resection was the most common surgery performed in 112 (59.6%). Histopathology revealed FCD type I in 102 (54.3%) patients. At last follow-up, 124 (66.0%) were seizure-free. Complete resection of FCD and type II FCD were predictors of seizure freedom. Localization of FCD on either MR imaging or PET or ictal SPECT had the highest sensitivity for seizure freedom at 97.5%. Among individual modalities, FDG-PET had the highest sensitivity (78.2%), followed by MR imaging (75.8%) and ictal SPECT (71.8%). The sensitivity of MR imaging to localize type I FCD (60.8%) was significantly lower than that for type II FCD (84.8%, $P < .001$). Among 37 patients with subtle MR imaging findings and a focal FDG-PET pattern, 30 patients had type I FCD.

CONCLUSIONS: During presurgical multimodality evaluation, localization of the extent of the epileptogenic zone in at least 2 imaging modalities helps achieve seizure freedom in about two-thirds of patients with refractory epilepsy due to FCD. FDG-PET is the most sensitive imaging modality for seizure freedom, especially in patients with type I FCD.

ABBREVIATIONS: EEG = electroencephalography; FCD = focal cortical dysplasia; ILAE = International League Against Epilepsy

Focal cortical dysplasia (FCD) is the most common malformation of cortical development[1] and an established etiology of drug-resistant epilepsies in children and adolescents.[2] It is the most frequent histopathology in children and the third most common etiology in adult patients undergoing epilepsy surgery.[3] These patients have a high seizure burden: More than 60% have daily seizures.[4] Precise localization of the extent of the epileptogenic zone may influence the surgical outcome. Therefore, in individuals with refractory epilepsy and FCD, the combination of multimodality imaging and electrophysiologic data during presurgical evaluation may help characterize the epileptogenic zone[5] and improve the outcome of the surgery.

Findings from scalp electroencephalography (EEG) in FCDs often have limitations in spatial resolution in recording readings from deeper cortical sites.[5] High-resolution MR imaging helps recognize features typical of FCDs in only two-thirds of patients.[6] Subtle MR imaging changes are often reported in the one-third of patients with FCDs characterized by disturbances in cortical organization that reorganize.[7] Frequent location of FCDs in a central region and poor localization on MR imaging make them a surgeon's challenge,[8] with reported seizure freedom in only one-third of patients postsurgery, significantly lower than the nearly 60% reported in all patients with FCD.[9]

FDG-PET offers a 3D, high-resolution analysis and is highly sensitive in detecting MR imaging negative for FCDs.[10] FDG-PET helps to delineate the cortical abnormalities with a higher sensitivity than MR imaging, especially in patients with mild type I FCD.[11] It has been reported that incorporating FDG-PET/MR

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imaging coregistration into the multimodality presurgical evaluation enhances the detection and successful surgical treatment of patients with FCD, especially those with type I FCD.[10] In patients in whom both MR imaging and FDG-PET fail to localize the epileptogenic zone, ictal SPECT has been associated with postsurgical seizure freedom in 86% of patients with FCD in whom the zone of ictal hyperperfusion detected on SPECT was completely resected.[12] Hence multimodality presurgical investigations are often required, with coregistration on FDG-PET or ictal SPECT in complex MR imaging negative cases[13] because each technique has its own limitations.[12]

With increasing use of noninvasive multimodality imaging in the evaluation of refractory epilepsy with suspected FCD, it becomes imminent to determine the number of modalities required to localize the extent of the epileptogenic zone and the sensitivity of each modality for long-term seizure freedom. Moreover, it is also imperative to determine how these modalities complement each other in selecting the patient and planning the extent of resection. In fact, most of the literature compares multimodality evaluation with intracranial EEG both for confirmation of the ictal onset zone and determining the extent of surgical resection.[14] Very few studies have investigated the role of presurgical multimodality evaluation with postoperative seizure freedom. In those studies that reported seizure freedom, the findings were observed in small study populations or with a short follow-up. We evaluated the role of presurgical noninvasive multimodality imaging techniques in selecting a patient with refractory epilepsy and FCD for epilepsy surgery and the imaging techniques influence on long-term seizure freedom in a large cohort.

MATERIALS AND METHODS

Of the 792 patients who underwent an epilepsy surgery between January 2005 and June 2016, data of 188 consecutive patients operated for drug-resistant epilepsy and a diagnosis of FCD were analyzed. The study was performed at a tertiary referral center with comprehensive epilepsy care and a dedicated epilepsy surgery program running for >14 years. The program comprises a neurologist, neuroradiologist, nuclear medicine specialist, neurosurgeon, and neuropathologist with substantial expertise. The inclusion criteria were the following: 1) type I or type II FCD within the surgical specimen, and 2) at least 2 years of postsurgery follow-up. Exclusion criteria were the following: 1) FCD type III, and 2) hemispheric dysplasia, tuberous sclerosis, and periventricular nodular heterotopias. The presurgical, surgical, and postsurgical data were collected using a structured data-collection form. Seizure classification was performed according to the International League Against Epilepsy (ILAE) Task Force on Classification and Terminology Guidelines.[15] The study was approved by the institutional ethics committee.

Presurgical Evaluation

Presurgical neurologic evaluation and surgery were performed after the necessary consents were obtained. Preoperative seizure frequency was calculated for the year preceding the surgery, excluding auras. A 3T brain MR imaging, FDG-PET with PET-MR imaging fusion, video-electroencephalography (video-EEG), and a detailed neuropsychological and developmental evaluation were performed in all patients. Ictal SPECT was performed in cases in which there was a discordance of the EEG data or in those with insufficient information on 3T MRI and/or FDG-PET. Functional MR imaging was performed in selected cases for lateralization of language, memory, and motor functions.

All the patients underwent MR imaging on a 3T scanner (Ingenia 3T; Philips Healthcare, Best, the Netherlands) with a dedicated epilepsy protocol. The protocol included a conventional DWI with b-values of 0 and 1000; 2D-FLAIR; axial 3D-volume T1; 3D-volume FLAIR; 3D-volume double inversion recovery sequences in the sagittal plane; and DTI with 15 directions using a dedicated 16-channel head coil. 3D imaging parameters were as follows—3D T1 fast-field echo: TR = 7.9 ms, TE = 3.6 ms, acquisition matrix = 232 × 224, acquired spatial voxel resolution = 0.99 × 1.00 × 1.00 mm, reconstructed spatial resolution = 0.53 × 0.50 × 0.50 with a data-acquisition time of 4 minutes and 17 seconds; 3D-FLAIR volume sequence: TR = 4800 ms, TE = 289 ms, TI = 1650 ms, acquisition matrix = 224 × 224, acquired spatial voxel resolution = 1.12 × 1.12 × 1.12 mm, reconstructed spatial resolution = 0.98 × 0.98 × 0.56 mm, data acquisition time = 4 minutes and 5 seconds; 3D double inversion recovery sequence: TR = 5000 ms, TE = 288 ms, TI = 2550 ms, acquisition matrix = 208 × 208, acquired spatial voxel resolution = 1.2 × 1.12 × 1.3 mm, reconstructed spatial resolution = 0.98 × 0.98 × 0.65 mm, data acquisition time = 5 minutes and 36 seconds.

The volume sequences were then processed by multiplanar reconstruction and volume-rendering in the axial, coronal, and sagittal planes for delineation of any sulcal, gyral abnormalities such as cortical laminar architectural abnormalities and blurring of gray-white matter interfaces. The MRIs were read by a neuroradiologist and neurologist with expertise in epilepsy imaging. The MR imaging data were reanalyzed after FDG-PET in cases in which the MR imaging findings were reported as normal or with minor gyral abnormalities. An MR imaging abnormality was classified as clear-cut FCD and subtle FCD (when the MR imaging lesion was indistinct and confirmed on the basis of FDG-PET hypo-/hypermetabolism).

Prolonged video-EEG monitoring was performed and at least 2 seizures were recorded. Interictal spikes were grouped as unilateral (when >75% of spikes were confined to the side of lesion), bilateral, and multifocal. The seizure semiology was grouped as lateralizing, nonlateralizing, and contralateral. The ictal EEG patterns were classified as focal, regional, hemispheric, generalized,[16] and contralateral. Unilateral spikes, lateralization on semiology, and regional ictal EEG onset patterns were compared for analysis with the rest of the parameters in the respective groups.

All patients underwent [^{18}F] FDG-PET using Biograph mCT (Siemens, Erlangen, Germany) in a 3D mode. PET-MR imaging fusion was performed using syngo MultiModality Workplace software (Siemens). FDG-PET and PET-MR imaging fusion images were analyzed in all 3 projections. The PET metabolism was classified as focal hypometabolism, hypermetabolism, and normal metabolism. The extent of hypo-/hypermetabolism was classified as focal when confined to the lesion/lobe, lateralized if it was beyond 1 lobe but in the same hemisphere, and not informative if it was normal or uncertain. For analysis, focal hypo-/hypermetabolism and the rest were organized into 2 groups.

Ictal SPECT was performed in 110 patients. Under video-EEG monitoring, 740-MBq of technetium Tc99m ethyl cysteinate dimmer (Tc99m-ECD) was injected during the ictal phase. Brain SPECT images were acquired using a Millennium MG (GE Healthcare, Milwaukee, Wisconsin) dual-head gamma camera equipped with low-energy, high-resolution, and parallel hole collimators. The SPECT hyperperfusion was classified as focal when confined to the lesion/lobe, lateralized if it was beyond 1 lobe but in the same hemisphere, and contralateral and noninformative if it was bilateral, normal, or uncertain. Focal hyperperfusion and the rest were separated into 2 groups for analysis.

Surgery

All patients underwent surgery after the review of the multimodality evaluation data in a multidisciplinary case conference. Surgery was performed only if there was a concordance in at least 2 imaging modalities: Namely, the lesion was clear-cut on MR imaging, or a localized FDG-PET pattern or a localized ictal SPECT pattern was present. The types of surgeries performed were focal resection (corticectomy/lesionectomy/lobectomy), multilobar resection, standard anterior temporal lobectomy with amygdalohippocampectomy, and posterior disconnection. During focal resections for a clear-cut lesion, the FCD along with a minimum of a 1-cm circumferential cortex was resected. However, when the extent of FDG-PET hypometabolism (in cases with a localized PET pattern in a noneloquent cortex) was more than that of the MR imaging lesion, the PET abnormality was also resected along with the lesion. All the resections were guided by neuronavigation and intraoperative electrocorticography. The motor cortex was defined by direct intraoperative cortical stimulation in cases in which the lesion was close to or overlapping the motor cortex.

Pathology

Pathologic examination of the resected tissue was performed by a neuropathologist with expertise in epilepsy pathology. The FCDs were classified as FCD type I, FCD type IIa, and FCD type IIb according to the ILAE classification.[17] FCD type I was characterized by isolated lesions, which present as either radial and/or tangential dyslamination of the neocortex. FCD type II was an isolated lesion characterized by cortical dyslamination and dysmorphic neurons without (type IIa) or with balloon cells (type IIb).[17]

Postsurgical Evaluation and Outcome

The postoperative hospital course, complications, and outcome data were analyzed. Acute postoperative seizures were defined as seizures occurring within 7 days after surgery. All the patients underwent routine interictal EEG, at 3 months and 1 year postsurgery. Brain MR imaging was performed at 1 year postsurgery. Outcome at the last follow-up was assessed according to ILAE classification where patients were categorized as ILAE class 1 (seizure-free) and the rest (persistent seizures).[15]

Statistical Analysis

The study population was divided into 2 groups based on seizure freedom or the type of FCD. Comparison between groups for categoric variables was performed using the Fisher exact test, whereas an independent Student t test was used for comparing continuous variables. Logistic regression was performed to evaluate predictors of seizure freedom. Comparison for sensitivities was performed using the McNemar test. Data analysis was performed using SPSS for Windows, Version 17.0 (IBM, New York). A P value $\leq .05$ was considered statistically significant.

RESULTS

Clinical Variables

The average age at onset of epilepsy was 7.93 ± 7.56 years (range, 0–50 years) with a mean duration of epilepsy of 9.75 ± 7.17 years (range, 0–29 years). The average age at the surgery was 17.31 ± 11.26 years (range, 2–64 years) with 92 (48.9%) women. Daily seizures were reported in 106 (56.4%). Febrile convulsions were reported in 23 (12.2%) patients, while there was a family history of epilepsy in 34 (18.1%), and 29 (15.4%) had history of status epilepticus. Developmental delay was reported in 47 (25.0%). Multiple seizure types were reported in 52 (27.7%) patients, and an aura was reported in 43 (22.9%) (Table 1).

Presurgical Variables

The interictal EEG showed regional epileptiform discharges in 93 (49.5%) patients, and 88 (46.8%) had regional ictal EEG onset. Interictal FDG-PET showed hypo- or hypermetabolism in 181 (96.3%) and a focal PET pattern in 144 (76.6%). In the110 patients in whom ictal SPECT was performed, focal hyperperfusion was noted in 77 (70.3%) patients. MR imaging showed clear-cut FCD in 136 (72.3%) patients. In the remaining 52 (27.7%) patients with subtle MR imaging findings, a regional interictal or ictal EEG onset pattern was noted in 27 patients. Among these 27 patients, a focal FDG-PET pattern was observed in 21 patients (Fig 1). In the remaining 6 patients, ictal SPECT showed focal hyperperfusion in 3. Among the 25 patients with subtle MR imaging findings and in whom ictal or interictal EEG was nonlocalizing, a focal FDG-PET pattern was observed in 16 patients. Among the remaining 9 patients, ictal SPECT showed focal hyperperfusion in 3 patients. Surgery was performed in the remaining 6 patients with subtle MR imaging findings after invasive EEG evaluation.

Surgical Variables

Focal resection was the most common surgery performed in 112 (59.6%), followed by amygdalohippocampectomy in 31 (16.5%) patients. Resections involved the frontal lobe in 101 (53.7%), the temporal lobe in 33 (17.6%), the parietal lobe in 17 (9.0%), and the occipital lobe in 10 (5.3%), and they were multilobar in 27 (14.4%). The FCD was close to an eloquent cortex in 36 (19.1%). There was no mortality. Postsurgery, 17 (9.0%) had complications, which improved by 3 months (motor weakness in 10, language dysfunction in 4, mutism in 2, and hemianopia in 1). Complete resection of the FCD was performed in 133 (70.7%) patients in whom the lesion was clear-cut on MR imaging. Histopathology was suggestive of FCD type I in 102 (54.3%), type II in 79 (42.0%), and mixed types I and II in the remaining 7 (3.7%) patients.

Table 1: Comparison of study variables for seizure freedom ($n = 188$)

Variable	Seizure-Free ($n = 124$)	Persistent ($n = 64$)	*P* Value
Age at surgery (mean) (yr)	18.68 ± 11.43	14.66 ± 10.50	.020
Age of onset (mean) (yr)	8.45 ± 8.18	6.91 ± 6.09	.198
Duration of epilepsy (mean) (%)	10.72 ± 7.31	7.90 ± 6.56	.012
Women (%)	56 (45.2%)	36 (56.3%)	.168
Febrile convulsions (%)	15 (12.1%)	8 (12.7%)	1.000
Multiple types of seizures (%)	21 (16.9%)	31 (48.4%)	<.001
Delayed development (%)	23 (18.5%)	24 (37.5%)	.007
Daily seizures (%)	63 (50.8%)	43 (67.2%)	.043
Presence of aura (%)	35 (28.2%)	8 (12.5%)	.017
Regional spikes on interictal EEG (%)	66 (54.1%)	27 (42.2%)	.168
Regional ictal EEG onset pattern (%)	62 (50.0%)	26 (46.2%)	.280
Clear-cut FCD on MRI (%)	94 (75.8%)	42 (65.6%)	.169
Focal FDG-PET pattern (%)	97 (78.2%)	47 (73.4%)	.472
Focal ictal SPECT pattern (%)	51 (71.8%)	26 (66.7%)	.664
Eloquent cortex location (%)	16 (12.9%)	20 (31.3%)	.003
FCD type I (%)	57 (47.5%)	45 (73.8%)	.001
FCD type II (%)	63 (52.5%)	16 (26.2%)	.001
FCD type I and II (%)	4 (3.2%)	3 (4.6%)	.691
Acute postoperative seizures (%)	32 (25.8%)	32 (50.0%)	.001
Complete resection (%)	105 (96.3%)	28 (54.9%)	<.001

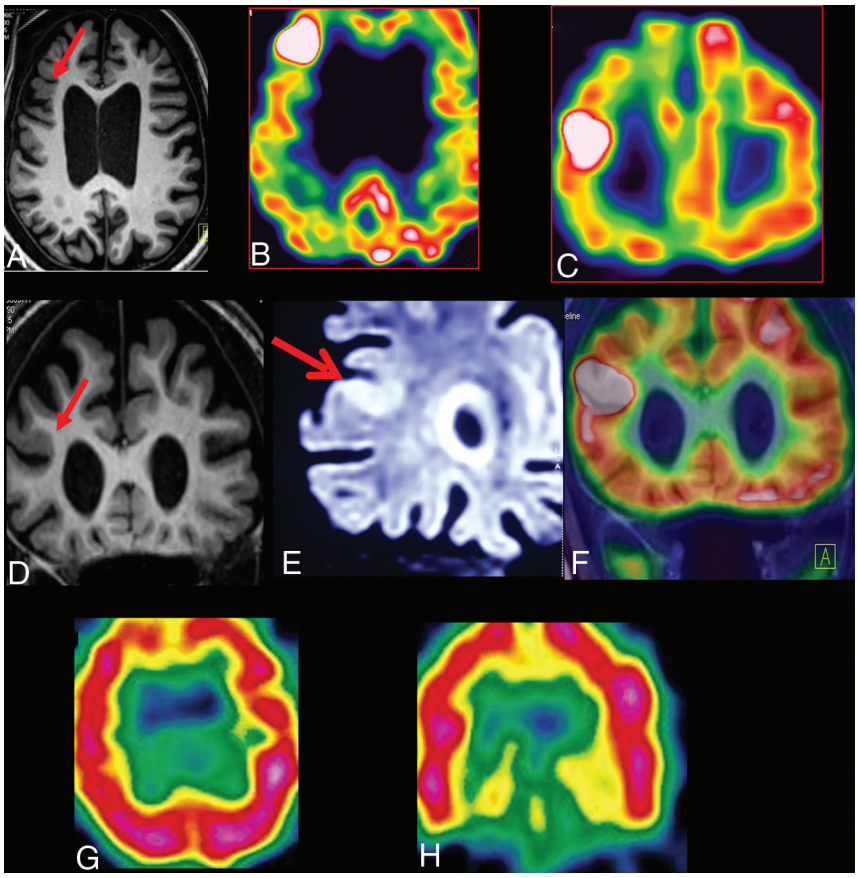

FIG 1. A case of refractory epilepsy with daily seizures of 21 years' duration with moderate mental retardation. Brain MR imaging 3D-T1 volume fast-field echo sequences of axial (*A*), coronal (*D*), and coronal (*E*) 3D-FLAIR volume show a right middle frontal gyrus cortical laminar architectural abnormality with cortical thickening (*arrow*). The MR imaging abnormality was detected retrospectively after the FDG-PET (*B* and *C*) and MR imaging/FDG-PET coregistration (*F*) showed the focal hypermetabolic focus. The ictal SPECT (*G* and *H*) findings were inconclusive.

Outcome

The postsurgery follow-up ranged from 2 to 13 years. At the latest follow-up, 124 (66.0%) patients were seizure-free (ILAE class 1) and an additional 20 (10.6%) had >90% seizure reduction (ILAE classes 2 and 3), while 20 (10.6%) had >50% seizure reduction (ILAE class 4).

Predictors of Outcome

On analysis of factors influencing seizure freedom, more patients with persistent seizures had daily seizures (50.8% versus 67.2%, $P = .043$), multiple types of seizures (16.9% versus 48.4%, $P < .001$), acute postoperative seizures (25.8% versus 50.0%, $P = .001$), and FCD close to an eloquent cortex (12.9% versus 31.3%, $P = .003$). Auras (28.2 versus 12.5%, $P = .017$), type II FCD (52.5% versus 26.2%, $P = .001$), and complete resection of the FCD (96.3% versus 54.9%, $P < .001$) were significantly more common in patients with seizure freedom (Table 1). On logistic regression analysis among the variables that were significantly associated with seizure freedom, complete resection of the FCD ($\beta = 0.043$, $P < .001$), type II FCD ($\beta = 3.07$, $P = .021$), and a single type of seizure ($\beta = 0.339$, $P = .042$) were predictors of seizure freedom, whereas acute postoperative seizures showed a trend for predicting persistent seizures ($\beta = -0.398$, $P = .072$).

Imaging Modalities and Sensitivity

On analysis of sensitivities of various modalities for seizure freedom, localization of FCD on either MR imaging or PET or ictal SPECT had the highest sensitivity at 97.5% followed by localization on either MR imaging or PET at 92.7%. Among individual modalities, localization on PET had a sensitivity of 78.2% followed by MR imaging with 75.8% and ictal SPECT with 71.8% (Fig 2*A*).

The sensitivity of localization of FCD either on MR imaging or PET or ictal SPECT was highest for both type I FCD (95.9%) and type II FCD (97.6%). This was followed by localization on either MR imaging or PET at 90.1% and 94.1% for type I and type II FCDs, respectively. The sensitivity of MR imaging to localize type I FCD (60.7%) was significantly lower ($P < .001$) than the sensitivity for localizing type II FCD (86.0%) (Fig 2*B*, -*C*). On the McNemar test, localization of FCD on either MR imaging or PET or ictal SPECT had significantly higher sensitivity ($P < .001$) for seizure freedom than any other individual technique.

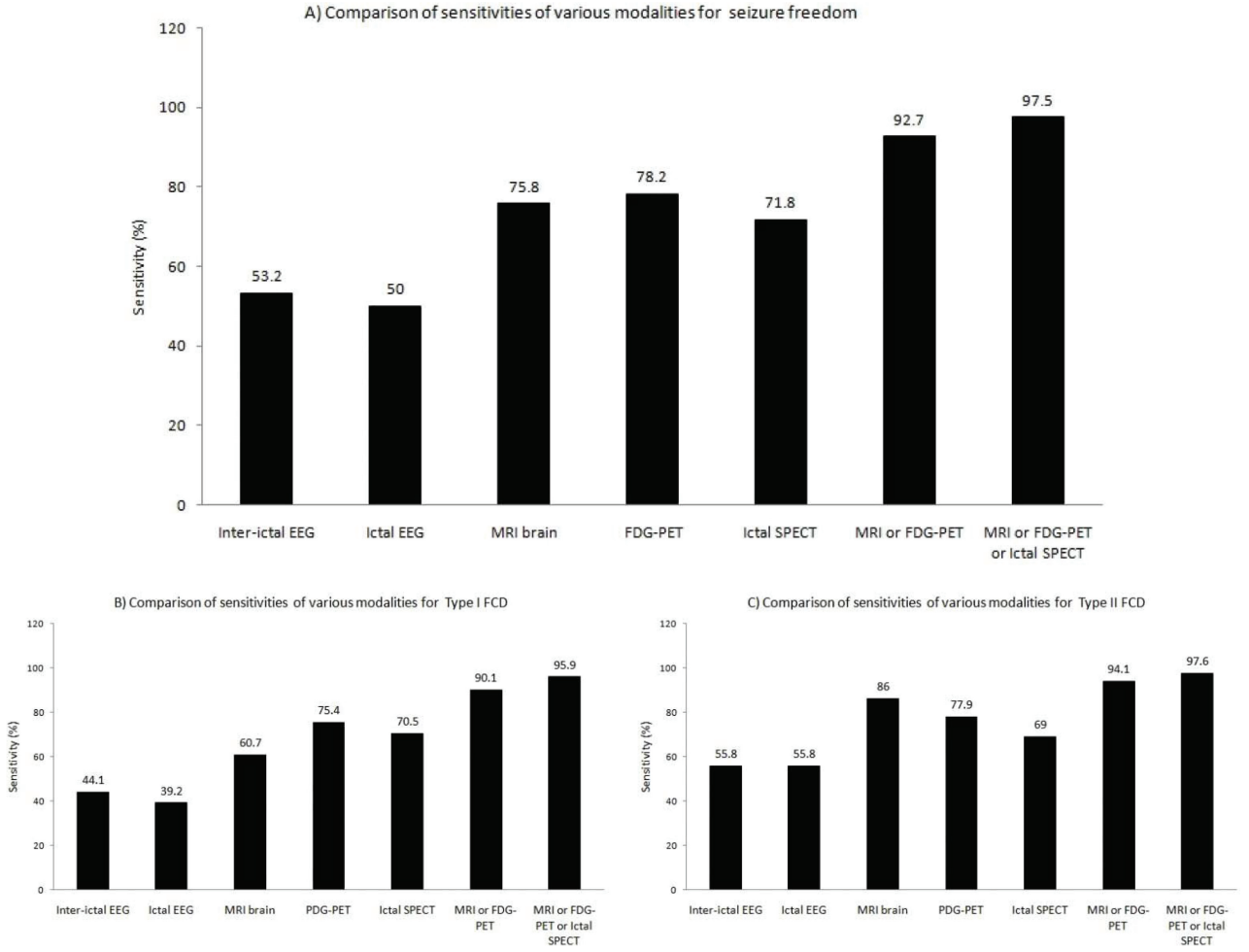

FIG 2. Comparison of sensitivities of various modalities for seizure freedom (*A*), type I FCD (*B*), and type II FCD (*C*).

Comparison of FCD Types I and II

On comparison of factors between type I and type II FCD, there were no differences between the types of FCD for demographic characteristics. More patients with type I FCD were multilobar in location (20.6% versus 3.8%; $P < .001$) and had developmental delay (31.4% versus 16.5%, $P = .025$). Clear-cut FCD on MR imaging (60.8% versus 84.8%, $P < .001$), a regional ictal EEG pattern (39.2% versus 58.4%, $P = .024$), and complete resection of FCD (77.8% versus 90.3%, $P = .048$) were more common in patients with type II FCD (Table 2). In a subset of 37 patients with subtle MR imaging findings and a focal FDG-PET pattern, 30 patients had type I FCD, while 7 had type II FCD. In this subset, there was no difference in seizure freedom based on the type of FCD (56.6% versus 57.1%, $P = 1.000$).

DISCUSSION

In the current study, we report that in patients with refractory epilepsy due to FCD, multimodality imaging helps achieve seizure freedom in nearly two-thirds of patients. More than one-fourth of the patients with FCD and refractory epilepsy had subtle MR imaging findings in which FDG-PET helped localize the epileptogenic zone in 71%. On correlating with histopathology, most (80%) of these patients in whom FDG-PET helped localize the epileptogenic zone had type I FCD. Predictors of postsurgical seizure freedom are a single type of seizure, complete resection of the FCD, and type II FCD. However, we could not replicate previously reported predictors such as younger age at the operation and shorter duration of epilepsy.[14]

We report seizure freedom in 66.0% of patients with an additional 10.6% of patients reporting a >90% seizure reduction. This result is similar to the 65% favorable outcome reported by Fauser et al[9] and the >56% seizure freedom reported by Kral et al.[18] The most common reason for incomplete resection in the current study was a lesion located in close proximity to the eloquent cortex, observed in 17.3% of our study population. Subtotal resections are common in these patients to avoid the risk of an unacceptable postoperative neurologic deficit.[3] Another commonly attributed reason for incomplete resection is type I FCD. Previously Kim et al[19] reported that patients with FCD of a severe-pathologic group (type II) had more chances of complete resection of FCD and subsequent seizure freedom. In the current study, we found that both completeness of resection and seizure freedom were higher in patients with type II FCD, possibly due to clear-cut focal lesions on MR imaging. In fact, having a dedicated 3T MR imaging protocol itself could have influenced the seizure outcome in the present study, as previously suggested by Ahmed et al.[20]

Table 2: Comparison of study variables for FCD types I and II ($n = 181$)

Variable	FCD Type I ($n = 102$)	FCD Type II ($n = 79$)	*P* Value
Age at surgery (mean) (yr)	16.54 ± 10.76	18.11 ± 11.05	.338
Age of onset (mean) (yr)	8.29 ± 7.88	7.76 ± 7.31	.655
Duration of epilepsy (mean) (%)	9.08 ± 6.91	10.82 ± 7.60	.117
Women (%)	50 (49.0%)	40 (50.6%)	.881
Multilobar distribution of FCD (%)	21 (20.6%)	3 (3.8%)	<.001
Febrile convulsions (%)	12 (11.9%)	9 (11.4%)	1.000
Multiple types of seizures (%)	31 (30.4%)	19 (24.1%)	.403
Delayed development (%)	32 (31.4%)	13 (16.5%)	.025
Daily seizures (%)	57 (55.9%)	48 (60.8%)	.546
Aura (%)	18 (17.6%)	23 (29.1%)	.076
Regional ictal EEG onset pattern (%)	40 (39.2%)	45 (58.4%)	.024
Clear-cut FCD on MRI (%)	62 (60.8%)	67 (84.8%)	<.001
Focal FDG-PET pattern (%)	77 ((75.5%)	63 (79.7%)	.592
Focal ictal SPECT pattern (%)	48 (70.6%)	29 (72.5%)	1.000
Eloquent cortex location (%)	21 (20.6%)	15 (19.0%)	.852
Seizure-free (%)	57 (55.8%)	63 (79.7%)	.008
Acute postoperative seizures (%)	38 (37.3%)	24 (30.4%)	.348
Complete resection (%)	63 (77.8%)	65 (90.3%)	.048

We also agree with Ahmed et al "that a dedicated 3T MR imaging protocol may increase the cost of presurgical evaluation, simultaneously considering the risks of administering general anesthetic for the MR imaging, especially in some children. However, additional MR imaging could improve not only the detection of a lesion, but could assist with subsequent management."[20]

The sensitivity of MR imaging to localize type II FCD was significantly higher than the sensitivity for type I FCD. This finding may be because of our concurrent findings that nearly one-fifth of patients with type I FCD had a multilobar distribution compared with a mere 3.8% of patients with type II FCD. This extensive distribution of type I FCD is perhaps the reason for our observation of higher rates of incomplete resection and persistent seizures in type I FCD. Furthermore, Jin et al[21] reported incomplete resection of FCD and habitual acute postoperative seizures as strong predictors of seizure recurrence after surgery, similar to the present study. As Hauptman and Mathern[3] suggested, given the poor localization with EEG and normal MR imaging findings, we need better and preferably noninvasive tools to not only identify the lesion but also provide ways to detect the borders of the histopathology and whether the lesion involves the functional cerebral cortex. The present study demonstrates that FDG-PET is complementary to MR imaging to detect the extent of epileptogenic zone, especially in type I FCD.

The sensitivity of a clear-cut FCD on MR imaging for seizure freedom in the current study at 75.8% is similar to previously reported sensitivities of 60%–90%.[10,14] Similarly, a sensitivity of 78.2% for localization of FCD on FDG-PET and a sensitivity of approximately 70% for ictal SPECT are similar to those reported by previous studies.[8] We report that evaluation with ≥2 modalities increases the sensitivity for seizure freedom in these patients. Most interesting, in 71% of 52 patients in whom MR imaging was not helpful, FDG-PET helped localize the FCD, and ictal SPECT, in 11.5% more patients in whom MR imaging and FDG-PET both were not helpful. Especially, in patients with type I FCD, in which MR imaging did not localize FCD, we report that FDG-PET helped localize the lesion and improve seizure freedom. These observations suggest that FDG-PET is a useful adjunct to MR imaging, especially in patients with type I FCD.

Limitations

The correlation between hypometabolism on FDG-PET and findings on MR imaging may not be precise because both evaluations were not studied within a short period. A retrospective design of the study did not permit us to determine false-negative reports. Furthermore, the retrospective design also did not allow blinding of any of the team members for diagnoses already performed, thus preventing us from observing variability between and within an observer. Ictal SPECT was performed in only a fraction of patients because coregistration of MR imaging/FDG-PET was sufficient in most patients.

Implications for Clinical Practice

In developing countries, the cost of epilepsy surgery using an invasive evaluation is 4 times that with noninvasive multimodality evaluation.[22] The findings of the current study that localization of FCD in ≥2 noninvasive imaging modalities is sufficient to achieve satisfactory seizure freedom may have potential cost-effective implications for the feasibility of epilepsy surgery after multimodality evaluation in countries with limited resources.

CONCLUSIONS

During presurgical multimodality evaluation, localization of the extent of the epileptogenic zone in at least 2 imaging modalities helps achieve seizure freedom in about two-thirds of patients with refractory epilepsy due to FCD. FDG-PET is the most sensitive imaging technique for seizure freedom, especially in patients with type I FCD.

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