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# Stepwise Diagnostic Evaluation in Pediatric Epilepsy: Predictors of MRI Positivity and Diagnostic Reclassification

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## Abstract:

**Objective:** This study aimed to evaluate the predictive value of clinical and electroencephalographic (EEG) findings for identifying epileptogenic structural lesions on cranial magnetic resonance imaging (MRI) in pediatric epilepsy, and to assess the contribution of MRI to diagnostic reclassification.

**Methods:** A total of 207 pediatric patients with a confirmed diagnosis of epilepsy were retrospectively analyzed. The diagnostic workflow was evaluated through a stepwise model integrating clinical assessment, EEG, and MRI. The primary endpoints comprised the MRI positivity rate, defined by the detection of epileptogenic structural lesions, and the diagnostic reclassification rate, defined as any modification in epilepsy type classification or etiological category following the incorporation of EEG and/or MRI findings. Independent predictors of MRI positivity were identified using multivariable logistic regression analysis.

**Results:** Epileptogenic structural lesions were identified in 9.7% of patients. Despite a relatively modest MRI positivity rate, imaging significantly contributed to diagnostic refinement. Among cases with normal EEG findings, MRI revealed structural pathology in 12%. The overall diagnostic reclassification rate following the addition of MRI was 9.7%. In multivariable analysis, focal-onset seizures (OR=2.63), developmental delay (OR=2.91), abnormal neurological examination (OR=3.08), and focal epileptiform EEG activity (OR=2.47) emerged as independent predictors of MRI positivity (all $P<0.05$). Agreement between EEG and MRI lateralization was moderate ($\kappa=0.60$).

**Conclusion:** In pediatric epilepsy, MRI may substantially contribute to etiological classification, particularly in the presence of high-risk clinical and electrophysiological features. These findings support the implementation of a risk-stratified, stepwise diagnostic approach to optimize clinical management.

**Keywords:** Pediatric Epilepsy, Magnetic Resonance Imaging, Electroencephalography

Epilepsy is a chronic neurological disorder characterized by recurrent seizures resulting from abnormal, synchronized electrical discharges within the central nervous system. In children, the prevalence of epilepsy ranges between 4 and 6 per 1,000, with incidence rates peaking in the early years of life, making it a major cause of neurological morbidity in childhood [1, 2]. Early and

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accurate diagnosis in the pediatric population is of critical importance, as ongoing epileptic activity and its underlying causes may adversely affect brain maturation, neurodevelopmental trajectories, and long-term cognitive and behavioral outcomes. Timely identification of etiology plays a pivotal role in guiding treatment selection, informing prognosis, and identifying patients who may benefit from targeted interventions, including epilepsy surgery. Reflecting this principle, the International League Against Epilepsy (ILAE) classification framework emphasizes determination of the underlying etiology as a core component of epilepsy evaluation [1]. Accordingly, the diagnostic assessment of pediatric epilepsy requires a multidimensional approach integrating clinical, electroencephalographic (EEG), and neuroimaging findings to achieve clinically meaningful conclusions.

EEG is a cornerstone diagnostic tool in epilepsy evaluation, playing a central role in demonstrating epileptiform activity and supporting seizure classification. Particularly in focal epilepsies, EEG may provide valuable information regarding lateralization and potential epileptogenic focus [3, 4]. However, EEG, although essential, has limited sensitivity for structural etiologies. A considerable proportion of patients with epilepsy may exhibit normal interictal EEG recordings, and EEG alone does not directly identify underlying structural abnormalities [3, 4]. Brain magnetic resonance imaging (MRI) is regarded as the gold standard imaging modality for detecting structural etiologies in epilepsy. It plays a critical role in identifying epileptogenic lesions such as malformations of cortical development, hippocampal sclerosis, epilepsy-associated tumors, and structural sequelae of perinatal injury [5, 6]. Early detection of such lesions not only clarifies etiology but also has significant implications for surgical candidacy assessment, treatment planning, and long-term prognostication. Nevertheless, whether cranial MRI provides uniform diagnostic yield across all patients with epilepsy remains a matter of debate. A key question in clinical practice is which pediatric patients derive the greatest diagnostic benefit from MRI and which clinical or electroencephalographic features may predict the need for imaging [6]. Determining the patient subgroups in whom MRI offers the highest diagnostic value is therefore essential for developing more rational and targeted diagnostic strategies.

Although EEG and cranial MRI are widely used together as complementary diagnostic tools in epilepsy evaluation, much of the existing literature has primarily focused on EEG–MRI concordance or correlation. In real-world clinical practice, however, the diagnostic process is not linear but rather stepwise and multidimensional. Patients are initially stratified based on clinical features and seizure semiology, followed by further refinement of epilepsy type and possible focus through EEG findings, and ultimately evaluation of structural etiology through MRI [7, 8]. Despite this staged diagnostic pathway, the extent to which MRI alters diagnostic classification—namely, its contribution to diagnostic reclassification—has not been systematically examined. Furthermore, the role of clinical and EEG characteristics in predicting the presence of epileptogenic structural lesions on MRI remains incompletely defined [7, 8]. This gap in the literature limits the development of evidence-based approaches aimed at identifying pediatric patients in whom imaging yields the greatest diagnostic benefit. Studies integrating clinical, electroencephalographic, and neuroimaging data are therefore needed to optimize the diagnostic process.

The present study aims to investigate the predictive value of clinical and electroencephalographic findings for the detection of epileptogenic structural lesions on cranial MRI in pediatric epilepsy. In addition, we systematically evaluate the complementary roles of EEG and MRI within the diagnostic pathway and quantify the contribution of MRI to diagnostic classification, particularly through assessment of the diagnostic reclassification rate. To this end, a stepwise, integrative diagnostic framework incorporating clinical, EEG, and neuroimaging data was employed. We hypothesize that this approach may support the development of more rational and targeted imaging strategies and ultimately contribute to optimization of diagnostic pathways in pediatric epilepsy.

## METHODS

### Study Design and Ethical Approval

This retrospective observational study was conducted at Balıkesir University Faculty of Medicine. Given the retrospective design and the use of fully anonymized data, the requirement for written informed consent was waived by the ethics committee. The study protocol was carried out in accordance with the principles outlined in the Declaration of Helsinki.

## Study Population

Patients followed in the Pediatric Neurology Clinic of Balıkesir University Health Practice and Research Hospital were consecutively screened through the institutional electronic medical record system. Only pediatric patients with a definitive diagnosis of epilepsy were eligible for inclusion. The diagnosis of epilepsy was established in accordance with the ILAE definition and diagnostic criteria, based on comprehensive clinical history, seizure semiology, neurological examination, and electroencephalographic evaluation. To ensure diagnostic consistency, only cases diagnosed by a pediatric neurologist with eight years of clinical experience were included. Patients without a clearly documented epilepsy diagnosis or with only suspected seizure events were excluded.

A total of 338 pediatric patients with suspected or confirmed epilepsy were initially screened during the study period. Patients were excluded for the following reasons: incomplete clinical, EEG, or MRI data (n=66); acute symptomatic seizures, isolated febrile seizures, or non-epileptic paroxysmal events (n=33); technically inadequate or non-interpretable EEG or MRI studies (n=19); and an interval exceeding six months between EEG and MRI examinations (n=13). Following application of all predefined eligibility criteria, 207 patients were included in the final study cohort for stepwise diagnostic analysis.

In line with the ILAE criteria, patients were classified as having epilepsy if they had experienced at least two unprovoked seizures occurring more than 24 hours apart, a single unprovoked seizure with a high risk of recurrence supported by clinical and EEG findings, or a defined epilepsy syndrome. Eligible participants were required to be between 0 and 18 years of age at the time of diagnosis, to have undergone routine EEG and cranial MRI as part of the diagnostic evaluation, and to have complete clinical documentation, including detailed medical history, neurological examination findings, and formal EEG and MRI reports.

Exclusion criteria comprised acute symptomatic seizures related to central nervous system infections, acute metabolic or toxic disturbances, or acute trauma; a history limited to febrile seizures; non-epileptic paroxysmal events such as syncope or psychogenic seizures; technically inadequate or non-interpretable EEG or MRI studies; and incomplete essential clinical data. To ensure comparability between EEG and MRI findings, the interval between the two examinations was limited to a maximum of six months. In patients with multiple EEG or MRI studies, the earliest examination performed closest to the time of diagnosis was selected for analysis.

## Clinical Data Collection

Demographic and clinical data were retrospectively extracted from the institutional electronic medical record system. For all patients, age at evaluation, sex, and age at seizure onset were recorded. Seizures were categorized according to the ILAE classification as focal, generalized, or of unknown onset.

Clinical variables assessed from medical records included the presence of developmental delay, abnormal neurological examination findings, a history of perinatal risk factors, a family history of epilepsy, and prior episodes of status epilepticus. Treatment-related data included the number of antiseizure medications administered. Drug resistance was defined in accordance with the ILAE criteria as the persistence of seizures despite adequate trials of at least two appropriately selected and tolerated antiseizure medications.

These variables were subsequently incorporated into the analysis to evaluate clinical and electroencephalographic factors associated with the presence of epileptogenic structural lesions on cranial MRI.

## EEG Acquisition and Classification of Findings

Standard scalp EEG recordings were obtained in all patients using surface electrodes placed according to the international 10–20 system. Interictal recordings were acquired for a minimum duration of 20 minutes. Activation procedures, including hyperventilation and intermittent photic stimulation, were performed when age-appropriate.

EEG findings were categorized into four principal groups: normal EEG, generalized epileptiform discharges, focal epileptiform discharges, and multifocal epileptiform discharges. In patients demonstrating focal epileptiform activity, lateralization of discharges [right, left, or bilateral] was documented, and lobar localization was specified whenever feasible.

All EEG recordings were reviewed and interpreted by the same pediatric neurologist with established expertise in pediatric epilepsy to ensure consistency of classification.

## MRI Protocol and Radiological Assessment

Cranial MRI examinations were performed using a 1.5-Tesla system (Ingenia, Philips Medical Systems, Best, The Netherlands) with a dedicated epilepsy imaging protocol. The standardized imaging protocol included axial T1-weighted spin-echo [TR/TE 450/15 ms], axial fat-suppressed T1-weighted spin-echo (TR/TE 633/15 ms), axial T2-weighted turbo spin-echo (TR/TE 5240/100 ms), axial diffusion-weighted imaging (b = 0 and 1000 s/mm²), coronal T2-weighted turbo spin-echo (TR/TE 3027/100 ms), coronal T1-weighted inversion recovery (TR/TE 3079/15 ms), coronal fluid-attenuated inversion recovery (FLAIR) (TR/TE 11,000/130 ms), three-dimensional FLAIR (TR/TE 4800/315 ms), and three-dimensional T1-weighted sequences. Intravenous contrast material was not administered in any case. The protocol was designed to provide comprehensive multiplanar and multisequence evaluation for the detection of epileptogenic structural abnormalities.

MRI findings were categorized into three groups. Group A comprised epileptogenic structural lesions, including malformations of cortical development, hippocampal sclerosis, tumors, vascular malformations, encephalomalacia related to perinatal injury, and other structural abnormalities considered potentially epileptogenic. Group B included nonspecific findings not directly associated with epilepsy, such as mild cerebral atrophy or nonspecific white matter signal alterations. Group C was defined as normal MRI. For the purposes of this study, MRI positivity was defined as the presence of Group A findings.

In patients with identified epileptogenic structural lesions, the anatomical location and hemispheric lateralization (right, left, bilateral, or midline) were systematically documented. All MRI examinations were independently reviewed by an experienced neuroradiologist with six years of subspecialty expertise to ensure consistency of interpretation. However, interobserver variability analysis was not performed, and it should be acknowledged that this approach may introduce observer-related bias.

## Stepwise Diagnostic Pathway

In this study, the diagnostic evaluation was structured using a stepwise model designed to reflect real-world clinical practice. In the first stage, patients were assessed exclusively on the basis of clinical findings, detailed seizure history, and seizure semiology, and an initial classification of epilepsy type was established according to clinical data alone.
In the second stage, EEG findings were incorporated into the evaluation. Diagnostic classification was subsequently refined based on EEG-derived information regarding epilepsy type, potential epileptogenic focus, and lateralization.

In the third stage, cranial MRI findings were integrated into the analysis to determine the final diagnostic classification and to assess the presence of a structural etiology.

This staged approach was designed to systematically evaluate the incremental contribution of clinical assessment, EEG, and MRI to the diagnostic process and to quantify classification changes occurring at each step of evaluation.

## Study Endpoints

The primary endpoints of this study were the diagnostic reclassification rate within the stepwise diagnostic model and the rate of epileptogenic structural lesion detection on cranial MRI (MRI positivity rate). Diagnostic reclassification was defined as any change in epilepsy type classification or etiological category between the initial classification based solely on clinical assessment and the final classification established after incorporation of EEG and/or MRI findings. MRI positivity was defined as the identification of an epileptogenic structural lesion on cranial MRI.

Secondary endpoints included the evaluation of the independent effects of clinical and electroencephalographic variables on MRI positivity, the assessment of the diagnostic yield of MRI in patients with normal routine EEG findings, and the analysis of concordance between EEG lateralization and lesion laterality on MRI in patients demonstrating focal EEG abnormalities.

### Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics (version 29.0; IBM Corp., Armonk, NY, USA) and RStudio (version 4.3.3; Posit Software, PBC, Boston, MA, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test. Variables demonstrating normal distribution were presented as mean±standard deviation, whereas non-normally distributed variables were reported as median (minimum–maximum). Categorical variables were expressed as counts and percentages. Between-group comparisons for categorical variables were conducted using the Pearson chi-square test or Fisher's exact test when expected cell counts were less than five. Continuous variables were compared using the independent samples t-test or the Mann–Whitney U test, as appropriate based on distributional assumptions. Agreement between EEG lateralization and lesion laterality on MRI was evaluated using Cohen's kappa coefficient. The strength of agreement was interpreted as poor (<0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), or very good (>0.80).

Logistic regression analysis was performed to identify factors associated with the presence of epileptogenic structural lesions on cranial MRI. Univariate analyses were conducted initially. The multivariable model was constructed by including variables that were statistically significant in univariate analyses and those considered clinically relevant. Given the limited number of MRI-positive cases, the number of variables entered into the multivariable model was restricted to reduce the risk of overfitting. Results were reported as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). Because of the exploratory nature of the study, no formal correction for multiple comparisons was applied. All statistical tests were two-sided, and a P-value <0.05 was considered statistically significant. Diagnostic reclassification was reported descriptively without formal statistical comparison, reflecting the staged clinical diagnostic pathway.

**TABLE 1. Baseline Clinical Characteristics of the Pediatric Epilepsy Cohort**

| Variable | Data |
|---|---|
| **Age (years)** | 11.39±4.3 |
| **Sex** | |
| Male | 100 (48.3%) |
| Female | 107 (51.7%) |
| **Age at seizure onset (years)** | 5.2 [2.1–9.4] |
| **Seizure type at initial clinical evaluation** | |
| Focal onset | 92 (44.4%) |
| Generalized onset | 58 (28.0%) |
| Unknown onset | 57 (27.5%) |
| **Developmental delay** | 49 (23.7%) |
| **Abnormal neurological examination** | 43 (20.8%) |
| **Perinatal risk history** | 38 (18.4%) |
| **History of status epilepticus** | 29 (14.0%) |
| **Number of antiseizure medications** | |
| Monotherapy | 122 (58.9%) |
| Polytherapy | 85 (41.1%) |
| **Drug-resistant epilepsy** | 44 (21.3%) |

Data are shown as mean±standard deviation or median [IQR=interquartile range], or number (%) where appropriate. ILAE, international league against epilepsy.

## RESULTS

### Demographic and Clinical Characteristics of the Study Population

The study cohort represented a clinically heterogeneous pediatric epilepsy population, encompassing a broad distribution of age, sex, age at seizure onset, and seizure type. Detailed baseline demographic and clinical characteristics—including neurodevelopmental status, neurological examination findings, history of perinatal risk factors, prior status epilepticus, number of antiseizure medications used, drug resistance status, and additional presenting clinical features—are summarized in Table 1.

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## Distribution of EEG Findings in the Study Population

EEG recordings demonstrated epileptiform activity in a substantial proportion of the cohort, with findings distributed across both generalized and focal patterns. Among patients exhibiting focal epileptiform discharges, hemispheric involvement was relatively balanced. In terms of lobar localization, temporal and frontal regions were most frequently implicated.
The detailed distribution of EEG findings is presented in Table 2.

## Distribution of MRI Findings in the Study Population

Cranial MRI examinations were normal in the majority of patients. Among those with structural abnormalities, epileptogenic lesions included encephalomalacia, intracranial tumors, malformations of cortical development, hippocampal sclerosis, and periventricular leukomalacia. Nonspecific findings comprised a heterogeneous group of abnormalities not directly considered epileptogenic, including hydrocephalus, cerebral atrophy, white matter signal alterations, arachnoid cysts, Blake's pouch cyst, Chiari type I malformation, and agenesis of the corpus callosum. The detailed distribution of MRI findings is presented in Table 3. An illustrative example of an epileptogenic lesion—a frontal lobe dysembryoplastic neuroepithelial tumor consistent with DNET—is shown in Figure 1.

## Diagnostic Reclassification

### Clinical Assessment Alone

In the first stage of the diagnostic pathway, patients were classified exclusively on the basis of clinical history and seizure semiology. Following clinical evaluation, 92 (44.4%) patients were categorized as having focal-onset epilepsy, 58 (28.0%) as generalized-onset epilepsy, and 57 (27.5%) as epilepsy of unknown onset.

### Diagnostic Refinement Following EEG

Incorporation of EEG findings into the diagnostic pathway resulted in notable changes in seizure classification. EEG demonstrated generalized epileptiform discharges in 107 (51.7%) patients and focal epileptiform discharges in 50 (24.2%) patients, while recordings were interpreted as normal in 50 (24.2%) patients. Among the 57 patients initially categorized as having epilepsy of unknown onset based on clinical assessment alone, EEG findings enabled determination of seizure onset type in 32 cases (32/57, 56.1%), corresponding to 15.5% of the overall cohort. Following this refinement, the proportion of epilepsy of unknown onset decreased from 27.5% to 12.1%.

### Diagnostic Reclassification Following MRI

Following the integration of cranial MRI findings into the diagnostic pathway, epileptogenic structural lesions were identified in 20 (9.7%) patients. These cases were subsequently reclassified into the structural etiological category compared with the classification established after clinical and EEG evaluation alone. The dynamic pattern of diagnostic reclassification across the clinical, EEG, and MRI stages, as well as

**TABLE 3. Distribution of Brain MRI Findings**

| | Data n (%) |
|---|---|
| **MRI category** | |
| Group A-Epileptogenic structural lesions | 20 (9.7%) |
| Group B-Nonspecific findings | 21 (10.1%) |
| Group C-Normal MRI | 166 (80.2%) |
| **Distribution of epileptogenic lesions (n=20)** | |
| Encephalomalacia | 5 (25.0%) |
| Brain tumor | 4 (20.0%) |
| Cortical malformations | 3 (15.0%) |
| Hippocampal sclerosis | 3 (15.0%) |
| Periventricular leukomalacia | 3 (15.0%) |
| Vascular malformation | 2 (10.0%) |
| **Distribution of nonspecific findings (n=21)** | |
| Hydrocephalus | 6 (28.6%) |
| Brain atrophy | 4 (19.0%) |
| White matter signal changes | 4 (19.0%) |
| Arachnoid cyst | 3 (14.3%) |
| Corpus callosum agenesis | 2 (9.5%) |
| Blake pouch cyst | 1 (4.8%) |
| Chiari malformation | 1 (4.8%) |

Data are shown as number (%). MRI positivity was defined as the presence of epileptogenic structural lesions [Group A]. Percentages for lesion types were calculated within the epileptogenic lesion group (n=20) and the nonspecific finding group (n=21), respectively.

the incremental contribution of each step, is illustrated in Figure 2.

## Diagnostic Yield of MRI in Patients with Normal EEG Findings

Patients with normal routine EEG recordings were analyzed as a predefined subgroup. In the study cohort, EEG findings were interpreted as normal in 50 (24.2%) patients. Among these individuals, cranial MRI identified epileptogenic structural lesions in 6 cases. Accordingly, the MRI positivity rate in patients with normal EEG findings was 12.0% (95% confidence interval [CI]: 4.5%–24.3%).

## Clinical and EEG Factors Associated with MRI Positivity

A univariate comparison of demographic, clinical, neurological, and electroencephalographic characteristics between MRI-positive and MRI-negative patient groups was performed prior to multivariable analysis. Patients with MRI-positive structural lesions demonstrated higher frequencies of focal seizure onset, developmental delay/regression, abnormal neurological examination findings, and focal epileptiform EEG abnormalities. Detailed results of the univariate analyses are presented in Table 4.

Univariate and multivariable logistic regression analyses were performed to identify clinical and electroencephalographic factors associated with the presence of epileptogenic structural lesions on cranial MRI. In univariate analyses, focal-onset seizures, developmental delay, abnormal neurological examination findings, drug-resistant epilepsy, and focal epileptiform EEG abnormalities were significantly associated with MRI positivity. These variables were subsequently entered into the multivariable logistic regression model. On multivariable analysis, focal-onset seizures, the presence of developmental delay, abnormal neurological examination findings, and focal epileptiform EEG abnormalities remained independently and significantly associated with epileptogenic structural lesions on MRI. In contrast, drug-resistant epilepsy did not retain statistical significance after adjustment. Odds ratios (OR), 95% CIs, and corresponding P-values are presented in Table 5.

ROC curve analysis demonstrated that the combined electroclinical multivariable model provided better discriminative performance for MRI positivity than individual predictors alone. Among the individual variables, abnormal neurological examination findings showed the strongest individual diagnostic contribution. Detailed ROC analysis results are presented in Table 6.

## EEG–MRI Concordance

Among the 50 patients with focal epileptiform activity on EEG, epileptogenic structural lesions were identified on cranial MRI in 12 cases. Concordance

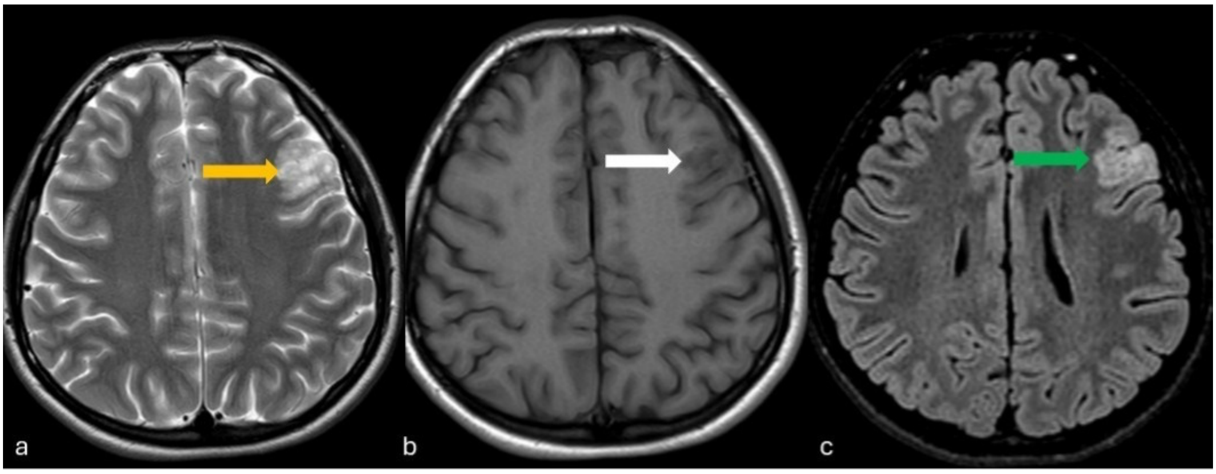


**FIGURE 1.** **Preoperative axial brain MRI of a 15-year-old patient with histopathologically confirmed dysembryoplastic neuroepithelial tumor (DNET). (a) Axial T2-weighted image demonstrates a cortically based lesion in the left inferior frontal gyrus with a characteristic "soap bubble" [bubbly] appearance (yellow arrow). (b) Axial T1-weighted image shows the same lesion as hypointense relative to the surrounding cortex (white arrow). (c) Axial FLAIR image reveals the lesion without complete signal suppression, maintaining hyperintense components (green arrow).**

between EEG lateralization and lesion laterality on MRI was subsequently evaluated within this subgroup.

Of the 12 patients with MRI-detected lesions, 9 (75.0%) demonstrated hemispheric concordance between EEG lateralization and lesion side, whereas hemispheric discordance was observed in 3 (25.0%) cases. Agreement between EEG lateralization and MRI lesion laterality was assessed using Cohen's kappa analysis, yielding a kappa coefficient of 0.60 (95% confidence interval: 0.18–1.00; P=0.008), indicating moderate agreement. However, the relatively wide confidence interval likely reflects the

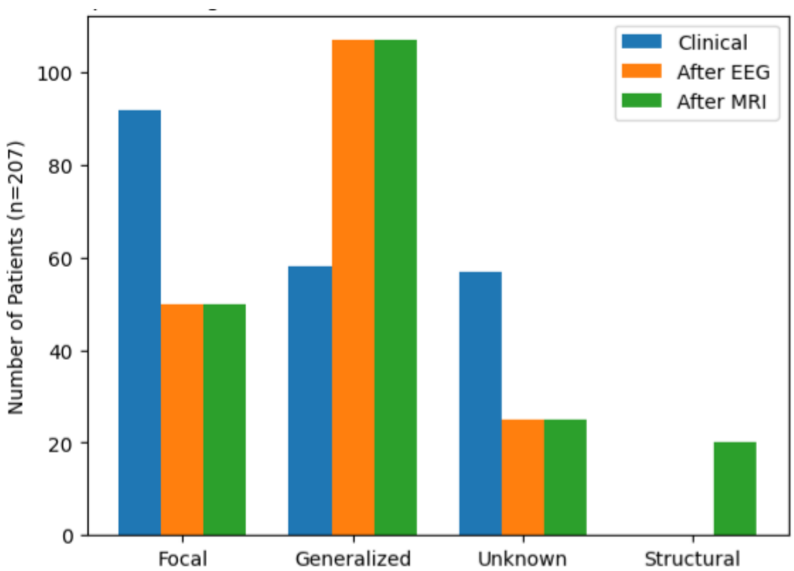


**FIGURE 2.** **Stepwise diagnostic reclassification across clinical, EEG, and MRI stages (n=207). Bar graph illustrating the distribution of seizure-onset categories at the clinical stage, after incorporation of EEG findings, and following MRI evaluation. EEG integration resulted in redistribution of seizure classification, with a reduction in unknown-onset cases and a shift between focal and generalized categories. MRI subsequently identified structural etiology in 20 (9.7%) patients, contributing additional etiological reclassification without further modification of seizure-onset type.**

**TABLE 4. Comparison of Clinical and Electroencephalographic Characteristics Between MRI-Positive and MRI-Negative Groups**

| Variable | MRI positive (n=20) | MRI negative (n=187) | P-value |
|---|---|---|---|
| **Age (years)** | 10.8±4.1 | 11.5±4.3 | 0.482 |
| **Sex** | | | |
| Male | 11 (55.0%) | 89 (47.6%) | 0.531 |
| Female | 9 (45.0%) | 98 (52.4%) | 0.531 |
| **Age at seizure onset (years)** | 4.2 [1.5–7.8] | 5.5 [2.2–9.6] | 0.214 |
| **Seizure type at initial clinical evaluation** | | | |
| Focal onset | 15 (75.0%) | 77 (41.2%) | **0.002** |
| Generalized onset | 3 (15.0%) | 55 (29.4%) | 0.184 |
| Unknown onset | 2 (10.0%) | 55 (29.4%) | 0.071 |
| **Developmental delay/regression** | 10 (50.0%) | 39 (20.9%) | **0.002** |
| **Abnormal neurological examination** | 11 (55.0%) | 32 (17.1%) | **<0.001** |
| **Perinatal risk history** | 6 (30.0%) | 32 (17.1%) | 0.168 |
| **History of status epilepticus** | 5 (25.0%) | 24 (12.8%) | 0.141 |
| **Number of antiseizure medications** | | | |
| Monotherapy | 8 (40.0%) | 114 (61.0%) | 0.071 |
| Polytherapy | 12 (60.0%) | 73 (39.0%) | 0.071 |
| **Drug-resistant epilepsy** | 7 (35.0%) | 37 (19.8%) | 0.082 |
| **EEG findings** | | | |
| Normal EEG | 2 (10.0%) | 48 (25.7%) | 0.146 |
| Generalized epileptiform discharges | 6 (30.0%) | 101 (54.0%) | 0.053 |
| Focal epileptiform EEG abnormalities | 10 (50.0%) | 40 (21.4%) | **0.007** |
| Multifocal epileptiform discharges | 0 (0%) | 0 (0%) | — |

Data are shown as mean±standard deviation or median [IQR=interquartile range], or number (%) where appropriate. EEG, electroencephalography; MRI, magnetic resonance imaging.

Continuous variables were compared using Student's t-test or Mann–Whitney U test according to distribution characteristics. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test where appropriate. MRI positivity was defined as the presence of epileptogenic structural lesions on cranial MRI.

Statistically significant P-values are shown in bold.

limited number of patients with both focal EEG abnormalities and MRI-positive epileptogenic lesions in the concordance subgroup.

## DISCUSSION

The present study demonstrates that diagnostic evaluation in pediatric epilepsy cannot rely on a single modality and that a stepwise, integrative approach substantially strengthens clinical decision-making. Our findings indicate that neuroimaging plays a decisive role in clarifying etiological classification and meaningfully reducing diagnostic uncertainty. Notably, the identification of epileptogenic structural lesions even in patients with normal interictal EEG underscores the independent diagnostic value of MRI within the evaluation algorithm [9–12]. At the same time, the strong association between specific clinical and electroencephalographic features and structural

**TABLE 5. Multivariable Logistic Regression Analysis of Factors Associated with MRI Positivity**

| Variable | Univariate OR [95% CI] | P-value | Multivariable OR [95% CI] | P-value |
|---|---|---|---|---|
| **Focal seizure onset** | 2.94 [1.46–5.90] | **0.002** | 2.63 [1.22–5.67] | **0.014** |
| **Developmental delay/regression** | 3.18 [1.55–6.53] | **0.002** | 2.91 [1.31–6.46] | **0.009** |
| **Abnormal neurological examination** | 3.52 [1.71–7.24] | **<0.001** | 3.08 [1.40–6.78] | **0.005** |
| **Focal epileptiform EEG** | 2.61 [1.29–5.29] | **0.007** | 2.47 [1.15–5.32] | **0.021** |
| **Drug-resistant epilepsy** | 1.88 [0.92–3.86] | 0.082 | 1.42 [0.64–3.17] | 0.380 |

OR, odds ratio; CI, confidence interval.

The multivariable model was constructed considering clinical relevance and to minimize overfitting due to the limited number of MRI-positive cases. Statistically significant P-values are shown in bold.

pathology provides a clinically actionable framework for developing targeted imaging strategies [13]. Collectively, these findings support an integrated model in which clinical assessment, EEG, and MRI are combined to enhance etiological accuracy and promote more rational patient management [9].

EEG remains a cornerstone of pediatric epilepsy assessment, particularly for demonstrating epileptiform activity and refining seizure classification. However, our results clearly highlight its limited sensitivity in identifying structural etiologies. A substantial proportion of children with epilepsy may exhibit normal interictal EEG recordings, a finding reflected in our cohort, where approximately one-quarter of patients had normal EEG results [12]. This observation reinforces the well-established principle that a normal EEG neither excludes the diagnosis of epilepsy nor rules out an underlying structural abnormality [12]. Conversely, focal epileptiform discharges were strongly associated with MRI-detected epileptogenic lesions, emphasizing their value as a marker of structural pathology. Nonetheless, the lack of complete concordance between electrical focus and structural lesion in some patients suggests that functional epileptogenic networks and structural abnormalities do not invariably align in a one-to-one manner [11]. Moreover, the relatively wide confidence interval observed in the EEG–MRI concordance analysis reflects the limited number of MRI-positive cases and warrants cautious interpretation. Overall, while EEG remains indispensable for seizure classification and clinical support, it is insufficient as a standalone tool for etiological determination.

**TABLE 6. Diagnostic Performance of Electroclinical Predictors for MRI Positivity**

| Variable | AUC | 95% CI | P-value | Interpretation |
|---|---|---|---|---|
| **Focal seizure onset** | 0.66 | 0.58–0.74 | **0.002** | Moderate |
| **Developmental delay/regression** | 0.69 | 0.61–0.77 | **<0.001** | Moderate |
| **Abnormal neurological examination** | 0.72 | 0.64–0.80 | **<0.001** | Moderate to good |
| **Focal epileptiform EEG** | 0.65 | 0.57–0.73 | **<0.005** | Moderate |
| **Drug-resistant epilepsy** | 0.68 | 0.60–0.76 | 0.061 | Moderate |
| **Combined electroclinical multivariable model** | 0.79 | 0.72–0.86 | **<0.001** | Good |

AUC, area under the receiver operating characteristic curve; CI, confidence interval; EEG, electroencephalography. Higher AUC values indicate better discriminative performance for predicting MRI positivity. The combined electroclinical multivariable model was constructed using variables that remained statistically significant in multivariable logistic regression analysis. Statistically significant P-values are shown in bold.

Cranial MRI represents one of the most influential diagnostic tools in establishing structural etiology in pediatric epilepsy [6, 10]. The MRI positivity rate of 9.7% observed in our cohort is consistent with previously reported rates in selected pediatric epilepsy populations [14, 15, 16]. The distribution of detected lesions—including encephalomalacia, malformations of cortical development, hippocampal sclerosis, and intracranial tumors—reflects the heterogeneous pathophysiology of structural epilepsy in childhood [10, 13]. These findings underscore the prominent role of early brain injury and developmental anomalies in epileptogenesis. From a clinical standpoint, identifying a structural epileptogenic focus extends beyond etiological clarification; it directly informs treatment planning, including evaluation for epilepsy surgery. In pharmacoresistant epilepsy, surgical candidacy is closely linked to lesion presence, localization, and lateralization [15]. Thus, the etiological information provided by MRI has direct implications for therapeutic strategy, seizure control prognosis, and long-term follow-up planning. Our findings strongly support the role of neuroimaging as a central component guiding clinical management in pediatric epilepsy.

A particularly important contribution of this study is the demonstration that the staged nature of the diagnostic pathway meaningfully influences final classification. While the addition of EEG substantially improved seizure-type determination following clinical assessment, incorporation of MRI led to a further and critical shift in etiological categorization. The reclassification of a subset of patients into the structural etiology category following MRI integration indicates that neuroimaging functions not merely as a confirmatory modality but as a diagnostic modifier [9, 10]. This observation aligns with the concept that epilepsy diagnosis in real-world practice is dynamic rather than linear [9]. Although clinical history and EEG findings often assist in defining seizure type, definitive etiological clarification frequently depends on neuroimaging. The transition of patients from “unknown etiology” to “structural etiology” following MRI emphasizes its unique and incremental contribution to the diagnostic algorithm. While prior studies have primarily focused on EEG–MRI concordance [11], systematic evaluation of MRI-driven diagnostic reclassification remains limited [13]. In this respect, our findings provide additional insight into the practical, stepwise structure of pediatric epilepsy evaluation. Stern *et al*. reported structural lesion detection rates of approximately 15–20% in pediatric epilepsy, particularly in cohorts enriched for focal semiology or abnormal neurological findings [6]. Likewise, Pastore *et al*. highlighted that optimized MRI protocols enhance detection of subtle cortical malformations in focal epilepsy populations [13]. In comparison, the MRI positivity rate observed in our cohort appears lower than that reported in several highly selected pediatric epilepsy series, particularly epilepsy surgery cohorts, likely reflecting the inclusion of a clinically heterogeneous real-world population rather than a preselected high-risk group enriched for focal, refractory, or structurally driven epilepsies. Although this resulted in a relatively modest overall lesion detection rate, it likely enhances the generalizability and practical clinical applicability of the study findings to routine pediatric epilepsy practice.

In addition, the systematic review by Gill *et al*. demonstrated that a substantial proportion of epilepsy cases remain MRI-negative despite modern imaging techniques [16]. Consistent with these observations, most patients in our cohort lacked identifiable structural abnormalities, underscoring that neuroimaging, while diagnostically pivotal, operates within a broader electroclinical framework.

Importantly, the diagnostic yield of MRI is not uniform across all patients. Identifying individuals with a higher likelihood of structural pathology is essential for rational resource utilization and prioritization. Multivariable analysis in our study demonstrated that focal-onset seizures, developmental delay or regression, abnormal neurological examination findings, and focal epileptiform EEG activity were independent predictors of MRI positivity. These features, often considered “red flags” in clinical practice, are widely recognized as indicators of focal or diffuse structural brain abnormalities [10, 13]. Developmental delay and abnormal neurological examination findings have been strongly associated with cortical malformations and sequelae of perinatal injury [10]. The combined presence of clinical and electrophysiological focality further increases the probability of detecting structural lesions, reinforcing the need for high-resolution imaging protocols in this subgroup. These findings support a risk-based and more targeted MRI utilization strategy rather than a uniform imaging approach for all pediatric epilepsy patients and may contribute to more rational and potentially more cost-effective neuroimaging utilization in routine clinical practice. In particular, prioritizing patients with high-risk clinical and electrophysiological features may help optimize diagnostic yield, especially in resource-limited clinical settings. Recent multimodal pediatric epilepsy studies integrating clinical semiology, EEG, and MRI findings further support the utility of stepwise diagnostic frameworks for improving etiological stratification and optimizing targeted neuroimaging utilization [7, 15]. In children exhibiting these high-risk features, early MRI evaluation appears both diagnostically justified and clinically impactful.

The superior discriminative performance of the combined electroclinical multivariable model compared with individual predictors further supports the value of integrated stepwise diagnostic evaluation in pediatric epilepsy. These findings suggest that combining clinical, neurological, and electrophysiological parameters may improve identification of patients with a higher likelihood of MRI-positive epileptogenic structural abnormalities.

Our findings also provide important perspective regarding the timing and prioritization of neuroimaging. The detection of structural lesions in approximately 12% of patients with normal EEG recordings indicates that normal routine EEG findings should not be interpreted as sufficient to exclude structural etiology. Reliance solely on EEG results when determining imaging necessity may therefore result in underdiagnosis in selected cases. A holistic, risk-profile–based approach integrating clinical features with electrophysiological data appears more appropriate. Early MRI planning in children with focal semiology, developmental delay or regression, abnormal neurological findings, or focal epileptiform activity may enhance diagnostic yield and facilitate timely etiological clarification, thereby enabling more rational therapeutic decision-making. Even in cases with normal EEG, MRI should be considered an essential complementary component of the diagnostic workup when clinical suspicion for epilepsy is established.

## Strengths and Limitations

Despite its contributions, this study has several limitations. The retrospective design and single-center cohort may limit generalizability. Interpretation of EEG and MRI studies by single experienced specialists ensured internal consistency but may reduce external validity. As such, this approach may introduce observer-related bias. Additionally, interobserver variability analysis was not performed. All MRI examinations were performed on a standardized 1.5-Tesla epilepsy protocol, reflecting routine clinical practice in many tertiary pediatric neurology centers where 1.5-T MRI remains the primary imaging platform for pediatric epilepsy evaluation. Nevertheless, higher-field imaging or advanced techniques available in other centers might yield different detection rates. The cross-sectional design precluded longitudinal assessment, and repeat imaging or delayed lesion emergence was not evaluated. An additional limitation of this study is the relatively limited number of MRI-positive cases, which constrained the number of variables that could be incorporated into the multivariable logistic regression model. Although variable selection was performed carefully to reduce the risk of overfitting, this limitation may have affected model stability and generalizability. Therefore, the predictive performance of the proposed electroclinical model should be interpreted cautiously and validated in larger prospective multicenter cohorts. Finally, genetic and metabolic investigations were not systematically incorporated, limiting comprehensive classification of non-structural etiologies.

Nevertheless, the study possesses notable strengths. The relatively sizable pediatric epilepsy cohort provides a clinically meaningful dataset. More importantly, the structured, stepwise evaluation of clinical, EEG, and MRI data reflects real-world practice and allows systematic assessment of incremental diagnostic contribution. By explicitly modeling the clinical → EEG → MRI pathway, this study offers a pragmatic framework for understanding diagnostic reclassification in pediatric epilepsy. In doing so, it reinforces the importance of multidisciplinary integration and supports a diagnostic strategy that extends beyond electrophysiological findings alone.

## CONCLUSION

Diagnostic evaluation in pediatric epilepsy requires a comprehensive, integrative approach that synthesizes information from multiple data sources. The findings of this study suggest that neuroimaging is not merely supportive but can play a decisive role in clarifying etiological classification, especially when integrated with clinical assessment and EEG findings within a stepwise diagnostic framework. The observed associations between specific clinical and electrophysiological features and structural pathology suggest that imaging decisions may be more effectively guided by a risk-based strategy rather than a uniform approach.

Overall, these results underscore the value of a multidisciplinary diagnostic framework in pediatric epilepsy, where the integration of clinical assessment, EEG, and MRI facilitates more accurate etiological determination and supports more rational, individualized patient management. These findings may additionally contribute to the development of more precision-based imaging strategies in pediatric epilepsy. Future prospective multicenter studies integrating advanced neuroimaging approaches, multimodal electroclinical assessment, and longitudinal follow-up may further refine targeted imaging strategies and optimize individualized diagnostic pathways in pediatric epilepsy.

*Ethics Approval and Consent to Participate*

This study was approved by the Balıkesir University Faculty of Medicine Clinical Research Ethics Committee. (Decision No: 2023/110; date: 23.08.2023). All procedures were conducted in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments. Given the retrospective design and the use of fully anonymized data, the requirement for written informed consent was waived by the ethics committee.

*Data Availability*

All data generated or analyzed during this study are included in this published article. The data that support the findings of this study are available on request from the corresponding author, upon reasonable request.

*Authors' Contribution*

Study Conception: AA; Study Design: AA; Supervision: AA; Funding: N/A; Materials: N/A; Data Collection and/or Processing: EA, İDÇ, MB, GD, BYK; Statistical Analysis and/or Data Interpretation: EB; Literature Review: EA, İDÇ, MB, BYK; Manuscript Preparation: AA, İDÇ; and Critical Review: EB, BYK, GD.

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*Editor's Note*

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