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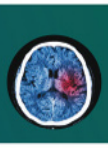

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ORIGINAL ARTICLE

Magnetic resonance imaging findings in focal-onset status epilepticus

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Abstract

Background and purpose: Magnetic resonance imaging (MRI) is commonly used in the diagnostic work-up for status epilepticus (SE). The purpose of this study was to characterize MRI features in SE patients and determine their association with clinical and electroencephalography (EEG) findings. The mid-term consequences of baseline MRI features were also analysed.

Methods: This is a prospective study including consecutive patients with SE who underwent brain MRI within 240 h after SE onset. The MRI protocol included T1-weighted (T1WI), T2-weighted (T2W), fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) sequences. Follow-up MRI was performed after SE resolution in some patients.

Results: Sixty patients (56.7% men, mean age 58.3 years) were included. SE-related MRI abnormalities were seen in 31 (51.7%), manifesting as hyperintensities on T2W/FLAIR imaging (58.1%) and DWI (74.2%) sequences. Hippocampal and pulvinar involvement was seen in 58.0% and 25.8% of patients, respectively. MRI abnormalities were associated with a longer SE duration ($p = 0.013$) and the presence of lateralized periodic discharges (LPDs) on EEG ($p < 0.001$). Amongst the 33 follow-up MRIs, nine (27.3%) showed mesial temporal sclerosis (MTS), which was associated with severe clinical status ($p = 0.031$), hippocampal oedema ($p = 0.001$) and LPDs ($p = 0.001$) at baseline. A poorer clinical outcome was associated with baseline T2W/FLAIR imaging hyperintensities ($p = 0.003$).

Conclusion: MRI showed abnormalities in more than half of SE patients. A longer SE duration and LPDs on EEG were associated with SE-related MRI abnormalities and the development of MTS.

KEYWORDS
diffusion-weighted imaging, magnetic resonance imaging, seizures, status epilepticus; epilepsy

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INTRODUCTION

Status epilepticus (SE) is defined as single or multiple seizures that persist with incomplete return to the baseline neurological status for a certain length of time. The time points for defining SE are based on a duration of 5 min for tonic–clonic convulsive SE and 10 min for focal SE with impaired consciousness. The critical duration of 30–60 min is associated with neuronal damage, which can lead to further consequences, such as brain atrophy or mesial temporal sclerosis (MTS) [1–3].

Magnetic resonance imaging (MRI) is often performed in focal-onset SE to detect underlying structural lesions. T2-weighted imaging (T2WI) and diffusion-weighted imaging (DWI) signal abnormalities can be seen in most cases with a cortico-subcortical distribution ipsilateral to the epileptogenic hemisphere; such abnormalities are potentially reversible and related to the duration of the SE [4–7]. The abnormalities are presumed to be a consequence of the excessive metabolic demand during prolonged epileptic activity, as seen in functional neuroimaging with nuclear medicine tracers involving positron emission tomography or single-photon emission computed tomography [8].

Although several publications describe SE-related MRI abnormalities, there are few available data on the correlation between the electroencephalography (EEG) patterns in SE and acute lesions seen on MRI. The main finding of these studies is that DWI signal abnormalities are more frequent in patients with lateralized periodic discharges (LPDs) on EEG [9,10]. Nonetheless, prospective MRI studies in a large series of patients with different ictal EEG patterns are lacking.

Some current topics of debate include the timing and duration of signal abnormalities on T2WI and DWI in SE, as well as their prognostic value at long-term follow-up.

The purpose of this study was to characterize MRI features in SE patients and determine their association with clinical and EEG findings. The radiological consequences of SE within the first few months after its resolution were also analysed.

METHODS

This is a prospective, single-centre and longitudinal study approved by the local ethics committee (PR (AG) 140/2018). From July 2017 to May 2019, patients older than 16 years with a diagnosis of focal-onset SE according to clinical and/or EEG criteria (Salzburg criteria) admitted to our epilepsy unit were included [11]. All included patients underwent a standardized brain MRI examination within the first 240 h after the diagnosis of SE.

All patients with hypoxic-ischaemic encephalopathy were excluded to avoid misdiagnosis of SE-related DWI findings. Patients were also excluded who presented with acute/subacute or chronic extensive brain infarction (>two-thirds of a vascular territory) or lobar haematoma or chronic traumatic injuries that produced a volume loss greater than one-third of a lobe to avoid misinterpreting follow-up MRI. Patients who underwent brain surgery with parenchymal resection were also excluded for the same reason.

Other patients excluded from this study were those who could not undergo an MRI examination during or immediately after the SE episode because of MRI contraindications (pacemakers and MR-incompatible prosthetic heart valves or metallic implants), critical illness (severe respiratory, cardiovascular or neurological derangement), the inability to remain still, or MRI unavailability. Patients with low diagnostic quality MRIs or incomplete MRI protocols were also excluded (Figure 1).

Follow-up MRI after the SE had resolved was performed between 3 and 18 months later in patients who agreed to undergo a second MRI for the purpose of the study.

The SE MRI study protocol (baseline and follow-up) included the following sequences performed with 3 T or 1.5 T magnets: (1) sagittal 3D T1-weighted (T1W) magnetization prepared rapid gradient-echo (MPRAGE) with multiplanar reconstructions along the main hippocampus axes; (2) transverse and coronal 2D T2W fast spin-echo; (3) transverse and coronal 2D T2W fluid-attenuated inversion recovery (FLAIR); and (4) transverse single-shot spin-echo echo-planar DW with diffusion sensitivity values of 0, 500 and 1000 s/mm^2 along all three orthogonal axes with the corresponding apparent diffusion coefficient (ADC) maps. Gadolinium enhanced sequences were used as part of the diagnostic work-up in selected cases and were not included in the study assessment. Details of the acquisition parameters are included in Table S1.

A staff neuroradiologist (SS, 15 years of experience) blinded to any clinical information other than the SE diagnosis visually assessed all the studies immediately after the imaging acquisition of each case. Structural and signal changes on T1W imaging (T1WI), T2WI, FLAIR and DWI were identified. High-signal areas on DWI, indicating restricted diffusivity, had to be confirmed on the corresponding ADC maps as low-signal areas. SE-related abnormalities were defined on T2W/FLAIR images with or without restricted diffusion as follows: (1) increased cortical signal intensity with or without thickening and blurring of the cortical grey and/or white matter borders (subcortical), (2) increased signal intensity in the pulvinar nucleus, (3) increased signal intensity and enlarged hippocampus and (4) increased signal intensity in the claustrum/peri-insular regions. Contralateral cerebellar T2W/FLAIR imaging hypersignals and DWI abnormalities were considered to be crossed cerebellar diaschisis caused by a prolonged seizure. SE-related MRI findings in aetiologies that may present local hypersignal in T2WI or DWI (tumours, encephalitis, infections or strokes) were included in the analysis only if they showed T2WI or DWI abnormalities independent from the primary lesion.

In addition, the observer visually assessed the presence of focal areas of restricted diffusivity associated with signal abnormalities detected on T2W/FLAIR. The observer specifically sought SE-related abnormalities, differentiating them from non-SE-related structural lesions. Signal abnormalities on T2W/FLAIR and DW images and hippocampal volume changes were visually assessed on the follow-up scans, with particular attention given to the identification of MTS (decreased hippocampal volume associated with a T2 hypersignal).

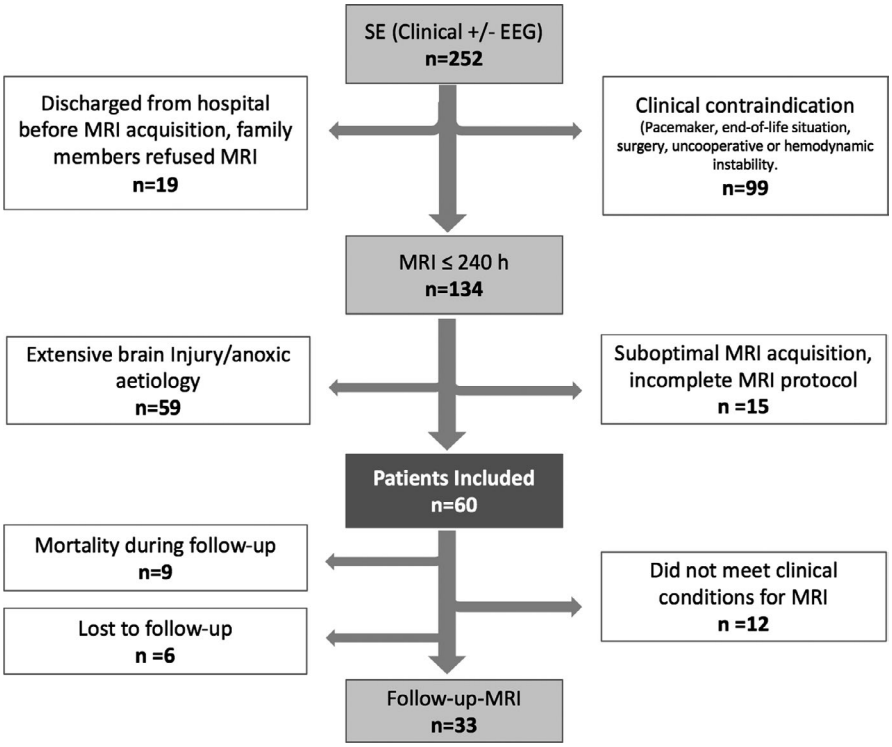

FIGURE 1 Patient recruitment flowchart. EEG, electroencephalography; MRI, magnetic resonance imaging; SE, status epilepticus

The type of SE was diagnosed and classified according to the International League Against Epilepsy (ILAE-2015), where SE is divided into SE with prominent motor symptoms (generalized convulsive SE, myoclonic SE and focal motor SE) or SE without prominent motor symptoms (non-convulsive status epilepticus [NCSE] without coma, NCSE with coma and focal SE) [1].

The SE video-EEG protocol included 21 scalp electrodes using the 10–20 international system, electrocardiogram, electromyogram and respiratory band with a duration range between 45 min and 4 h. Serial video-EEGs with time gaps from 6 to 24 h were performed as part of the routine diagnostic work-up. The duration and frequency of the consecutive video-EEG recordings depended upon the clinical evolution up to the cessation of seizures. An expert neurophysiologist (MS) read the EEGs according to the 2012 consensus of the American Clinical Neurophysiology Society [12] and Salzburg's Consensus EEG Criteria [11]. The EEGs were classified according to the Epidemiology-based Mortality Score in Status Epilepticus (EMSE), which in brief includes the following patterns: spontaneous burst-suppression, after status ictal discharge (ASID), generalized periodic discharges (GPDs), LPD or none of the previous patterns [13].

Demographics, clinical data and baseline functional status using the modified Rankin Scale were prospectively recorded on admission.

The aetiology of the SE was classified as acute symptomatic, remote symptomatic, progressive and unknown (cause not identified after complete study). In acute symptomatic SE, the precipitating aetiology occurs within a few weeks prior to SE onset and can include, for example, stroke, traumatic brain injury or central nervous system (CNS) infection. In remote symptomatic SE, the aetiology is related to chronic brain lesions. Progressive SE occurs in the context of a progressive neurological disease, such as CNS neoplasm, mitochondrial encephalopathies and CNS storage disorders [1].

The severity of the SE was determined by two scores: the modified Status Epilepticus Severity Score (mSTESS) calculated for each patient at admission [14] and the EMSE determined at 24 h [15]. Refractory SE was established when seizures persisted despite the use of at least two drugs (benzodiazepine and one antiepileptic drug) at appropriate doses.

The duration of the SE was determined clinically or by EEG. SE onset was the time at which symptoms began or the last time the patient was seen to be asymptomatic. The conclusion or end-point was the time EEG monitoring recorded seizure suppression. In comatose NCSE patients with an unknown starting time, SE onset was considered the last time they were seen to be asymptomatic. The time interval from SE onset to the MRI study was also determined.

Poor outcome was defined as the development of a new disability or an increase in the modified Rankin Scale score. Good outcome was considered when the functional status returned to baseline.

Statistical analysis

Descriptive and frequency statistical analyses were performed, and comparisons were made using IBM SPSS Statistics 22.0 software. Categorical variables are reported as frequencies (percentages), continuous variables as the mean ± standard deviation (SD) and non-normally distributed quantitative variables as the median and interquartile range (IQR). The normality assumption for quantitative variables was checked with the use of quantile–quantile (Q-Q) plots.

Statistical significance in the comparisons of MRI abnormalities in patients with a poor prognosis and development of MTS was assessed by Pearson's chi-squared or Fisher's exact test for categorical variables, Student's *t* test for continuous variables and the Mann–Whitney *U* test for non-normally distributed quantitative variables. A receiver operating characteristic curve was plotted to calculate the cut-off point for SE duration with the best sensitivity and specificity in predicting MRI abnormalities; the optimal cut-off point was obtained using the maximum value of Youden's index (sensitivity + specificity − 1). Variables in the univariable analysis associated with a p value <0.1 were entered into multiple logistic regression models to identify factors independently associated with SE-related MRI abnormalities and MTS on follow-up MRI. Because of the small follow-up sample size, the results of this last regression model should be considered exploratory. p values <0.05 were considered statistically significant.

RESULTS

Demographics and clinical characteristics

In all, 252 patients were admitted during the study period, of whom 60 met the inclusion criteria of the study (Figure 1). They were 56.7% (n = 34) men, and the mean age of the enrolled cohort was 58.3 (±20.6) years. The patients' demographic and clinical characteristics are summarized in Table 1. The median mSTESS score was 3 (IQR 1–4), and the median EMSE was 62 (IQR 39–81). Video-EEG findings showed ictal patterns in 48 (80%) patients as focal seizures (Table 1), 18 (30%) LPDs plus and eight (13.3%) rhythmic delta activity plus. According to the EMSE EEG score 18 (30%) LPDs, 20 (33.3%) ASIDs and one (1.7%) GPDs were observed (Table 1).

The median SE duration was 26.4 h (IQR 9.1–92.9 h), and 36 (60%) episodes were refractory/super-refractory SE with a median duration of 46.2 h (IQR 15.2–108.3 h). The median time interval from SE onset to the MRI study was 123 h (IQR 76.8–183.8 h) (Table 1).

Radiological findings

In the overall MRI analysis, 49 patients (81.7%) presented with abnormal findings, but these were considered to be SE related in 31 (63.3%). SE-related features included DWI abnormalities in 23 patients (74.2%) and hyperintensities on T2W/FLAIR imaging suggestive of oedema in 18 (58.1%) (Figure 2). The most frequent finding was an abnormality in the ipsilateral hippocampus (Figure 3). A unilateral claustrum/periinsular T2W/FLAIR hyperintensity was seen in a single patient with SE secondary to herpes simplex virus 1 encephalitis. Crossed cerebellar diaschisis was seen in five patients (15%) (Table 2).

Analysis of the factors associated with the presence of SE-related hyperintensities on T2W/FLAIR or DW images revealed a relationship with higher EMSE scores (median 74, IQR 61–88 vs. 42, IQR 21–65; $p < 0.001$) and specific aetiologies, such as chronic cerebrovascular disease or traumatic brain injury (19.4% vs. 6.9%; $p = 0.037$).

TABLE 1 Demographic and clinical variables of the patients

Men	34 (56.7%)
Mean age, years, mean ± SD	58.3 ± 20.6
Aetiology	
Acute symptomatic	26 (43.3%)
Remote symptomatic	14 (23.3%)
Progressive symptomatic	13 (21.7%)
Unknown	7 (11.7%)
Aetiology	
Cerebral neoplasm	16 (26.7%)
Toxic/drug overdose	9 (15%)
Chronic cerebrovascular disease or chronic traumatic brain injury	8 (13.3%)
Unknown cause	7 (11.7%)
Non-adherence	6 (10%)
Acute stroke	6 (10%)
Acute infection	3 (5%)
Inflammatory/autoimmune	3 (5%)
Metabolic	2 (3.3%)
Pre-existing seizure	22 (36.7%)
mSTESS score, median (IQR)	3 (1–4)
EMSE score, median (IQR)	62 (39–81)
EEG	
Ictal focal activity	48 (80%)
Findings on EEG (EMSE EEG):	
LPDs	18 (30%)
ASID	20 (33.3%)
GPDs	1 (1.7%)
SE duration, h, median (IQR)	26.4 (9.1–92.9)
Refractory/super-refractory SE duration, h, median (IQR)	46.2 (15.2–108.3)
ILAE classification	
Prominent motor symptoms	
Generalized seizures	16 (26.7%)
Focal motor seizures	15 (25%)
No prominent motor symptoms	
Without coma	26 (43.3%)
With coma	3 (5%)
Time interval to MRI examination, h, median (IQR)	123 (76.8–183.8)
Outcome at discharge	
Unfavourable	23 (38.3%)
Returned to baseline status	37 (61.7%)

Abbreviations: ASID, after status ictal discharge; EEG, electroencephalography; EMSE, Epidemiology-based Mortality Score in Status Epilepticus; GPDs, generalized periodic discharges; ILAE, International League Against Epilepsy; IQR, interquartile range; LPDs, lateralized periodic discharges; mSTESS, modified Status Epilepticus Severity Score; MRI, magnetic resonance imaging; SE, status epilepticus.

SE-related MRI signal abnormalities were also associated with the median SE duration (69.6 h, IQR 13–109 vs. 15 h, IQR 3.1–43.2; $p = 0.013$), and the best cut-off point (sensitivity 51.6%, specificity 86.2%) was >60 h duration ($p = 0.002$). No significant association was found with the time interval between symptom onset and MRI examination ($p = 0.985$) (Table 3). There was a strong association between SE-related abnormalities and the presence of LPDs (48.4% vs. 10.3%) or ASIDs (41.9% vs. 24.1%) ($p < 0.001$) on EEG (Table 3).

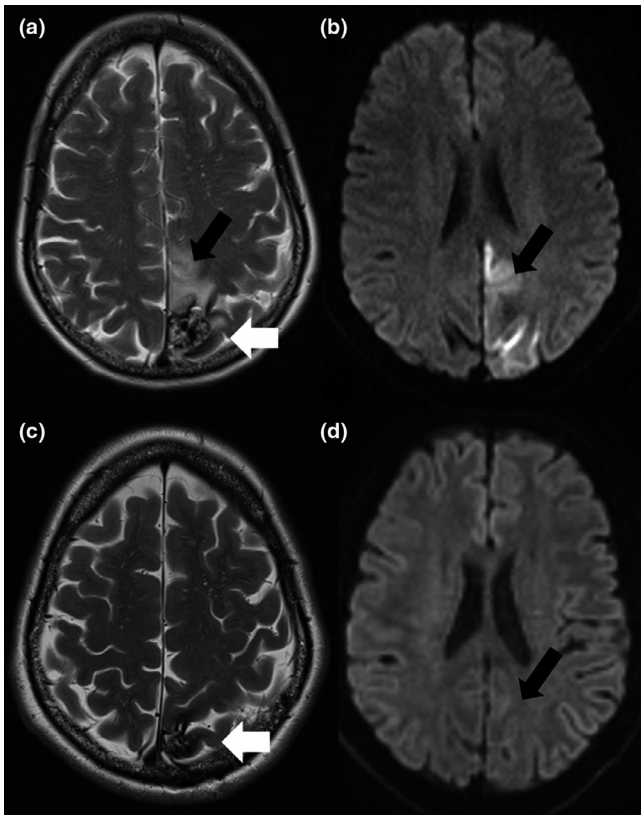

FIGURE 2 A 46-year-old man with new-onset status epilepticus. (a), (c) Axial T2WI and (b), (d) DWI show an irregularly shaped node (10-mm diameter) with peripheral haemosiderin staining in the left parietal lobe, consistent with a cavernous malformation (a, white arrow). The hypersignal and cortical thickening beyond the oedema surrounding the cavernoma (a, b, black arrows) are probably due to cytotoxic oedema. (c), (d) Follow-up MRI at 6 months shows resection of the cavernoma (c, arrow) and resolution of abnormalities associated with status epilepticus (d, arrow)

All MRI findings in our series were unilateral and ipsilateral to the epileptic source. The single patient with GPDs on EEG had a normal MRI. According to the seizure onset localization on EEG, lesions on DWI (73.9% vs. 37.8%, $p = 0.007$) and in the hippocampus (78.6% vs. 43.5%, $p = 0.021$) were more probably seen in temporal lobe origin SE.

After performing multiple logistic regression analysis, the presence of LPDs (odds ratio [OR] 7.485, 95% confidence interval [CI] 1.075–52.120; $p = 0.042$) and prolonged SE duration (>60 h) (OR 4.467, 95% CI 1.005–19.843; $p = 0.049$) were found to predict SE-related abnormalities on DWI and T2W/FLAIR imaging. All patients with LPDs and SE duration >60 h showed MRI abnormalities (Figure S1).

The 14 patients (23.3%) who underwent MRI during the active SE seizure were more likely to have T2W/FLAIR imaging hyperintensities (44.4% vs. 14.3%, $p = 0.019$), but there were no significant differences regarding DWI abnormalities. In this subset of patients, the median SE duration was 165.6 h (IQR 72–319 h), and 57.1% had a temporal lobe origin.

At hospital discharge, 23 (38.3%) patients had a poor outcome, and 37 (61.7%) returned to their baseline clinical status. Patients with MRI abnormalities tended to have poorer outcomes (65.2% vs. 43.2%, $p = 0.098$), particularly those with SE-related T2W/FLAIR imaging hyperintensities (52.2% vs. 16.2%, $p = 0.003$).

Magnetic resonance imaging findings at follow-up

Follow-up MRI was performed in 33 of the 60 patients (55%) at a mean interval of 9.7 months (3.2–17.4 months) after SE cessation. T2W/FLAIR and DW MRI abnormalities recovered in 15 of the 33 patients (45%), whereas in the 10 patients who had normal baseline findings MRI remained normal at follow-up.

TABLE 2 Radiological findings

MRI examinations	*N* (%)
MRI abnormal	49 (81.7%)
Cortical lesions	24 (49%)
MTS at baseline	2 (4%)
SE-related	31 (63.3%)
DWI abnormalities (restricted diffusivity)	23 (74.2%)
↑ T2W/FLAIR imaging (with/without cortical thickening)	18 (58.1%)
Hippocampal ↑ T2W/FLAIR imaging + enlargement	13 (41.9%)
Pulvinar nucleus ↑ T2W/FLAIR imaging (+ DWI)	8 (25.8%)
Crossed cerebellar diaschisis (↑ T2W/FLAIR)	5 (16%)
Claustrum/peri-insular ↑ T2W/FLAIR	1 (3.2%)

Abbreviations: ↑, increased signal; DWI, diffusion-weighted imaging; FLAIR, T2W fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; MTS, mesial temporal sclerosis; SE, status epilepticus; T2W, T2-weighted.

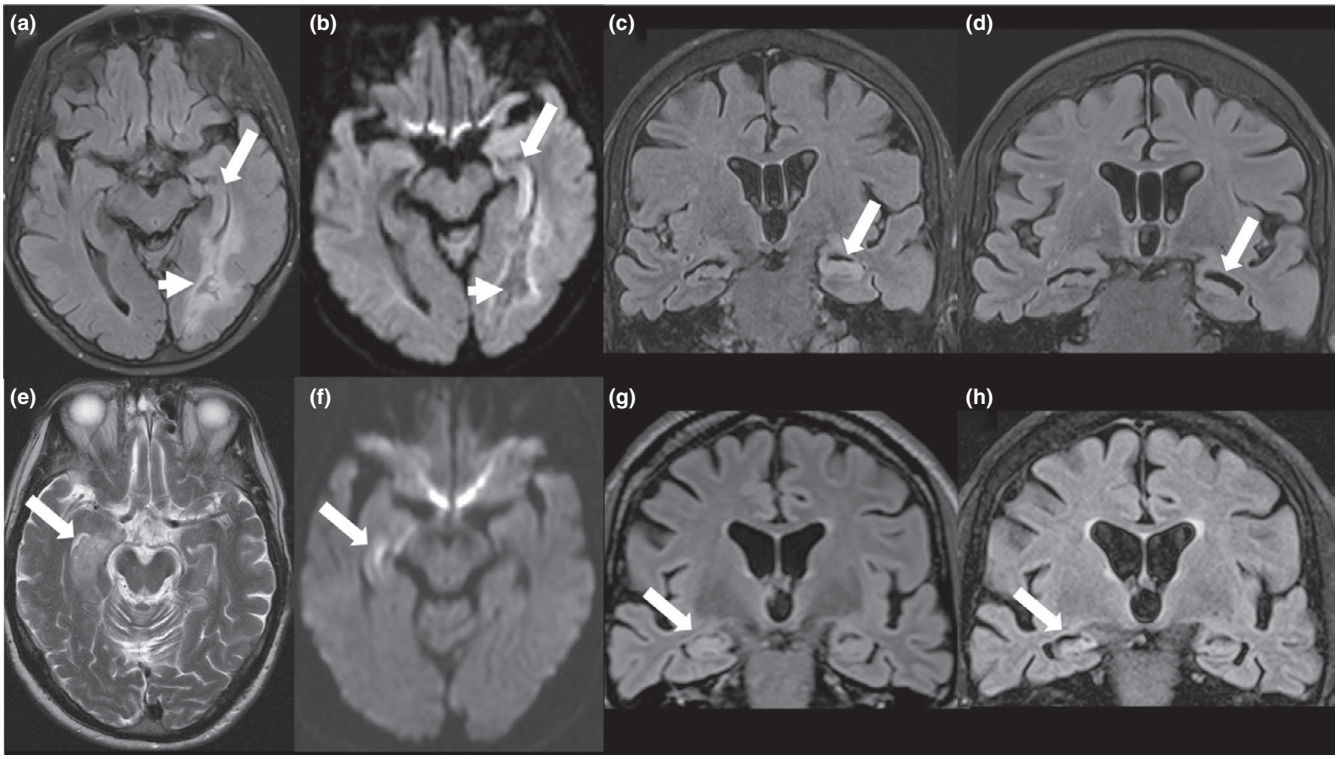

FIGURE 3 Two illustrative cases with temporal onset SE. (a)–(d) Case 1: a 76-year-old woman with an SE secondary to a subacute left posterior cerebral artery infarction (a, b, arrowheads). In baseline MRI, FLAIR hyperintensity (a, arrow) and DWI restriction (b, arrow) were observed in the left hippocampus. Moreover, a coronal FLAIR image showed hippocampal enlargement and hyperintensity (c, arrow). The 6-month follow-up MRI showed left mesial temporal sclerosis (d, arrow). (e)–(h) Case 2: a 65-year-old man with nonconvulsive SE of unknown aetiology. In baseline MRI, right hippocampus hyperintensity and enlargement on axial T2WI (e, arrow) and coronal FLAIR (g, arrow), as well as restriction on DWI (f, arrow) were observed. The 9-month follow-up MRI showed right mesial temporal sclerosis (h, arrow)

MTS is was seen in two patients on baseline MRI, one of which was related to the epileptogenic focus (Table 2). On follow-up MRI, eight patients (24.2%) with a mean age of 58 (±5.5) years had developed unilateral MTS, whereas one patient with unilateral MTS at baseline showed progressive hippocampal atrophy, considered a consequence of the SE. One patient had a history of SE 1 year before and another one had active epilepsy.

The development of MTS was associated with a higher percentage of LPDs on EEG (77.8% vs. 12.5%, $p < 0.001$) and a lower median EMSE score (55, IQR 33–72, vs. 69, IQR 64–77; $p = 0.031$). The temporal lobe was the most likely epileptic source of the SE in patients with MTS on follow-up MRI (seven patients, 77.8%).

Following multiple regression analysis, the factors independently associated with MTS on follow-up MRI were T2W/FLAIR and DWI abnormalities in the hippocampus (OR 28.074, 95% CI 1.990–396.131; $p = 0.014$) and LPDs on EEG (OR 14.061, 95% CI 1.095–180.486; $p = 0.042$) during the SE episode (Table S2).

DISCUSSION

This is a prospective study of patients who underwent MRI during an episode of SE, where it was observed that the presence of SE-related MRI abnormalities was associated with some clinical features and certain EEG patterns. Unlike other studies, a mid-term follow-up MRI in some patients showed that acute SE-related abnormalities in the temporal lobe implied a risk for further MTS development.

Status-epilepticus-related MRI abnormalities were seen at a higher rate than in previous studies [5,10,16,17]. As expected, abnormal findings were commonly observed in patients with an acute symptomatic aetiology, malignant tumours and chronic cerebral lesions [18–20]. The two main factors associated with the development of MRI abnormalities were the duration of the SE episode and the presence of LPDs on EEG examination. The relevance of the duration of the ictal activity is in line with previous publications, which showed that signal abnormalities on T2WI and DWI were observed more frequently in patients with prolonged SE [2,4,16,17].

Our study showed a large heterogeneity of EEG findings. However, the main EEG pattern observed was the presence of LPDs in line with other studies [10]. LPDs commonly described in SE are attributed to disconnection of the cortex from subcortical structures in the presence of brain lesions such as strokes, encephalitis or malignancies [21,22]. In our study, LPDs were strongly associated with SE-related MRI abnormalities, particularly in the hippocampal and pulvinar regions, even in the absence of underlying lesions [21].

As has been observed in previous studies, SE-related MRI abnormalities occur ipsilateral to ictal activity on EEG [2,21,22]. It was found that specific alterations in the hippocampus (41.9%) and

TABLE 3 Status-epilepticus-related hyperintensities on DWI and T2W/FLAIR imaging

	SE-related abnormalities		
n	**Yes**	**No**	***p***
Mean age, years, mean ± SD	55.87 ± 12.29	60.97 ± 22.81	0.343
Type of seizures (worst)			
Focal	14 (45.2%)	11 (37.9%)	0.478
Generalized	14 (45.2%)	17 (58.6%)	
NCSE with coma	3 (9.7%)	1 (3.4%)	
mSTESS, median (IQR)	2 (1–3)	3 (2–4)	0.142
EMSE, median (IQR)	74 (61–88)	42 (21–65)	<0.001
ILAE classification			
Prominent motor symptoms	14 (45.2%)	17 (58.6%)	0.297
No prominent motor symptoms	17 (54.8%)	12 (41.4%)	
ILAE aetiology			
Acute	19 (32.3%)	16 (55.2%)	0.363
Remote	9 (29.0%)	5 (17.2%)	
Progressive	8 (25.8%)	5 (17.2%)	
Unknown	4 (12.9%)	3 (10.3%)	
Findings on EEG (EMSE EEG)			
LPDs	15 (48.4%)	3 (10.3%)	<0.001
ASID	13 (41.9%)	7 (24.1%)	
GPDs	0	1 (3.4%)	
No LPD/ASID/GPD	3 (9.7%)	18 (62.1%)	
SE duration, h, median (IQR)	69.6 (13–109)	15 (3.1–43.2)	0.013
Time interval to MRI examination, h, median (IQR)	120.7 (73.6–162.9)	126.5 (90.6–212.9)	0.985
Duration >60 h	25 (80.1%)	11 (37.9%)	0.002

Abbreviations: ASID, after status ictal discharge; DWI, diffusion-weighted imaging; EEG, electroencephalography; EMSE, Epidemiology-based Mortality Score in Status Epilepticus; FLAIR, T2W fluid-attenuated inversion recovery; GPDs, generalized periodic discharges; ILAE, International League Against Epilepsy; IQR, interquartile range; LPDs, lateralized periodic discharges; MRI, magnetic resonance imaging; mSTESS, modified Status Epilepticus Severity Score; NCSE, non-convulsive SE; SD, standard deviation; SE, status epilepticus; T2W, T2-weighted.

pulvinar nucleus (25.8%) were strongly related to the temporal origin of the SE. However, this type of involvement can be seen regardless of the origin of SE as a consequence of seizure propagation [4,22–24]. The involvement of mesial temporal structures is widely recognized in epilepsy, whilst the thalamic pulvinar nucleus has gained less attention. Although not directly involved in epileptogenesis, this structure is especially prone to changes induced by seizure propagation [4,22–24]. The claustrum/peri-insular involvement described in aggressive forms of febrile SE was rare in our series [25].

A quarter of the patients with follow-up MRI presented with MTS. This feature was strongly associated with baseline hippocampal abnormalities on DW and T2W/FLAIR images and with LPDs and temporal-lobe-onset seizures on EEG. Although the duration of the SE was not found to be a risk factor for developing MTS, more evidence is required to confirm this.

Despite the potential reversibility of the MRI abnormalities in SE, T2W/FLAIR imaging hyperintensities may indicate a poor prognosis. Moreover, it was found that the presence of lesions on T2W/FLAIR imaging increased the risk of a poor functional outcome at hospital discharge and the development of MTS, which supports previous findings [2]. Due to the limited number of patients in whom a follow-up MRI was obtained, no firm conclusions can be drawn regarding the value of the follow-up findings as a marker of permanent functional and structural damage.

Due to the high number of refractory SE, the lack of early availability for MRI and incomplete or suboptimal MRI quality, a dynamic evaluation of SE-related abnormalities on MRI was not possible for all patients. However, according to a previous retrospective study published by our group, the main predictive factor for the presence of SE-related MRI abnormalities was the duration of the SE [2], which could explain the lack of relation between early MRI acquisition after SE onset and the presence of SE-related abnormalities on MRI. Several reports describe the dynamics of quantitative changes in multi-parametric MRI. However, all these studies were carried out in rats [6,26], and therefore the factors and timing of MRI abnormalities in humans are not yet known. Moreover, gadolinium contrast enhancement was not

included in the protocol, which has been shown to be a promising diagnostic tool in recent studies of new-onset SE. An initial diffuse leptomeningeal enhancement has been documented [27].

In summary, our study shows that SE-related MRI abnormalities are associated with the duration of SE and the presence of LPDs on EEG examination. Mesial temporal structures and the pulvinar nucleus are the most susceptible to ictal epileptic damage. The presence of hyperintensities in the hippocampus on T2W/FLAIR imaging together with LPDs on EEG may be predictive of a poor functional outcome.

AUTHOR CONTRIBUTIONS

Silvana Sarria Estrada: Conceptualization (lead); formal analysis (lead); investigation (lead); methodology (lead); validation (lead); visualization (lead); writing—original draft (lead); writing—review and editing (lead). Estevo Santamarina: Conceptualization (equal); formal analysis (supporting); investigation (supporting); methodology (supporting); supervision (equal); validation (equal); writing—original draft (supporting); writing—review and editing (supporting). Manuel Quintana: Conceptualization (supporting); formal analysis (equal); investigation (supporting); methodology (supporting); supervision (supporting); validation (supporting); writing—original draft (supporting); writing—review and editing (supporting). Deborah Pareto: Conceptualization (supporting); formal analysis (supporting); software (supporting). Maria Sueiras: Conceptualization (supporting); investigation (supporting); supervision (supporting); writing—review and editing (supporting). Cristina Auger: Conceptualization (supporting); investigation (supporting); writing—review and editing (supporting). Manuel Toledo: Conceptualization (lead); formal analysis (equal); investigation (equal); methodology (equal); supervision (equal); writing—original draft (supporting); writing—review and editing (equal). Alex Rovira: Formal analysis (supporting); investigation (supporting); methodology (supporting); supervision (supporting); validation (supporting); writing—original draft (supporting); writing—review and editing (equal).

DATA AVAILABILITY STATEMENT

Data available on request from the authors. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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