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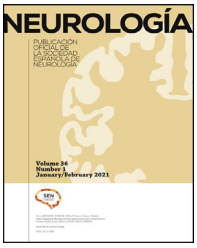

ORIGINAL ARTICLE

Current management of urgent epileptic seizures in a tertiary referral hospital in the Community of Madrid: a descriptive study

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KEYWORDS
Epilepsy;
Urgent seizure;
Status epilepticus;
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Abstract
Objective: Analyse the current status of the management of urgent epileptic seizures (ES) in a tertiary referral hospital in the Community of Madrid at each stage of the care process and by the different medical teams involved, including out-of-hospital emergency services, hospital emergency departments and neurology teams.
Method: Cross-sectional descriptive study with a subsequent 30-day prospective longitudinal follow-up of a consecutive sample of patients with urgent EC, recruited between October 2021 and March 2022.
Results: 53 patients were included. The mean age was 57.6 (21.2) years. 39.6% were women. 35.8% had a previous diagnosis of epilepsy. The most frequent cause of urgent ES was high-risk seizures (57%), followed by status epilepticus (24%) and cluster seizures (19%). A total of 90.5% of the seizures occurred in the out-of-hospital setting. The median time between ES and emergency services assessment was 40 (27—78) minutes, and between ES and neurology assessment 165 (97.5—290) minutes. 86.8% were treated with benzodiazepines and 81.1% with at least one anti-crisis medication. Urgent video-EEG monitoring was performed in 60.4%. The most frequent destination after emergency management was hospital discharge (47.2%), followed by hospitalisation (39.6%). At 30 days, 20.8% of patients had a new ES and 5.7% had died.

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Conclusions: Analysis of the current state of emergency EC management shows significant delays at all levels, both in assessment and drug administration.

PALABRAS CLAVE
Epilepsia;
Crisis epiléptica urgente;
Estado epiléptico;
Tratamiento agudo;
Atención urgente prehospitalaria y hospitalaria

Manejo actual de las crisis epilépticas urgentes en un hospital de tercer nivel de la Comunidad de Madrid, estudio descriptivo

Resumen
Objetivo: Analizar el estado actual del manejo de las crisis epilépticas (CE) urgentes en un hospital de tercer nivel de la Comunidad de Madrid en cada etapa del proceso asistencial y por parte de los diferentes equipos médicos implicados, entre ellos los servicios de urgencias extrahospitalarios (SUEH), servicios de urgencias hospitalarios (SUH) y equipos de Neurología.
Método: Estudio descriptivo transversal con posterior seguimiento prospectivo longitudinal a 30 días de una muestra consecutiva de pacientes con CE urgentes, reclutados entre octubre 2021 y marzo 2022.
Resultados: Se incluyeron 53 pacientes. La edad media fue de 57,6 años. El 39,6% eran mujeres. El 35,8% tenía diagnóstico previo de epilepsia. La causa más frecuente de CE urgente fue crisis de alto riesgo (57%), seguido de estado epiléptico (24%) y crisis en acúmulos (19%). El 90,5% de las CE sucedieron en ámbito extrahospitalario. La mediana de tiempo entre CE y valoración por SUEH fue 40 (27—78) minutos, y entre CE y valoración por Neurología 165 (97,5—290) minutos. Globalmente, el 86,8% recibió tratamiento con benzodiacepinas y el 81,1% tratamiento con al menos un medicamento anticrisis (MAC). Se realizó monitorización video-EEG urgente en el 60,4%. El destino más frecuente tras el manejo urgente fue el alta hospitalaria (47,2%), seguido de la hospitalización (39,6%). A los 30 días, el 20,8% de los pacientes presentó una nueva CE y el 5,7% había fallecido.
Conclusiones: El análisis del estado actual del manejo de las CE urgentes muestra importantes retrasos en todos los niveles, tanto en la valoración como en la administración de fármacos.

Introduction

Epilepsy presents a high incidence and prevalence worldwide. In Spain, lifetime prevalence amounts to 15 cases per 1 000 population.[1] According to the World Health Organization (WHO), one in every 10 people is estimated to present an epileptic seizure (ES) in their lifetime. Seizures account for 1% of consultations at emergency departments and are associated with significant morbidity, mortality, and use of resources.[2]

Given the incidence of the disease and the lack of clear protocols for the comprehensive care of these patients at different levels, several scientific associations and professionals from different Spanish hospitals participating in the management of epilepsy have worked to establish a consensus and create a treatment protocol to improve the care of these patients. As a result of this work, a consensus statement on the management of patients with ES at emergency departments was recently published by the Spanish Society of Epilepsy, the Spanish Society of Neurology's Epilepsy Study Group, and the Spanish Society of Emergency Medicine.[3] This document, which describes the relevance of early management of ES, introduces the concept of urgent ES, including status epilepticus (SE), in accordance with the current definition of the International League Against Epilepsy (ILAE),[4] as well as seizure clusters and high-risk ES. The term seizure cluster refers to the occurrence of repeated acute seizures within a short period of time; however, there is no universally accepted definition, and several have been proposed: recurrence of 3 or more seizures within 24 hours, 2 or more seizures within 6 hours, or 2 or more seizures within 24 hours, always with recovery periods between seizures (therefore, SE criteria are not met). Lastly, high-risk ES is a novel concept encompassing a series of situations that imply greater severity than the presence of an isolated ES. These situations include: first ES, score > 1 on the ADAN prehospital assessment scale,[5] pregnancy, paediatric age, associated fever, severe psychiatric comorbidity, poor treatment adherence (more than 24 h without taking standard treatment), and presence of complications associated with seizures (such as head trauma).

The importance of time in the treatment of ES has received greater attention in recent years. Numerous studies underscore the relevance of early, efficient management of ES and SE, as seizure duration is directly associated with prognosis.[6,7]

The aim of this study is to analyse the current situation of the management of these patients, assessing management

times and care of urgent ES in every stage of the care provided by the different medical teams involved. This study also underscores the relevance of prehospital emergency services (PES), hospital emergency departments (HED), and neurology departments.

Material and methods

Study design and setting

We performed a descriptive, cross-sectional study with a subsequent longitudinal prospective follow-up at 30 days of a series of consecutive patients with urgent ES assessed by the PES, the HED, and at in-hospital consultations at a tertiary hospital of the Region of Madrid.

Study period and population

The study period was from October 2021 to March 2022. We included all patients aged $\geq$ 12 years who presented an urgent ES (defined according to the previously described criteria) in the prehospital or hospital setting and who were assessed by a neurologist in the acute phase. Prospective follow-up was conducted by a telephone interview at 30 days after the initial event. We excluded terminally ill patients in the last days of life, in whom therapeutic effort is limited, as well as patients with suspected non-epileptic paroxysmal disorder.

Study variables

We collected data on a series of variables at different levels from patients' clinical records and reports from the PES. We considered demographic data (sex, age), personal history of epilepsy (type of epilepsy and treatment with antiseizure drugs [ASD]), baseline situation (assessed using the modified Rankin Scale [mRS]), and characteristics of the ES: type of seizure (according to the current ILAE classification), urgent seizure criteria (SE, seizure cluster, and high-risk seizure), as well as the ADAN prehospital assessment scale.

Furthermore, we gathered relevant healthcare data: type of care provided by the PES (at home, in a public space, etc), care by the HED or physicians working at in-hospital consultations, and care by the neurology department. With regard to these parameters, we also recorded management times (date and time). We also gathered data on the acute treatment administered in the different interventions (type of drug, date and time of administration). Data were also recorded from the main supplementary tests (blood analysis, neuroimaging studies, lumbar puncture) as well as cases undergoing emergency video-EEG monitoring (in the first 24 hours after the ES), including the duration, date and time of the study, and findings.

Lastly, we included clinical progression variables: patients' initial destination, duration of stay in the emergency department, and treatment changes (onset of treatment, dose change, or addition of an ASD). We recorded variables on progression at 30 days (new ES, visits to the emergency department, hospital admissions, and death).

From the data collected, we extracted the times between different interventions: ''ES—assessment by the PES,'' ''ES—administration of a benzodiazepine by PES,'' ''ES—assessment at the HED,'' ''ES—administration of a benzodiazepine at the HED,'' ''ES—administration of an ASD at the HED,'' ''arrival at hospital—assessment by the neurology department,'' ''ES—administration of a benzodiazepine by the neurology department,'' ''ES—administration of an ASD by the neurology department,'' ''ES—administration of first-line treatment (benzodiazepine or ASD),'' and ''ES—emergency video-EEG monitoring.''

Statistical analysis

Quantitative variables are expressed as means and standard deviations, or as median and quartiles 1 and 3 (Q_1-Q_3) when variables were not normally distributed, according to the Kolmogorov-Smirnov test. For qualitative variables, we used absolute values and percentages.

We performed a descriptive analysis of the collected variables from the total patient sample. We subsequently analysed the parameters referring to management times and drugs administered by patient subgroup, according to the place of assessment by healthcare professionals. Lastly, we performed a descriptive analysis of clinical progression at 30 days after the initial seizure.

Statistical analysis was performed using the IBM SPSS® software (version 26.0) for Windows.

Ethical considerations

The study was approved by the clinical research ethics committee of the hospital where the study was performed (21/676-E), and complied with the Declaration of Helsinki. All participants, or their representatives, gave their written consent to participate in the study.

Results

During the study period, we recruited a total of 53 patients with diagnosis of urgent ES. Twenty-one (39.6%) patients were women, mean age was 57.6 years (21.2), and baseline mRS score was 1 (Q_1-Q_3: 0—1.5); 19 (35.8%) patients had a previous diagnosis of epilepsy, of whom 15 (78.9%) presented focal epilepsy, 1 (5.3%) presented idiopathic generalised epilepsy, and 3 (15.8%) presented epilepsy of unknown cause. All patients with a diagnosis of epilepsy were under treatment with some ASD, 11 (57.9%) with one drug, 5 (26.3%) with 2, and 3 (15.8%) with 3 or more drugs.

Epileptic seizures were focal aware seizures in 10 (18.9%) patients, focal impaired awareness seizures in 5 (9.4%), focal with progression to bilateral tonic-clonic in 19 (35.8%), of generalised onset in 18 (34%), and of unknown onset in 1 (1.9%).

Forty-eight (90.5%) ES occurred outside of the hospital, with 35 (66%) occurring at the patient's home and 13 (24.5%) in public spaces. All ES occurring outside of the hospital were subsequently assessed at the emergency department;

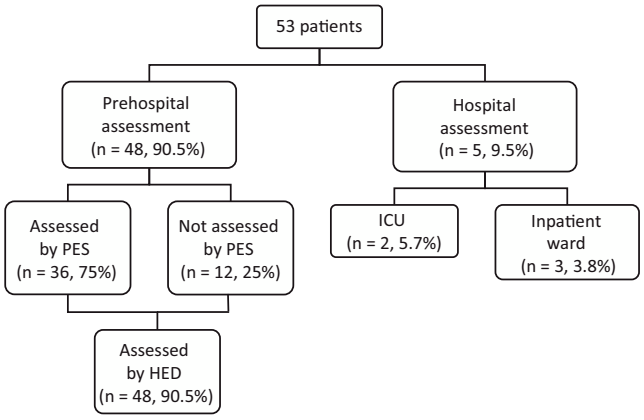

Figure 1 Flow diagram showing the location of seizure occurrence and assessment.
HED: hospital emergency department; ICU: intensive care unit; PES: prehospital emergency services.

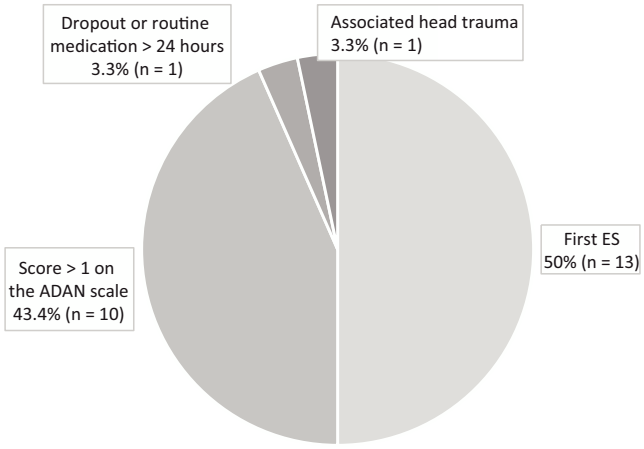

Figure 2 Distribution of criteria for high-risk seizures.
ES: epileptic seizure.

5 (9.5%) ES occurred in the hospital. The distribution of locations where the ES occurred and patients were assessed are shown in Fig. 1.

Of the 48 patients with ES occurring outside of the hospital, 36 (75%) were assessed by the PES and 12 (25%) came to hospital by other means. In 8 (22.2%) of the 36 cases, the on-call neurology department was alerted due to code stroke activation.

Fig. 2 shows the distribution of criteria for high-risk ES (n = 30). Fig. 3 shows the distribution of reasons for which ES was defined as urgent.

Regarding management times and drug administration times, these were analysed according to where ES onset occurred and the appropriate medical assessment was conducted in each situation.

In the subgroup of patients presenting an ES outside of the hospital and subsequently assessed at the emergency department (regardless of the previous assessment by the PES) (48 patients), mean time between the ES and assessment at the HED was 90.8 (53.4) minutes. Regarding the assessment at the HED, a benzodiazepine was administered to 15 (31.3%) patients, with the median time between the ES and drug administration being 150 minutes (Q_1-Q_3: 92—229). Eighteen (37.5%) patients received at least one ASD, with 150.5 minutes (Q_1-Q_3: 115.5—221.3) between the ES and drug administration. Of the total sample, 20 (41.7%) patients received first-line treatment, with the time between the ES and treatment administration being 135 minutes (Q_1-Q_3: 73—416).

In the subgroup of patients presenting an ES outside of the hospital and subsequently assessed by the PES (36 patients), time between the ES and the assessment was 40 minutes (Q_1-Q_3: 27—78). Regarding management, 9 (25%) patients received a benzodiazepine, with the time between the ES and drug administration being 58.6 (25.7) minutes. Three (8.3%) patients received at least one ASD, having previously received a benzodiazepine. Regarding the intervention by the PES, 9 (25%) patients received first-line treatment, with the mean time between the ES and treatment administration being 58.6 (25.7) minutes.

A benzodiazepine was administered before assessment by the neurology department in 22 (41.5%) patients: 6 (46.2%) in the SE group, 5 (50%) in the seizure cluster group, and 11 (36.7%) in the high-risk seizure group. Twenty-one (39.6%) patients received an ASD before assessment by the neurology department. Of the total patient sample, 23 (43.4%) patients received first-line treatment before assessment by the neurology department, with the time between the median ES and treatment administration being 104 minutes (Q_1-Q_3: 25—416).

All patients underwent assessment by the neurology department. The time between the ES and the assessment was 165 minutes (Q_1-Q_3: 97.5—290); in the subgroup of patients who suffered the ES outside of the hospital (n = 48), the time between arrival at hospital and the assessment was 111 minutes (Q_1-Q_3: 70.5—277.3). Benzodiazepines were administered to 25 (47.2%) patients, with the time between the ES and drug administration being 170 minutes (Q_1-Q_3: 140—353). At least one ASD was administered to 43 (81.1%) patients, with the time between the ES and drug administration being 205 minutes (Q_1-Q_3: 159.8—347.8). At least 2 ASDs were administered to 14 (26.4%) patients. Of the total sample, 45 (84.9%) patients received first-line treatment, with the time between the ES and treatment administration being 210 minutes (Q_1-Q_3: 23—558).

Of the total sample, 46 (86.8%) patients received a benzodiazepine at some point during the emergency assessment; benzodiazepines were the first treatment administered in 42 (79.2%) cases. Fig. 4 shows the settings in which benzodiazepines were administered in the subgroup of patients assessed by the PES and subsequently transferred to the emergency department and assessed by the neurology department (n = 36).

Neuroimaging studies were performed in 42 (79.2%) patients, with 18 (42.9%) displaying abnormal findings. The most frequent abnormal findings were of vascular origin (infarction, intraparenchymal haemorrhage, subarachnoid haemorrhage, subdural haematoma) in 9 (17%) patients, followed by tumour in 6 (11.3%), leukoaraiosis in 2 (3.8%), and other in 1 (1.95%). Lumbar puncture was performed in 4 (7.5%) patients; results of the analysis were abnormal in 2, showing elevated protein level (< 45 mg/dL) with no pleocytosis.

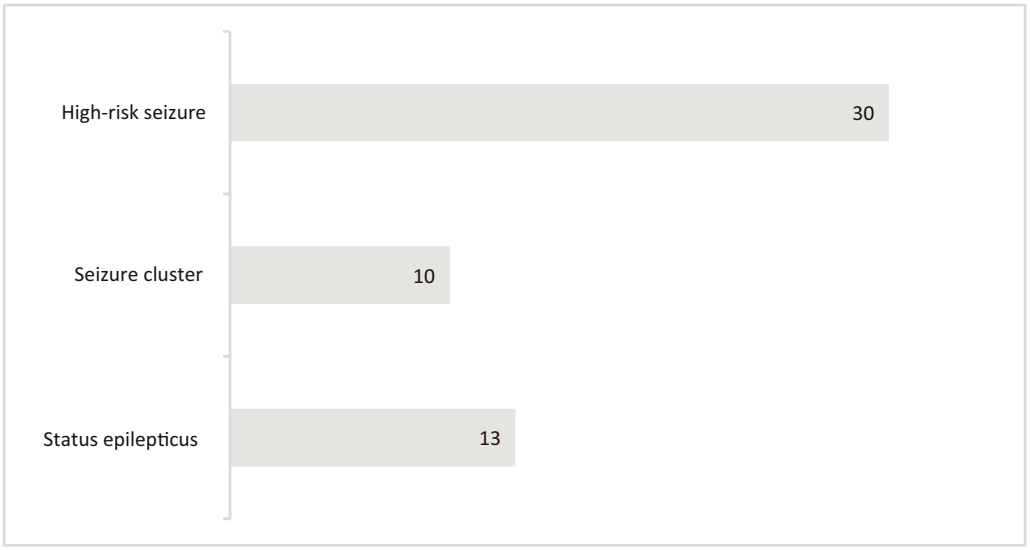

Figure 3 Distribution of urgent seizures.

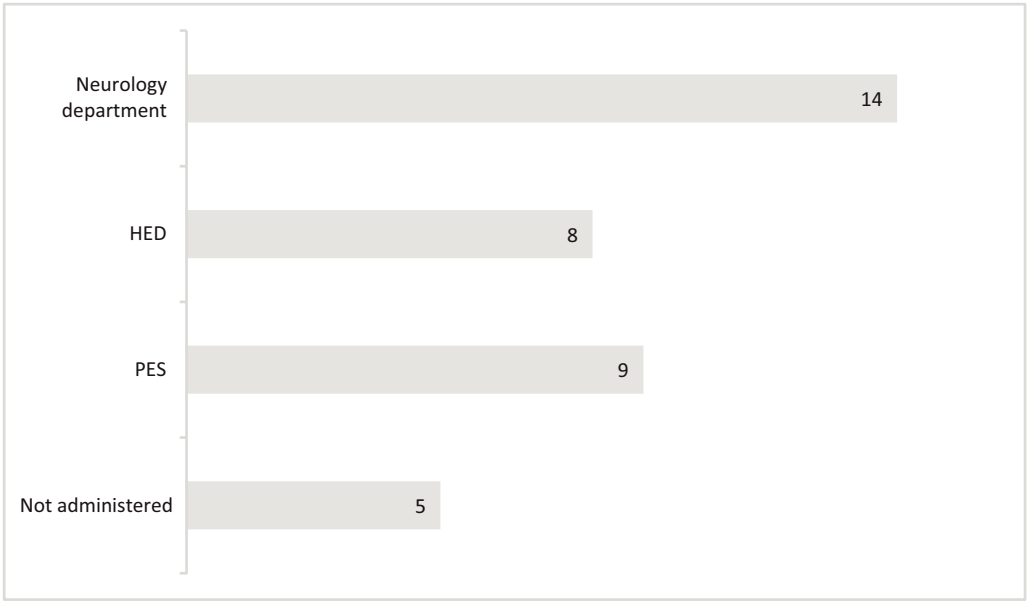

Figure 4 Distribution of the administration of benzodiazepines in the subgroup of patients assessed by prehospital emergency services and subsequently transferred to the emergency department and assessed by the neurology department.
HED: hospital emergency department; PES: prehospital emergency services.

Emergency video-EEG monitoring was performed in 22 (60.4%) patients. Median duration of monitoring was 43 minutes (Q_1-Q_3: 20—119) and the time between the ES and the video-EEG study was 6.8 hours (Q_1-Q_3: 2.8—15.2). The results of the monitoring are shown in Fig. 5.

The mean duration of the emergency department stay was 21 hours (Q_1-Q_3: 9—27). The destination of patients was discharge in 25 (47.2%) patients, hospitalisation in 21 (39.6%), and referral or admission to an intensive care unit in 7 (13.2%). All patients (n = 6) who showed an SE or ES pattern in the video-EEG monitoring required hospital admission; 3 (5.7%) patients died during hospitalisation, of whom 2 had a diagnosis of SE and 1 with seizure cluster.

Of the total sample, 52 (98.1%) underwent some treatment modification after the ES. All patients (n = 31) with no treatment prior to the ES and who did not die during the initial admission started treatment with at least one ASD, which was maintained after discharge. In 18 (94.7%) patients with a previous diagnosis of epilepsy and under treatment with ASDs, some treatment modification was performed, which consisted in all cases in a dose modification or the addition of a new drug. One (1.9%) patient who was already receiving previous treatment with an ASD underwent no treatment modification after the assessment.

In the prospective follow-up at 30 days, 11 (20.8%) patients presented a new ES and 4 (7.5%) visited the emergency department at least once more, with subsequent

Figure 5 Distribution of emergency video-EEG monitoring findings.

admission to an inpatient ward. All patients presenting new ES were receiving treatment with at least one ASD. During this period, no additional deaths were recorded, regardless of the already mentioned initial in-hospital mortality rate.

Discussion

This study describes the characteristics of a group of patients with urgent ES according to the definition proposed in the consensus statement,[3] as well as the care provided by the different healthcare levels in our setting; the largest subgroup included those who were first attended outside of hospital.

Although the sample is heterogeneous in its composition, all patients presented an urgent ES, defined as seizures requiring priority management and care. Our analysis revealed a pronounced delay in management times at the different healthcare levels with regard to the recommendations of the current international guidelines on the management of SE, for both assessment and treatment administration.[8] We should mention that these recommendations refer to the management of SE, but they have been extrapolated in this case for comparison with our sample of urgent ES. Similarly, the results obtained regarding the delay in management times are in line with other recently published Spanish[6,7] and international studies[9] analysing the management, care, and prognosis of patients with SE.

In our study, the delay between the onset of an urgent ES and assessment by prehospital healthcare professionals was 40 minutes, and the delay between the urgent ES and assessment by the neurology department at the hospital was 165 minutes. We should underscore that these times are calculated from the onset of the ES, not from the first telephone contact with the PES and the start of the emergency assessment process.

Regarding therapeutic management, we should stress the pronounced delay in the administration of a first-line treatment (benzodiazepines or ASD) at the different healthcare levels, which was almost an hour in the case of PES, more than 2 hours at the HED, and up to 4 hours in the case of assessments by the neurology department.

It is also significant that more than 20% of patients did not receive a benzodiazepine as the first treatment. In the subgroup analysis, a benzodiazepine was administered to 25% of patients managed by the PES, with almost one hour between the seizure and drug administration. The overall percentage of patients receiving this treatment before assessment by the neurology department was 41.6%. In this line, it is also relevant to highlight the lower rates of administration of benzodiazepines in patients with high-risk seizures (36.7%), compared to patients with SE and seizure clusters (46.2%). Regarding ASD, fewer than half of patients received at least one drug prior to assessment by the neurology department.

Video-EEG monitoring was used as part of the management process in 60.4% of the patients, with almost 20% of these showing an EEG pattern of SE or presence of recurrent ES. We should mention that this subgroup of patients required hospital admission, which shows the usefulness of this test in healthcare management.

We should also underscore that the introduction of the concepts of high-risk ES and seizure cluster, which account for more than 80% of our sample, enables us to include a higher number of patients with an urgent ES that require early management. Although we found no differences between the clinical scenarios considered in the different management times assessed in this study, we did identify a lower tendency for the PES and HED to administer drugs to the group with high-risk ES, compared to the other groups.

Lastly, follow-up at 30 days showed ES recurrence in more than 20% of the patients. The overall mortality rate amounted to almost 6%, with deaths occurring exclusively

in association with the initial admission. In general terms, this rate is lower than those reported by other studies evaluating mortality in series of patients with SE, which report in-hospital mortality rates of up to 28%.[10] This disparity may be associated with the mortality derived from longer hospital stays and the associated complications, with a rate of hospital admission of approximately 50% in our sample.

Our study presents several limitations. Firstly, it is subject to the limitations inherent to observational studies, as well as the loss of patients in the recruitment process, mainly those assessed by the PES but not referred to the hospital, and those patients who, although assessed at hospital, were not assessed by the neurology department; this may result in underestimation of the real incidence of these cases. Secondly, there is a potential for bias in the selection of patients, as the inclusion criteria included assessment by a neurologist. Thirdly, our single-centre study was performed at a tertiary hospital in the Region of Madrid, which has an on-call neurology department and the capacity to perform an emergency video-EEG monitoring; this may represent an obstacle to extrapolating our data to other Spanish regions and may have influenced the sample characteristics.

In conclusion, despite the limitations mentioned, this study offers an updated perspective of the management of patients with urgent ES at different healthcare levels, as well as, in general terms, the significant delay in care and drug administration in these situations. These conclusions may support the implementation and launch of a specific healthcare process for the management of urgent ES to improve care and management times, in a disease in which early intervention directly and independently determines outcomes.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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