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Impact of Treatment Delays in Epileptic Seizures

Time to Hospital Care and to EEG Increases Risk of Status Epilepticus and ICU Admission in Epileptic Seizures

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ABSTRACT

Background: Delays in the provision of care to patients experiencing seizures can result in evolution into status epilepticus (SE) and admission to the intensive care unit (ICU). However, data on specific response times and its implications remain sparse. Our aim is to report the time intervals of care delivery in patients with urgent seizures and evaluate its impact on the diagnosis of SE and the requirement for ICU admission.

Methods: A consecutive cohort analysis was conducted across two tertiary hospitals between December 2022 and March 2024. Of 1493 emergency episodes, 1139 cases were analyzed after excluding non-epilepsy diagnoses and incomplete data. Demographic data and time intervals (seizure onset, extra-hospital emergency activation, hospital admission, and EEG performance) were recorded. Associations between these intervals and SE diagnosis or ICU admission were evaluated.

Results: From our sample, 236 patients were diagnosed with SE, and 128 required ICU admission. Patients with SE had longer commute times (55 vs. 48 min, $p = 0.040$) and higher rates of prehospital anti-seizure drug administration ($p < 0.001$). Delays in EEG acquisition were associated with increased ICU admissions (22.1 vs. 16.5 h, $p < 0.001$). In multivariable analysis, prehospital treatment showed a strong association with SE (OR = 24.5, $p < 0.001$). Commute to hospital (OR = 4.95, $p < 0.001$) and seizure-to-EEG timelapse (OR = 5.05, $p < 0.001$) were associated with ICU admission.

Conclusion: Pre-hospital treatment administration, commute home to hospital and delayed EEG acquisition are associated with SE diagnosis and ICU admission, underscoring the need to optimize urgent care protocols for epileptic seizures.

1 | Introduction

Epileptic seizures represent one of the main reasons for admission in emergency services [1]. In its most severe manifestation, the failure of physiological mechanisms to terminate the seizure can lead to status epilepticus (SE), a condition in which timely intervention is critical due to its high risk of mortality and permanent neurological sequelae [2]. Therefore, early identification and timely treatment of epileptic seizures and SE are essential to improve clinical outcomes.

In recent years, advances in scientific evidence have allowed for the optimization of both diagnosis [3] and treatment of acute seizures and SE [4]. However, significant delays persist in the delivery of care for these patients, which could directly impact their prognosis [5, 6]. Critical factors such as the time elapsed from the onset of symptoms to prehospital care, the prehospital administration of anti-seizure drugs (ASD), and urgent EEG have been identified as key factors in the effective management of acute epileptic seizures [7].

Recently, the importance of early identification and treatment of these patients has been emphasized, highlighting the need for effective strategies in the prehospital setting, starting with the detection of urgent high-risk seizures that may evolve into SE or need more specialized care [8]. Tools such as the ADAN scale have demonstrated potential to improve the referral stratification of patients towards appropriate care pathways [9, 10]. However, real data on the time frame of response for seizures and its impact on specific outcomes is scarce [11].

This study analyzes the impact of delays in various phases of care for patients with acute epileptic seizures. The hypothesis is that there may be an association between delays in prehospital activation, hospital transport, and acquisition of urgent EEG with clinical outcomes, measured by the diagnosis of SE and the need for ICU admission as an indicator of severity.

2 | Methods

Data for this study was sourced from a structured data repository, extracted from a medical epilepsy form that is part of the electronic health record of adult patients at two tertiary hospitals in the metropolitan area of Barcelona: Hospital Universitari Bellvitge (HUB) and Hospital Universitari Vall d'Hebron (HUVB). This form was designed by a panel of epileptologists and personnel from the Institut Català de la Salut in 2021 for the follow-up of patients with epileptic seizures and was progressively implemented during 2022. The attending neurologists received specific training for completing the forms, and the system has been systematically used in daily clinical practice since November 2022. The form collects demographic and clinical characteristics as well as comorbidities and functional status (assessed with the modified Rankin Score, mRS) [12]. For this study, a structured form was used that mandatorily recorded the date and time of the epileptic seizure that prompted the emergency admission, the date and time of activation of the Extrahospital Medical Services (EMS), the date and time of arrival at the Emergency Department (ED), and the date and time of the EEG performed during the episode. Additionally, the prehospital treatment administered by the EMS (none, ASD, benzodiazepines, and/or endotracheal intubation) was recorded. A review of cases entered between December 2022 and March 2024 was conducted for this study.

The registry also included the final diagnosis of the episode in the ED (SE, acute symptomatic seizures, or epileptic seizure in a patient with epilepsy) and the patient's destination (discharge, hospital admission, or ICU admission). The ADAN scale score at the time of evaluation in the ED was recorded as an instrument to stratify the risk of SE. The ADAN scale considers the presence of 4 clinical data (Speech Alteration, Eye Deviation, Automatism, and Number of Seizures) to predict the risk of the patient being in SE [9, 10]. All patients were evaluated by specialist neurologists, and data registry was completed by these same professionals consecutively.

SE diagnosis was done by neurologists, according to clinical [2] and EEG criteria [3] Patient treatment was decided by emergency doctors, neurologists, and intensive care physicians, who requested the EEG acquisition and determined the escalation of therapy, including pharmacological sedation and intubation. Both centers used the same treatment protocols as recommended by the Catalan Neurology Society [13].

EEG was conducted on all patients using the 10/20 international system with a minimum duration of 30 min. The EEG findings were described according to the glossary of the International Federation of Clinical Neurophysiology and the Standardized Terminology for Critical Care EEG of the American Clinical Neurophysiology Society [3, 14]. Urgent

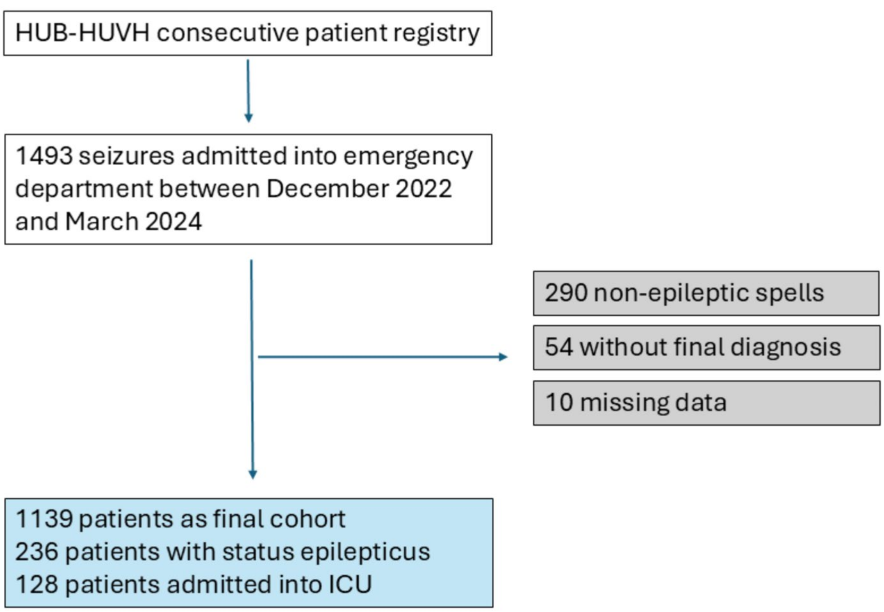

FIGURE 1 | Study flowchart. HUB, Hospital Universitari Bellvitge; HUVH, Hospital Universitari Vall Hebrón.

EEGs were available from 8:00am to 3:00pm Mondays to Fridays at HUB, and from 8:00am to 8:00pm every day at HUVH. We recorded whether patients arrived at the ED during these periods of EEG availability.

The registry was approved by the ethics committee of both centers (ReCU-2024.1; PR(AG)429/2024 and PR143/24).

For statistical analysis, IBM SPSS Statistics 25.0 software was used. Categorical variables were expressed as the number of cases (percentage) and numerical variables as the mean (standard deviation) or median (interquartile range [IQR]) in case they did not meet normality criteria (Q-Q plot). Characteristics associated with the diagnosis of SE and ICU admission were evaluated using Pearson's chi-square test or Fisher's exact test for categorical variables, the linear trend chi-square test for ordinal variables, the Student's *t*-test for age comparison, and the Mann–Whitney i test for other numerical variables. Adjusted logistic regression models were performed to identify variables independently associated with SE diagnosis and ICU admission. A *p*-value of less than 0.05 was considered statistically significant.

3 | Results

3.1 | Cohort Characteristics

In the registry, a total of 1493 episodes of urgent care for suspected epileptic seizures were included. Of these, 64.3% of cases arrived at the ED through pre-hospital care; 17.9% arrived by their own means, and 11% were referred from another hospital or primary care center. From the global sample, 19.6% (290 cases) were non-epileptic episodes, 3.6% (54 cases) had no recorded diagnosis, and 0.6% (10 cases) were not correctly recorded; these cases were not analyzed. Finally, from a sample of 1139 cases, 236 patients (20.71%) were diagnosed with SE in the ED. Additionally, 128 patients (11.23%) required ICU admission. For the global characteristics of the sample, see Figure 1 and Table 1.

TABLE 1 | Descriptive variables for the final sample.

Variables	$N = 1493$
Sex	
Male	789 (52.8%)
Age, mean ± SD (range)	58.4 ± 20.6 (16–98)
Previous Rankin, median (IQR)	1 (0–3)
Patient arrival method	
EMS	960 (64.3%)
Own means	267 (17.9%)
Other hospitals	153 (10.2%)
Primary care	12 (0.8%)
Not specified	101 (6.8%)
Pre-hospital treatment ($n = 809$)	
Benzodiazepines	65 (9.5%)
Antiseizure medications	14 (2.0%)
Orotracheal intubation	60 (8.8%)
No treatment	545 (79.7%)
ADAN scale, median (IQR)	1 (0–2)
Seizure – EMS time (min), median (IQR)	40 (15–244)
EMS – admission time (min), median (IQR)	50 (37–71)
Seizure – EEG time (hours), median (IQR)	19.0 (11.4–26.8)
Final diagnosis ($n = 1483$)	
Acute symptomatic seizure	145 (9.8%)
Epilepsy	575 (38.8%)
First unprovoked seizure	183 (12.3%)
Status epilepticus	236 (15.9%)
Non-epileptic paroxysmal episode	290 (19.6%)
Unknown	54 (3.6%)

Abbreviations: EEG, electroencephalogram; EMS, extra-hospital medical service; IQR, interquartile range; Min, minutes; SD, standard deviation.

3.2 | Prehospital Delays

Regarding pre-hospital time frames, the median time between the seizure and the EMS 112 call was 40 min (IQR 15–244 min); the median timelapse between EMS activation and ED admission was 50 min (IQR 37–71 min), and the global time between the seizure onset and the EEG acquisition was 19 h (IQR 11.4–26.8 h) (Figure 2A).

In patients with a final diagnosis of SE, a longer time was observed between EMS activation and commute to the ED compared with non-SE patients (55 vs. 48 min $p = 0.040$). No differences were observed between the time from seizure to EMS activation, nor between seizure onset and EEG. Patients with a final diagnosis of SE received more pre-hospital treatment ($p < 0.001$) and were older ($p < 0.001$). In patients with a final diagnosis of SE, the ADAN scale score was higher ($p < 0.001$) (see Table 2), Figure 2A). We conducted a logistic regression analysis including time from EMS activation to ED admission, age, previous mRS, and pre-hospital treatment. Only pre-hospital treatment showed a significant association with SE diagnosis (OR = 4.78, 95% CI: 2.57–8.67, $p < 0.001$).

In patients requiring ICU admission, there was a longer transfer time from EMS to the emergency department (69 vs. 46.5 min, $p < 0.001$) and a longer time from seizure onset to EEG performance (22.1 vs. 16.5 h, $p < 0.001$). It was also observed that patients requiring ICU admission had a higher ADAN score ($p < 0.001$) and had received more pre-hospital treatment ($p < 0.001$) (see Table 3).

Finally, a logistic regression including time from EMS activation to ED admission and timelapse from seizure onset to EEG,

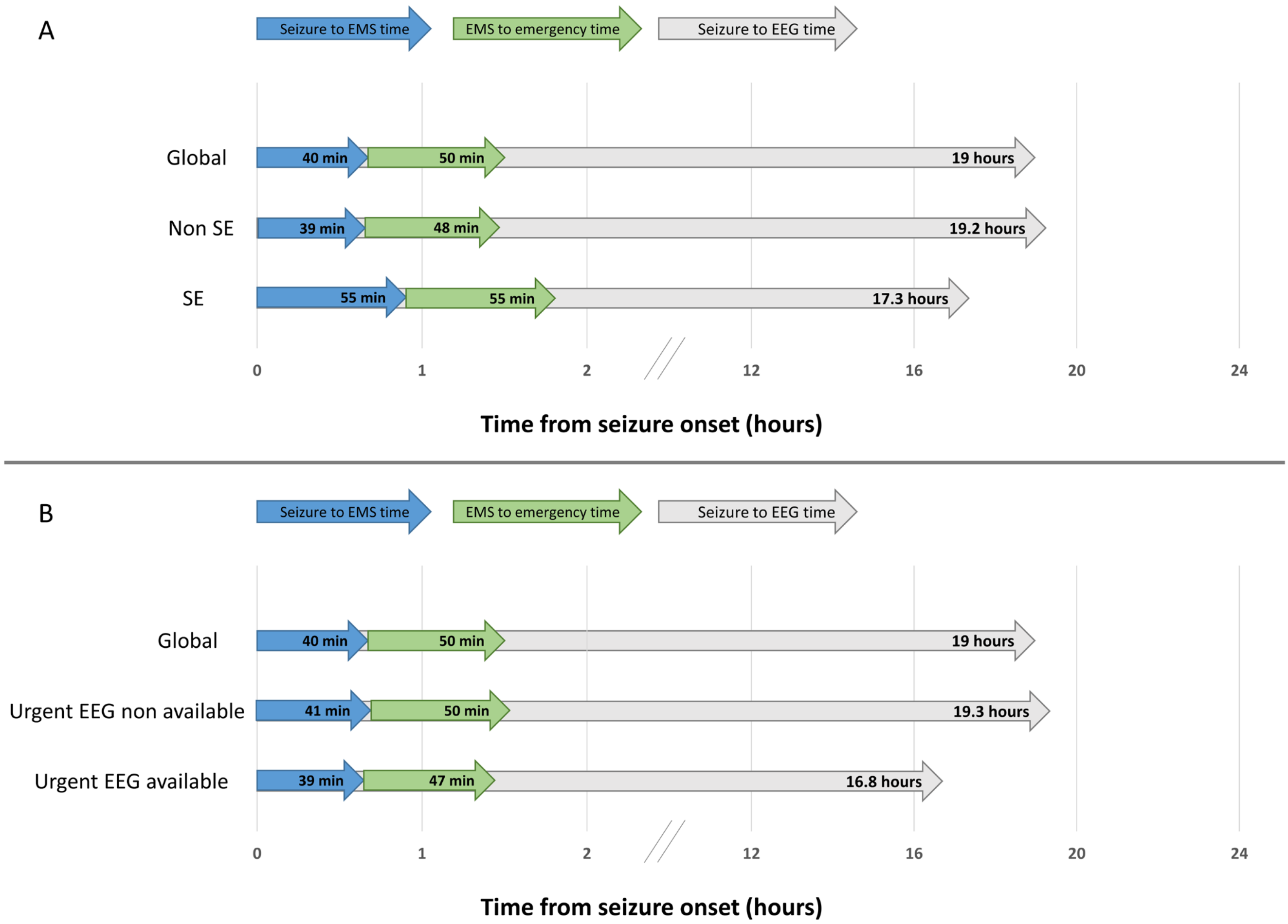

FIGURE 2 | Care delivery mean times according to the final diagnosis of SE and based on EEG availability. In the upper section (A), differences in care times are reported between the overall sample and the final SE diagnosis groups; prehospital care and transport times were significantly longer. In the lower section (B), care times are reported based on EEG availability. For patients arriving when EEG was unavailable, significantly longer delays in acquisition were observed, along with a higher proportion of patients requiring ICU admission. EEG, electroencephalogram; EMS, extra-hospital medical service; SE, status epilepticus.

pre-hospital treatment, age and mRS was performed. We found that the longer time between EMS activation to ED admission (OR = 4.95, 95% CI: 2.38–10.3, $p < 0.001$), between seizure onset and EEG acquisition (OR = 5.05, 95% CI: 2.39–10.68, $p < 0.001$), and the administration of prehospital treatment (OR = 18.97, 95% CI: 8.62–41.75, $p < 0.001$) were significantly associated with increased ICU admissions.

3.3 | EEG Availability

To assess the impact of EEG availability, times were compared according to whether the EEG was available at patient arrival. Overall, the proportion of patients that required ICU admission was higher when EEG was not available (15.3% vs. 7.4%, $p < 0.001$, Table 3). For patients arriving within EEG availability, no differences in EEG access times were observed depending on ICU admission requirement. In contrast, for patients admitted during EEG unavailability, access to EEG was significantly delayed for those admitted in the ICU compared to those who did not require ICU (22.8 vs. 17.4 h, $p < 0.001$) (Figure 2B, Table 3, Figure 3). In a logistic regression model adjusted for age, baseline functional status (mRS), and prehospital treatment, timelapse to EEG (OR = 4.59, 95% CI: 2.28–9.22, $p < 0.001$) and prehospital treatment were risk factors for ICU admission (OR = 24.5, 95% CI: 11.87–50.57, $p < 0.001$).

3.4 | Clinical Characteristics

Upon arrival at the ED, ADAN scale scores were analyzed for all patients. Scores > 2 showed an association with a final diagnosis of SE ($p < 0.001$), while scores ≤ 2 were significantly associated with absence of SE ($p < 0.001$; Table 2). However, no differences in the time frame of delivery of care were observed between patients stratified by ADAN score and final SE diagnosis.

We analyzed patients presenting with two or more motor seizures in the 12 h prior to consultation, as this variable is included in the ADAN score and might serve as a surrogate marker for seizure clustering. Based on this definition, we identified 194 patients (17%) from our cohort that would classify as having seizure clusters. These patients had longer commute to hospital (EMS call-to-admission times, $p < 0.004$), but this finding was not significant ($p = 0.208$) when adjusted by pre-hospital treatment, age and mRs.

TABLE 2 | Demographic and delivery of care timings in patients with Status epilepticus as final diagnosis compared to patients without Status epilepticus.

Variables	No SE ($n=903$)	SE ($n=236$)	p
Sex, male	662 (52.7%)	127 (53.8%)	0.867
Age, mean ± SD	57.4 ± 21.0	63.7 ± 17.2	< 0.001
Previous diagnosis of epilepsy	341 (36.3%)	81 (39.7%)	0.357
Previous mRs, median (IQR)	1 (0–2)	1 (1–3)	< 0.001
Pre-hospital treatment	81 (15.0%)	58 (40.6%)	< 0.001
Pre-hospital treatment			
Benzodiazepines	35 (6.5%)	30 (21.0%)	< 0.001
Antiseizure drugs	7 (1.3%)	7 (4.9%)	< 0.001
Orotracheal intubation	39 (7.2%)	21 (14.7%)	< 0.001
None	460 (85.0%)	85 (59.4%)	< 0.001
ADAN scale—median (IQR)			
Low risk (0–1)	618 (49.2%)	11 (4.7%)	< 0.001
Moderate (2)	356 (28.3%)	32 (13.6%)	< 0.001
High risk (> 2)	283 (22.5%)	193 (81.8%)	< 0.001
Seizure to EMS time, minutes—median (IQR)	39 (15–220)	55 (14–283)	0.625
EMS to admission time, minutes—median (IQR)	48 (37–70)	55 (40–80)	0.040
Seizure to EEG time, hours—median (IQR)	19.2 (11.8–26.8)	17.3 (8.0–26.9)	0.148
Available EEG			
Seizure to EEG time, hours, median (IQR)	17.5 (4.6–25.3)	8.5 (4.7–20.7)	0.193
Unavailable EEG			
Seizure to EEG time, hours, median (IQR)	19.5 (14.0–30.3)	19.0 (13.7–28.6)	0.867

Abbreviations: EEG, electroencephalogram; EMS, extra-hospital medical service; IQR, interquartile range; mRs, modified Rankin scale; SD, standard deviation; SE, status epilepticus.

4 | Discussion

In our data registry, delays at key points in the management of urgent seizures were associated with clinically relevant outcomes. Patients with SE experienced longer commute times, likely reflecting the need for prehospital treatment. Moreover, prolonged transport duration, prehospital medication administration, and delayed EEG acquisition were all independently associated with increased ICU admission.

In acute seizures and SE, the timely administration of antiseizure medication at appropriate doses is crucial for favorable clinical outcomes. Delays in hospital arrival and treatment delivery, which are often correlated, have been reported to impact seizure duration, and proposed to be a key modifiable factor in the development and outcome of SE [15, 16]. In a recent analysis of the published evidence from multiple studies [11], the mean time to first ASD administration was 42.4 min for patients with SE and 40.2 min for patients with epileptic seizures. The mean reported time from the onset of SE to the arrival of pre-hospital services was 22 min, and to hospital arrival was 56 min. Delays in prehospital treatment were common and multifactorial; 12.8% of patients were treated by their families/caregivers, while 51.8% were treated by pre-hospital services. Data from a more recent multicenter registry again emphasize the time to treatment as a key factor in the management of SE with motor symptoms [17]. It has also been observed that response times to seizures can exceed the recommended time window for initiating treatment, indicating a structural problem in the care of these patients [7].

While most studies focus on treatment administration timelines, our work assesses activation times, hospital transport logistics, and EEG access time not only in SE patients but also in those with suspected acute seizure emergencies. Our case series identifies prehospital transport delays and delayed EEG acquisition as factors associated with both the diagnosis of SE and the need for ICU admission.

In the initial phase of prehospital emergency medical services activation, our case series demonstrates data consistent with prior studies, albeit with moderately prolonged delays [11]. Our analysis revealed no significant differences between final clinical diagnoses and prehospital activation intervals. This finding is likely attributable to public recognition of epileptic seizures or acute neurological impairment scenarios prompting timely emergency activation.

TABLE 3 | Demographic and delivery of care timings in patients requiring ICU admission.

Variables	No ICU (n = 1011)	ICU (n = 128)	p
Sex, male	541 (53.5%)	72 (56.3%)	0.558
Age, mean ± SD	57.8 ± 21.4	55.1 ± 15.8	0.087
Previous epilepsy	352 (40.7%)	32 (35.2%)	0.306
Previous mRs, median (IQR)	1 (0–3)	1 (0–2)	0.001
Pre-hospital treatment	54 (13.0%)	57 (69.5%)	< 0.001
Pre-hospital treatment			
Benzodiazepines	41 (9.9%)	15 (18.3%)	< 0.001
Antiseizure drugs	8 (1.9%)	5 (6.1%)	< 0.001
Orotracheal intubation	5 (1.2%)	37 (45.1%)	< 0.001
None	362 (87.0%)	25 (30.5%)	< 0.001
ADAN scale, median (IQR)			
Low risk (0–1)	447 (44.2%)	21 (16.4%)	< 0.001
Moderate (2)	246 (24.3%)	19 (14.8%)	< 0.001
High risk (> 2)	318 (31.5%)	88 (68.8%)	< 0.001
Seizure to EMS time, median (IQR)	31 (13–100)	23.5 (12–97)	0.412
EMS to admission time, median (IQR)	46.5 (36–65.5)	69 (54–140)	< 0.001
Seizure to EEG time, median (IQR)	16.5 (8.0–23.0)	22.1 (12.2–33.7)	< 0.001
Arrival with EEG availability			
Seizure to EEG time, hours, median (IQR)	9.5 (4.5–22.7)	8.5 (4.7–20.7)	0.730
Arrival without EEG availability			
Seizure to EEG time, hours, median (IQR)	17.4 (11.6–23.3)	22.8 (16.0–38.0)	< 0.001

Abbreviations: EEG, electroencephalogram; EMS, extra-hospital medical service; ICU, intensive care unit; IQR, interquartile range; mRs, modified Rankin scale; SD, standard deviation.

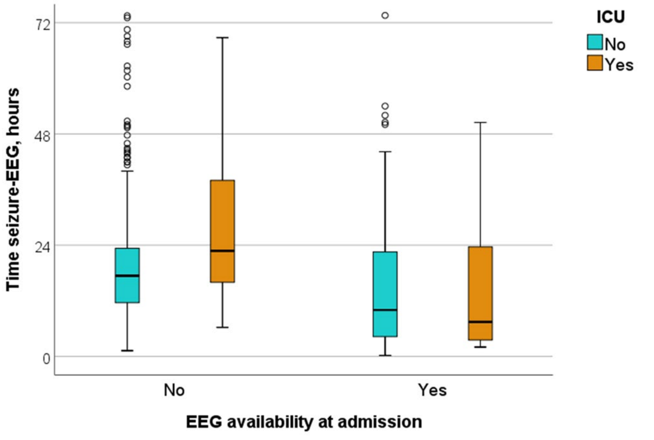

FIGURE 3 | Association between seizure-to-EEG time, EEG availability, and ICU admission. A significant relationship was observed between longer seizure-to-EEG intervals and ICU admission, specifically in patients who arrived during hours when EEG was not available. ICU, intensive care unit.

Pre-Hospital treatment and hospital transfer intervals demonstrated significant differences in both final diagnosis of SE and ICU admission requirements. Particularly, a definitive SE diagnosis was associated with pre-hospital treatment administration. Furthermore, pre-hospital treatment administration and transport time were both independently related to ICU admission. The administration of prehospital treatment in suspected SE cases is imperative, but it probably needs to be alongside optimizing prehospital diagnostic tools and prioritizing expedited referral for specialist evaluation [8]. In our setting, out-of-hospital seizure calls are initially attended by a basic, non-medical ambulance with limited treatment capabilities. When a pharmacological intervention is required, a second, medically equipped unit must be dispatched, which may contribute to significant delays in treatment delivery and transport. In this context, accurate prehospital risk stratification could enhance resource allocation and response efficiency, particularly in high-prevalence conditions such as epileptic seizures. In the current scenario, the need for use of pre-hospital medications may serve as an alert to consider those patients at risk of SE, likely requiring ICU admission. Also, validated clinical tools such as the ADAN scale may facilitate prehospital triage prioritization.

Finally, prolonged EEG acquisition intervals demonstrated a statistically significant association with increased ICU admission requirements, specifically when patients arrived outside

EEG availability hours. EEG remains a critical diagnostic and therapeutic tool in managing acute seizure emergencies, enabling tailored pharmacological management and preventing unnecessary overtreatment [18] Furthermore, patients presenting outside urgent EEG availability windows exhibited higher ICU admission rates, with this subgroup demonstrating the most pronounced disparities in EEG acquisition times. These findings suggest that implementing urgent EEG accessibility protocols in such cases could mitigate ICU admission rates by facilitating timely clinical decision-making, optimizing therapeutic management, and potentially reducing treatment aggressiveness. Importantly, the association between seizure-to-EEG timelapse and ICU admission was only observed during the EEG off-time, revealing the impact of this tool. However, there is a potential selection bias that may reflect systemic constraints rather than clinical decision-making, and this should be clarified with further prospective studies.

Notably, despite advances in evidence-based treatment and diagnostic approaches for SE, mortality rates have shown no significant improvement in recent years. While this trend may be multifactorial, delays in prehospital activation and acute care intervals emerge as a key modifiable determinant [19]. The implementation of standardized seizure management protocols to optimize response timelines may provide enhanced therapeutic efficacy, reinforcing the adage 'time is brain' in acute seizure emergencies and SE management [20, 21]. Our study aims to establish a systematic registry of acute seizure care timelines within our clinical setting, identifying critical junctures to refine acute-phase management. Distinct temporal demarcation of intervention phases is imperative, as each requires a tailored quality improvement strategy. Based on our findings, integrating prehospital risk stratification, expedited transfer protocols for high-risk patients (e.g., high ADAN scale scores), and rapid EEG acquisition could reduce SE incidence, ICU admission requirements, and hopefully associated complications.

Key limitations of our study include the absence of seizure etiology stratification—a critical determinant of therapeutic management and prognostic outcomes—and its exclusive focus on adult populations, thereby precluding generalizability to pediatric cohorts. Additionally, SE semiology, a potential independent confounding variable, was not analyzed, nor were seizure clusters, which were not explicitly defined or recorded as a separate outcome in our registry. As such, any inference regarding clustering must be interpreted with caution. Moreover, EEG findings were not structured in the data collection form, so we were unable to assess their influence in clinical decision-making or outcomes. Lastly, while clinical protocols were uniformly followed, the specific antiseizure medications administered were not documented in our registry.

Nevertheless, this work provides a comprehensive registry of acute seizure care activation timelines, underscoring the critical implications of care delays. These findings aim to inform quality improvement initiatives and standardized protocols for acute seizure management, with the goal of optimizing resource allocation and timely intervention in SE-risk scenarios and ICU management optimization.

5 | Conclusion

Delivery of care timelines in seizure emergency management are critical. The use of pre-hospital medication, longer commute to hospital, and delayed EEG acquisitions are risk factors associated with SE and ICU admission.

Author Contributions

Jacint Sala-Padró and Elena Fonseca contributed equally to the conception, design, data acquisition, analysis, and drafting of the manuscript and are recognized as co-first authors. All remaining authors contributed equally to the interpretation of data, critical revision of the manuscript for important intellectual content, and approved the final version for submission.

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The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data supporting the findings of this study are not publicly available due to privacy and ethical restrictions but can be obtained from the corresponding author upon reasonable request.

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