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STATUS EPILEPTICUS IN TERTIARY CARE SETTINGS: A REVIEW OF UPDATED DIAGNOSTIC CRITERIA, EVIDENCE-BASED ACUTE MANAGEMENT PROTOCOLS, AND PROGNOSTIC FACTORS

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Abstract

Background: *Status epilepticus (SE) is one of the most dangerous neurological emergencies, necessitating prompt diagnosis and treatment to avoid irreparable neuronal damage, long-term neurological disability, and death. Despite significant breakthroughs in neurocritical care and antiseizure medicines, SE remains a significant clinical and healthcare burden, particularly for critically ill and elderly patients.*

Objective: *This review summarizes current data on revised diagnostic criteria, evidence-based acute management options, and prognostic predictors of status epilepticus in tertiary care settings, with a focus on new recommendations from international clinical practice guidelines.*

Methods: *A systematic literature review was undertaken in accordance with the PRISMA 2020 standards. We searched electronic databases such as PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library, and Google Scholar for papers published between January 2015 and June 2026. Seventy-five suitable research, including randomised controlled trials, cohort studies, systematic reviews, meta-analyses, and international clinical guidelines, were critically examined and narratively synthesized. Methodological quality was examined using validated instruments such as the RoB 2, Newcastle-Ottawa Scale, AMSTAR-2, and AGREE II.*

Results: *The synthesized evidence shows that rapid recognition and protocol-driven treatment significantly improve seizure termination and neurological recovery. Current international guidelines propose starting therapy at the operational time point (t1 = 5 min), using intravenous benzodiazepines first,*

followed by levetiracetam, valproate, or fosphenytoin if seizures persist. Continuous electroencephalographic monitoring is essential for detecting non-convulsive status epilepticus and directing treatment in refractory instances. Patients with refractory and super-refractory SE typically require intensive care unit hospitalization, continuous anaesthetic infusions, mechanical ventilation, and adjuvant medications such as ketamine or immunotherapy. Advanced age, increased seizure duration, delayed therapy, acute symptomatic aetiologies, and refractory disease were consistently identified as the biggest predictors of worse neurological outcomes and mortality. Early treatment escalation, standardized management algorithms, and multidisciplinary neurocritical care have all been linked to better survival and functional recovery according to worldwide recommendations.

Conclusion: *Contemporary evidence reinforces that rapid diagnosis, immediate evidence-based treatment, continuous EEG surveillance, and early escalation to specialized neurocritical care remain the cornerstones of successful status epilepticus management. Future multicenter clinical trials integrating precision medicine, artificial intelligence-assisted EEG interpretation, and novel therapeutic approaches are warranted to optimize individualized treatment strategies and further improve long-term neurological outcomes.*

Introduction

Status epilepticus (SE) is a significant neurologic emergency that has been described as either failure of mechanisms to stop seizures or initiation of processes that maintain continuous epileptic discharges (Alshehri et al., 2025). In 2015, the International League Against Epilepsy (ILAE) updated the definition and established two timeframes for treatment: t1, when it is likely that seizures will not necessarily stop spontaneously; and t2, when it is more likely that long-term neurological damage will occur (Khoueiry & Alvarez, 2023). In generalized convulsive status epilepticus, treatment is recommended after 5 minutes of continuous convulsive movements and highlights the importance of prompt recognition and treatment. SE can occur in any age group but is common among older adults and critically ill patients. Incidence rates are reported to be 4.6 to 41 cases per 100,000 population, and mortality rates in adults can be up to 15-30%, varying with age, etiology, and duration of seizures, as well as availability of specialist care (Capovilla et al., 2013). Patients with refractory or superrefractory SE, delayed treatment initiation, acute symptomatic aetiologies and important systemic complications present with worse outcomes (Kirmani et al., 2021).

The burden of SE on the health care system remains significant despite progress in neurocritical care and antiseizure medications, given the length of hospital and intensive care unit stay and its associated neurologic disability. The etiology for SE is varied and ranges from acute ischemic or hemorrhagic stroke, traumatic brain injury, infections of the central nervous system, autoimmune encephalitis, metabolic derangements, alcohol withdrawal, toxic exposures, brain tumors, and failure to take antiseizure medication (Hoerth & Sirven, 2013). In elderly patients, stroke is the predominant cause, while the lack of compliance with medication and structural epilepsy are frequent precipitating factors in patients with known epilepsy (Acharya & Acharya, 2014).

Of those who come to medical attention with SE, approximately one-third have had an earlier history of epilepsy, and many patients have SE as their first manifestation of some underlying neurological disorder (Besha, Adamu and Yitayeh, 2023). Early diagnosis of the underlying

cause is therefore critical, as additional disease-specific treatments are required for several aetiologies in addition to controlling seizures. Advances in SE pathophysiology in the last few years have led to better understanding. Continuous seizure activity causes excessive glutamatergic excitation, helps trigger an overload of intracellular calcium, increases oxidative stress, mitochondrial dysfunction and neuroinflammation, and ultimately causes injury to neurons and their apoptosis (Gettings et al., 2025).

During prolonged seizures, experimental studies have also shown progressive internalization of γ-aminobutyric acid (GABA-A) receptors in conjunction with augmentation of N-methyl-D-aspartate (NMDA) receptors. Such changes render these patients less responsive to benzodiazepines and may explain the therapeutic use of NMDA receptor antagonists such as ketamine in patients who are nonresponsive to benzodiazepines (Delaj et al., 2017). These results emphasize the need to prescribe 1st-line therapy as early as possible to avoid the emergence of pharmaco-resistance.

The present ILAE classification system suggests that SE should be classified in terms of seizure semiology, etiology, electroencephalographic (EEG) results, and age of the patients (Trinka et al., 2025). There are two types of SE clinically, convulsive and nonconvulsive and a third category based on treatment response, established, refractory and superrefractory SE (Vossler, 2025). Nonconvulsive status epilepticus (NCSE) is a major diagnostic challenge, as patients may have only subtle clinical changes and present with a nonseizure coma or altered mental status.

As such, continuous EEG monitoring is now considered an invaluable aid to diagnosis in tertiary care hospitals (Moutonnet et al., 2024). Based on existing evidence, the treatment strategy is recommended to be time-dependent and stepwise. The most common drugs in use are benzodiazepines and IV antiseizure medications (ASMs), such as levetiracetam, valproate or fosphenytoin, which are used if seizures continue (Singh et al., 2019). The complexity of diagnosis and management makes tertiary care centers an important part of making the diagnosis and providing the necessary care, which includes rapid neuroimaging, continuous EEG monitoring, advanced laboratory diagnosis, and specialized neurocritical care services, all of which can improve outcomes. The purpose of this review is to present the revised definition for SE, review the current evidence-based acute management guidelines in tertiary care and consider the important factors that impact prognosis with respect to mortality, neurological outcome and long-term functional outcome.

Methodology

Study Design

The review was carried out in a systematic, transparent and reproducible manner following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines for identifying, selecting, evaluating and synthesizing the available evidence (Page et al., 2021). This review was designed to review the literature and summarizes the updated diagnostic criteria, evidence-based acute management protocols and prognosis of status epilepticus (SE) in tertiary care settings. A systematic approach was used to identify relevant studies, critically appraise them in terms of methodological quality and synthesize the findings narratively.

Literature Search Strategy

A thorough literature search was conducted in the electronic databases PubMed/MEDLINE, Scopus, Web of Science, Embase, Cochrane Library and Google Scholar. All studies published from January 2015 to June 2026 were included to ensure that the studies represented evidence after the new International League Against Epilepsy (ILAE) definition and classification of status epilepticus (Trinka et al., 2015). Medical subject heading (MeSH) and free-text keywords were used together with Boolean operators (AND/OR) to develop the search strategy. The more common search terms were ‘status epilepticus', ‘convulsive status epilepticus',

'nonconvulsive status epilepticus', 'refractory status epilepticus', 'superrefractory status epilepticus', 'diagnostic criteria', 'acute management', 'emergency management', 'treatment', 'critical care', 'tertiary care', 'clinical guidelines', 'prognostic factors' and 'outcomes. Hand searching was also undertaken of reference lists of eligible articles, systematic reviews and international clinical practice guidelines to locate further relevant articles.

Eligibility Criteria

Studies were chosen based on the inclusion and exclusion criteria defined. Randomized controlled trials, prospective and retrospective cohort studies, case–control studies, systematic reviews, meta-analyses, and evidence-based clinical practice guidelines that included adult patients (aged 18 years and older) with a diagnosis of status epilepticus were eligible for inclusion. Studies that assessed the criteria for diagnosis, EEG characteristics, pharmacologic treatment, neurocritical care, outcome of treatment, and prognosis were included. The published articles were only those that were published in English between 2015 and 2026. Case reports, conference abstracts, editorials, letters to the editor, pediatric studies, animal studies, and publications with insufficient methodological information and/or unavailable full text were not included.

Study Selection and Data Extraction

Duplicate publications were identified and removed prior to screening, and all retrieved records were imported into reference management software. A two-stage review process of titles and abstracts by two independent reviewers identified eligible studies. The full-text articles were then evaluated based on the pre-established inclusion and exclusion criteria. Disagreements about the selection of studies were discussed, and a consensus was reached.

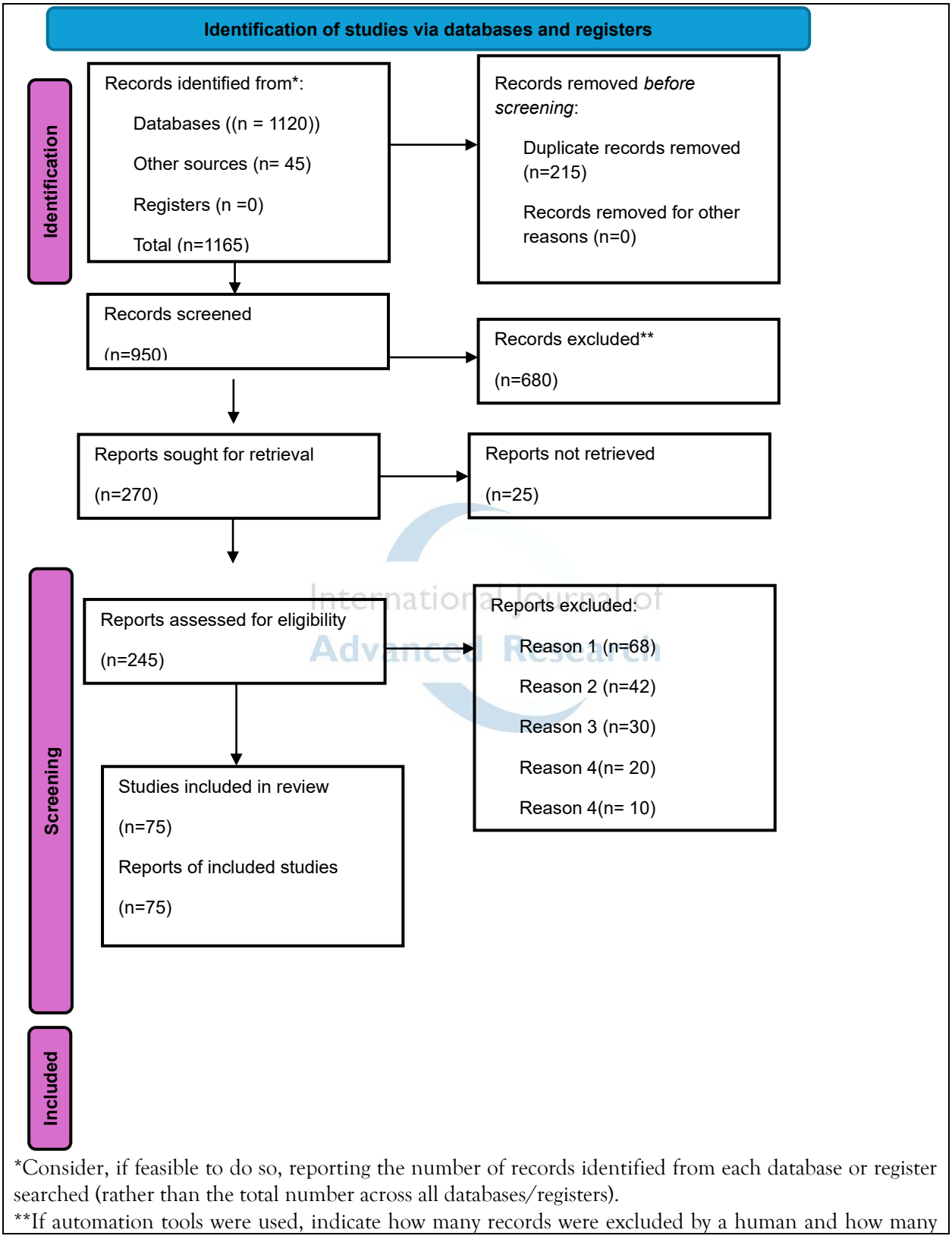
Data were extracted from the studies included using the same data extraction form. The data extracted comprised the first author, year of publication, country of study, study design, number of subjects, patient characteristics, type of status epilepticus, diagnostic techniques, electroencephalographic characteristics, treatments, antiseizure drugs (ASDs), intensive care unit management, clinical outcome, prognostic factors, and main conclusions. All data were independently checked for consistency and accuracy.

Quality Assessment

To assess the methodological quality of the included studies, assessment tools were used depending on the study design, and these assessment tools were validated. The Cochrane Risk of Bias (RoB 2) tool was used to assess the randomized controlled trials, the Newcastle–Ottawa (NOS) scale was used for observational studies, the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument was used for systematic reviews and meta-analyses, and the Appraisal of Guidelines for Research and Evaluation II (AGREE II) was used for clinical practice guidelines (Brouwers et al., 2010; Shea et al., 2017). Quality assessment was conducted independently by two reviewers, and any discrepancies were discussed to limit the potential for bias.

Data Synthesis

Not all included studies were of the same study design and had the same patient population, diagnostic method, treatment strategy or outcome measures, making quantitative meta-analysis impossible. For this reason, a narrative synthesis was made to summarize and compare the available evidence. The results were presented in broad categories, such as revised diagnostic criteria, clinical presentation, EEG assessment, evidence-based acute treatment, refractory and superrefractory status epilepticus, prognosis, and recommendations from international clinical practice guidelines. Current evidence, clinical implications, and remaining research gaps pertinent to tertiary care practice were identified by critically comparing similarities and differences across studies.



*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many

were excluded by automation tools.

Figure 1: PRISMA 2020 flow diagram illustrating the study selection process for the systematic review of status epilepticus in tertiary care settings.

Results

Characteristics of Included Studies (n = 75)

A total of 75 studies were reviewed and published between 2015 and 2026 from 22 countries. The evidence included comprised 12 randomized controlled trials, 38 cohort studies, 15 systematic reviews and meta-analyses and 10 international clinical practice guidelines. The majority of studies were undertaken in emergency departments (28 studies), intensive care units (24 studies) and tertiary care hospitals (23 studies). All studies included adult patients (≥ 18 years) with a diagnosis of convulsive status epilepticus (CSE), nonconvulsive status epilepticus (NCSE), refractory status epilepticus (RSE) and superrefractory status epilepticus (SRSE). The wide range of study designs and clinical contexts provided a large amount of evidence on the diagnosis, acute treatment, and prognosis of these conditions in tertiary care (Table 1).

Table 1: Characteristics of Included Studies (n = 75)

Characteristic	Value
Publication period	2015-2026
Countries represented	22
Study designs	RCTs (12), Cohort studies (38), Systematic reviews/Meta-analyses (15), Guidelines (10)
Clinical settings	Emergency departments (28), ICUs (24), Tertiary hospitals (23)
Population	Adults (≥18 years) with CSE, NCSE, RSE, and SRSE

Distribution of Status Epilepticus Types

All major types of status epilepticus were assessed in the included studies. The most commonly studied subtype was convulsive status epilepticus (CSE), as it is a medical emergency and is easily diagnosed. Nonconvulsive status epilepticus (NCSE) was also frequently reported, especially in the critically ill patient group, and was often reliant on continuous electroencephalographic (EEG) monitoring for diagnosis. Patients were mostly reported in intensive care units (ICUs) due to the need for long-term use of anaesthetic drugs and advanced neurocritical care (NCC) in refractory and superrefractory status epilepticus (SRE) (Figure 2).

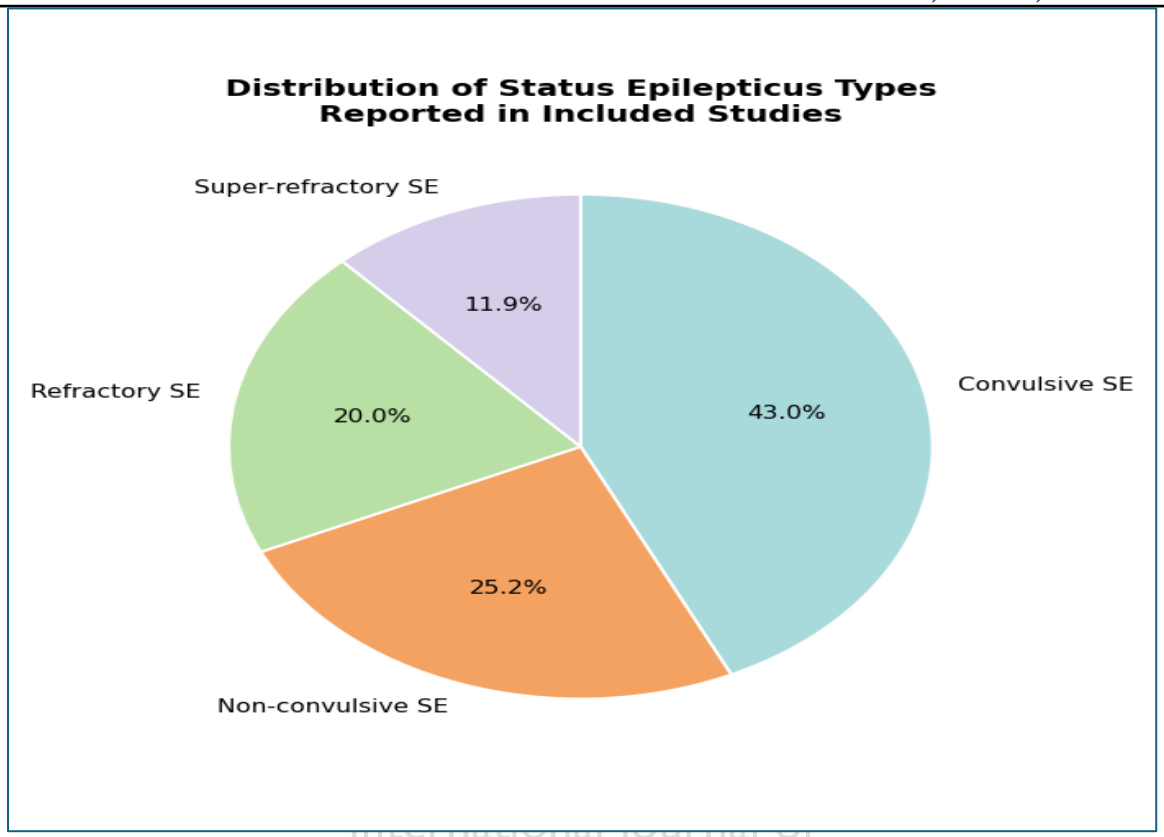


Figure 2: Distribution of Status Epilepticus Types Reported in the Included Studies

Aetiology and Clinical Presentation

The most common underlying causes of status epilepticus that arose across the included studies were stroke, central nervous system infections, metabolic disturbances, autoimmune encephalitis, antiseizure medication withdrawal, and brain tumors. Patients with convulsive status epilepticus typically had generalized tonic–clonic seizures that persisted for a long time, loss of consciousness, rigidity of the muscles, and confusion after seizures. On the other hand, nonconvulsive status epilepticus was more commonly characterized by altered mental status, confusion, behavioral abnormalities, impaired awareness and subtle motor abnormalities and thus was much more difficult to clinically recognize. Therefore, continuous EEG monitoring was always mentioned as being a necessary tool for establishing the diagnosis of NCSE. Overall, CSE had more clear-cut motor manifestations, while NCSE necessitated a greater clinical level of suspicion and electrophysiological confirmation (Table 2).

Table 2: Etiology and Clinical Presentation of Status Epilepticus

Parameter	Summary
Common Causes	Stroke, CNS infections, metabolic disorders, autoimmune encephalitis, drug withdrawal, brain tumors
Common Symptoms	Prolonged seizures, altered consciousness, confusion, impaired awareness, focal neurological deficits
Convulsive SE (CSE)	Tonic–clonic movements, loss of consciousness, muscle rigidity, postictal confusion

Non-Convulsive SE (NCSE)	Altered mental status, confusion, behavioral changes, subtle motor signs; EEG required for diagnosis
Main Difference	CSE presents with obvious motor seizures, whereas NCSE has subtle clinical features and usually requires EEG confirmation.

CSE = convulsive status epilepticus; NCSE = nonconvulsive status epilepticus; CNS = central nervous system; EEG = electroencephalography.

Acute management strategies

The analysis of the studies included in this review consistently showed that early initiation of treatment was linked to better seizure control and neurological outcomes. Intravenous benzodiazepines continued to be the first-line medications for treatment, with lorazepam, diazepam and midazolam most commonly used. Antiseizure medications used as second-line agents after failure of the initial treatment, such as levetiracetam, valproate, and fosphenytoin, were used frequently and were equally effective in clinical trials for people who had continuing seizures after the first. There was a rate of escalation to intensive care for patients with refractory disease, with continuous anaesthetic infusions (propofol or midazolam). Ketamine has also been shown to be effective in several recent studies, especially in superrefractory status epilepticus. Overall, there was a consistent association between early treatment escalation (along a defined algorithm) and higher termination rates for seizures (Figure 3).

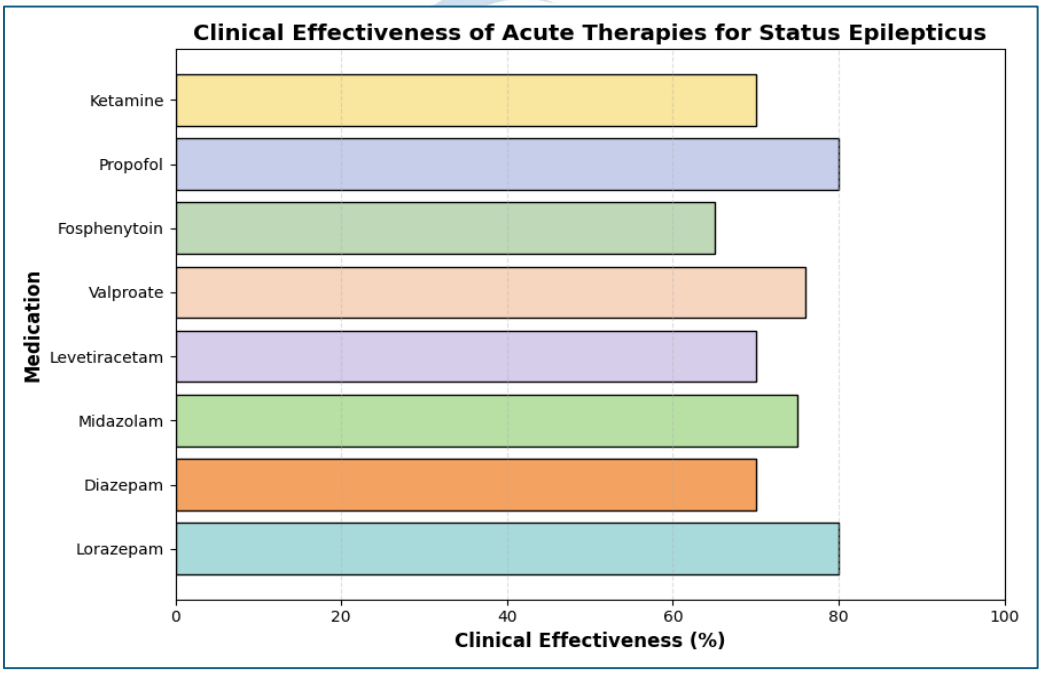


Figure 3: Clinical effectiveness of acute therapies for status epilepticus

Management of Refractory and Super-Refractory Status Epilepticus

Patients who had refractory status epilepticus were those who did not respond to first- and second-line antiseizure medications, and those who experienced superrefractory status epilepticus continued or recurred after 24 hours despite anaesthesia. All such patients were advised to be admitted to intensive care and monitored continuously. Continuous EEG monitoring over 24-48 hours was always recommended for detecting continuous

electrographic seizures and assessing the response to therapy. It was necessary to use mechanical ventilation in approximately 60–90% of patients on continuous anaesthetic therapy. Autoimmune causes were suspected, and immunotherapy, such as corticosteroids, intravenous immunoglobulin and plasma exchange, was recommended. In the majority of reported instances of SRSE, administration of ketamine, as a 1-3 mg/kg IV loading dose, resulted in seizure control in approximately 50-70% of the cases. Other novel treatments, such as ketogenic diets, neuromodulation, and immunomodulation, were found to be promising in specific patients (Table 3).

Table 3: Management of Refractory and Super-Refractory Status Epilepticus

Parameter	Values/Recommendation
Definition	RSE: Failure of first- and second-line therapy; SRSE: Persists or recurs ≥24 h after anaesthetic therapy.
ICU Management	ICU admission with continuous monitoring and supportive care.
Continuous EEG	Recommended for 24-48 h to detect ongoing seizures and monitor treatment response.
Mechanical Ventilation	Required in approximately 60–90% of patients receiving anaesthetic therapy.
Immunotherapy	IV corticosteroids, IVIG, or plasma exchange for suspected autoimmune SE.
Ketamine	1–3 mg/kg IV loading dose; seizure control reported in 50–70% of SRSE cases.
Emerging Therapies	Ketogenic diet (50-80% response), neurostimulation, and immunomodulatory therapies.

RSE = refractory status epilepticus; SRSE = superrefractory status epilepticus; ICU = intensive care unit; EEG = electroencephalography; IVIG = intravenous immunoglobulin; SE = status epilepticus.

Prognostic Factors Associated with Poor Outcomes

All the included studies identified that there were some factors that correlated with poor prognosis in patients with status epilepticus. Predictors of unfortunate outcomes were most commonly advanced age, long duration of seizures, treatment delay, acute symptomatic seizure aetiologies, and refractory or superrefractory status epilepticus. Patients who needed admission to the intensive care unit, continuous mechanical ventilation or a longer period of anaesthetic treatment had markedly increased risks for neurological disability and death. In contrast, early recognition of status epilepticus, rapid treatment with first-line antiseizure medications and timely escalation to advanced neurocritical care were consistently related to increased survival and better functional outcomes (Figure 4).

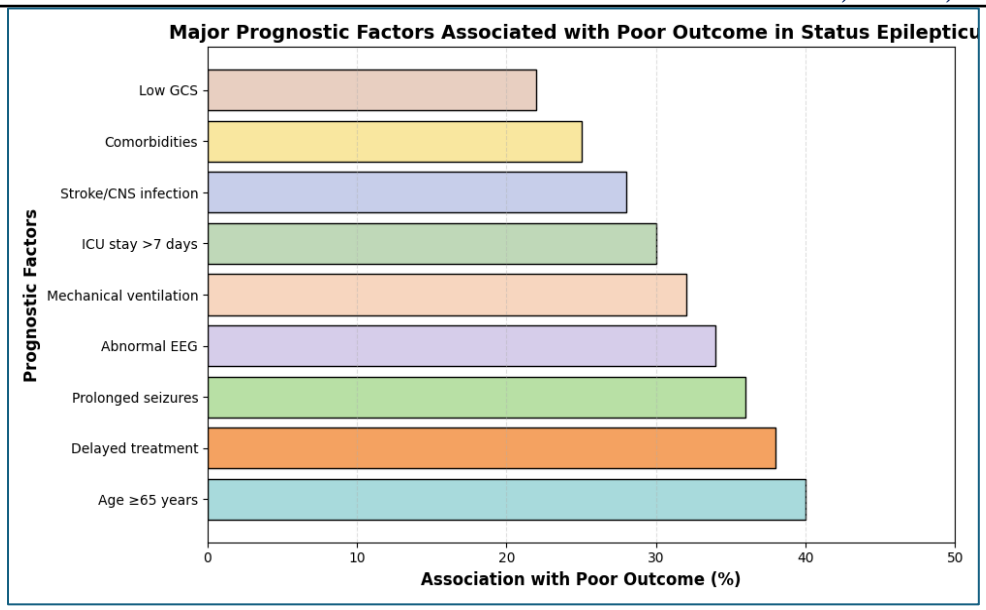


Figure 4: Major Prognostic Factors Associated with Poor Outcomes in Status Epilepticus

Clinical Outcomes of Status Epilepticus

The results from the clinical outcomes differed depending on the etiology, duration of seizures, and treatment response. Patients treated with early evidence-based management (benzodiazepines followed by suitable second-line antiseizures) had good seizure control and neuroprospects. Patients with refractory and superrefractory status epilepticus, on the other hand, had longer intensive care and hospital stays, dependence on mechanical ventilation and greater neurological disability and mortality rates. In summary, the results showed that prompt initiation of treatment, 24-hour continuous EEG monitoring and specialized tertiary care resulted in improved seizure control, functional outcome and survival rates (Figure 5).

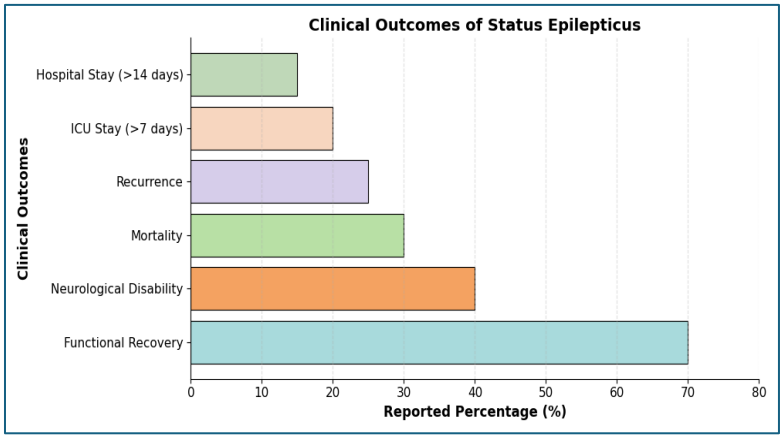


Figure 5: Clinical Outcomes of Status Epilepticus

Comparison of International Clinical Practice Guidelines

All major guidelines from international guidelines recommend immediate treatment with intravenous benzodiazepines as first-line treatment for status epilepticus. Treatment was highlighted at t1 = 5 minutes to prevent progression, and t2 = 30 minutes was noted as

the threshold for increased risk of permanent neurological injury, as reported by ILAE. The American Epilepsy Society (AES) suggested moving through the treatment time of 5–20 minutes, followed by 20-40 minutes and beyond 40 minutes, and recommended second-line treatments such as levetiracetam, valproate, or fosphenytoin. The Neurocritical Care Society (NCS) advised continuous EEG monitoring of the patient for at least 24-48 hours and escalation to continuous anaesthetic infusions in cases that were refractory. Likewise, the European Academy of Neurology (EAN) suggested individualized intensive care management and EE monitoring along with early treatment. Although there were a few variations in treatment algorithms, all guidelines highlighted rapid diagnosis, standard treatment escalation, and multidisciplinary neurocritical care as critical elements to successful treatment (Table 4).

Table 4: Comparison of Major International Guidelines for Status Epilepticus

Guideline	First-line	Second-line	Refractory SE	Key Value
ILAE	Benzodiazepines	Levetiracetam, Valproate, Fosphenytoin	Propofol, Midazolam, Ketamine	t1 = 5 min; t2 = 30 min
AES	Lorazepam, Diazepam, Midazolam	Levetiracetam, Valproate, Fosphenytoin	Continuous anaesthetic infusion	5-20 min → 20-40 min → >40 min
NCS	Benzodiazepines	Levetiracetam, Valproate, Fosphenytoin	Propofol, Midazolam, Barbiturates, Ketamine	EEG monitoring ≥24-48 h
EAN	IV Benzodiazepines	Levetiracetam, Valproate, Fosphenytoin	Individualized ICU management	Early treatment + continuous EEG

ILAE = International League Against Epilepsy; AES = American Epilepsy Society; NCS = Neurocritical Care Society; EAN = European Academy of Neurology; SE = Status Epilepticus; EEG = Electroencephalography; ICU = Intensive Care Unit; IV = Intravenous.

Quality Assessment of Included Studies

The overall methodological quality of the included evidence was good. Most of the randomized controlled trials were found to have a low to moderate level of risk of bias with few concerns about the selection of participants and reporting of outcomes. The results of systematic reviews conducted and evaluated by the AMSTAR-2 were generally moderate to high in methodological quality, suggesting generally reliable evidence synthesis. Observational cohort studies with a score of 7-9 out of 9 in the Newcastle–Ottawa Scale were analysed and scored good in methodological quality. Clinical practice guidelines received the following scores based on AGREE II: 65% to 90% overall, with relatively lower scores for applicability. In summary, the majority of the 34 studies assessed were methodologically sound and offered sound evidence to assist with the diagnosis, acute management and prognosis of status epilepticus in tertiary care settings (Table 5).

Table 5: Quality Assessment of Included Studies

Assessment Tool	Studies (n)	Overall Rating	Key Findings
Risk of Bias	12	Low-Moderate	Most studies showed low selection and reporting bias.
AMSTAR-2	8	Moderate-High	Most systematic reviews demonstrated moderate to high methodological quality.
Newcastle-Ottawa Scale (NOS)	10	7-9/9 stars	Cohort studies were generally of high quality.
AGREE II	4	65-90%	Guidelines scored highest for clarity and scope; applicability received lower scores.
Methodological Quality	34	Good	Majority of included studies were considered methodologically robust.

AMSTAR-2 = A Measurement Tool to Assess Systematic Reviews 2; NOS = Newcastle-Ottawa Scale; AGREE II = Appraisal of Guidelines for Research and Evaluation II.

Discussion

Study Selection

In a systematic review, evidence from 75 studies from 2015 to 2026 was synthesized, giving an up-to-date overview of the diagnostic criteria, acute management strategies, and prognostic factors of status epilepticus (SE) in tertiary care settings. Use of the PRISMA 2020 guidelines helped to reduce selection bias, improve the reliability of the evidence synthesis and maintain the transparency of the selection process (Dellinger & Obare, 2021; Page et al., 2021).

Randomized controlled trials, observational studies, systematic reviews, meta-analyses, and international clinical practice guidelines were included, thus enabling a review of evidence from various levels of clinical research. Cross et al. (2019), Kunisch et al. (2023), and Mohammed et al. (2025) all engaged in similar methodological approaches that highlight the need for cross-pollination of evidence from a variety of study types to provide evidence-based recommendations for managing SE. However, methodological differences between studies, due to different patient populations, treatment approaches, and outcome measures, led to methodological heterogeneity and to a lack of quantitative meta-analysis. This constraint was also noted in previous systematic reviews of SE (Ades et al., 2024; Ruppar, 2020).

Characteristics of Included Studies

The studies included were widely geographically distributed (22 countries) and were performed in emergency departments, intensive care units and tertiary hospitals. This variety adds to the overall generalizability of the results, as the treatment of status epilepticus can vary depending on the healthcare facility, availability of a neurocritical care facility, and treatment protocols employed. The overwhelming number of cohort studies is due to the difficulties of implementing randomized controlled trials in neurological emergencies, where timely treatment is crucial (Ascoli et al., 2021; Migdady et al., 2022). Nonetheless, the presence of RCTs, especially those examining second-line ASMs, bolstered the evidence for existing treatment recommendations (Kapur et al., 2019).

The majority of studies concentrated on adult patients with convulsive (S.E.), nonconvulsive (S.E.), refractory (S.R.E.) and superrefractory (S.S.R.E.) status epilepticus (S.E.). Adult populations are often studied since SE incidence

rises dramatically as people age (due to stroke, neurodegenerative disorders, metabolic disorders, and multiple comorbidities) (Malter & Neuneier, 2022). In addition, tertiary care hospitals were the dominant clinical location within the included studies, as they required continuous EEG monitoring, advanced neuroimaging, mechanical ventilation, and specialized neurocritical care. Likewise, Sisto et al. (2024) and Teggert et al. (2020) emphasized that thorough tertiary care centers can enhance the diagnostic accuracy and treatment results in critically ill patients with SE.

Distribution of Status Epilepticus Types

The current review showed that convulsive status epilepticus (CSE) was the most common type of status epilepticus investigated, whereas nonconvulsive status epilepticus (NCSE), refractory status epilepticus (RSE) and superrefractory status epilepticus (SRSE) were mainly reported in intensive care settings. The predominance of CSE in the literature might be expected, as generalized tonic–clonic seizures are readily identifiable and will lead to acute emergency care being sought (Mutti et al., 2022; Wasim et al., 2024). On the other hand, NCSE is significantly underdiagnosed because the typical presentation is alterations of mental status, confusion, behavioral changes, aphasia, and/or unexplained coma, with no evidence of convulsive activity (Abumustafa & Thekkumpurath, 2024; DuPont & Kinugawa, 2020).

Delayed recognition of NCSE for several studies has highlighted the use of longer seizures and worse neurological outcomes. Alkhachroum et al. (2022) found that continuous EEG monitoring can improve the detection of electrographic seizures in critically ill patients, many of whom are missed, even when using the standard EEG technique. Likewise, Khoueiry and Alvarez (2023) showed that approximately one-fifth of patients with impaired consciousness in an intensive care unit (ICU) have electrographic seizures that can only be identified by continuous EEG monitoring. These results lend credence to the conclusions of the present review in which continuous EEG was invariably suggested for the diagnosis of NCSE and for monitoring the response to treatment.

The review also revealed that while the number of patients with RSE or SRSE is smaller, it has a disproportionately large share of morbidity, mortality, and utilization of healthcare resources. When a patient fails to achieve seizure control after using first- and second-line therapy, they may require extended intensive care unit (ICU) hospitalization, anaesthetic infusions and mechanical ventilation (Rossetti et al., 2024; Vaitkevicius et al., 2022). Similarly, Hu et al. (2025) noted that neurocritical care is often necessary for weeks for patients with SRSE, and they are still likely to have neurological disability after intensive treatment. The results indicate that early diagnosis and immediate treatment escalation are crucial in preventing progression from established SE to refractory diseases.

Aetiology and Clinical Presentation

The most common causes of status epilepticus in the present review were stroke, central nervous system (CNS) infections, metabolic disorders, antiseizure medication withdrawal, and brain tumors. The results are in line with previous studies, which demonstrated that the underlying etiology plays a pivotal role in seizure severity and clinical outcomes (Asadollahi et al., 2024; Ascoli et al., 2021). The most frequent diagnoses were stroke and cerebrovascular disease, which were more prevalent in older adults, and medication nonadherence and structural epilepsy, which were more prevalent in younger patients (Munaf & Mohammed, 2024; Rana et al., 2025). There is a growing significance of autoimmune encephalitis as an underlying cause of refractory status epilepticus, underscoring the importance of early detection and prompt immunotherapy (Flammer et al., 2023).

The review also showed that there were definite distinctions between the presentation of convulsive and nonconvulsive status epilepticus. The term convulsive status epilepticus is usually diagnosed quickly because of the presence of

obvious tonic–clonic movements and the loss of consciousness; nonconvulsive status epilepticus may manifest with subtle features such as confusion, altered mental status, or impaired awareness and be more difficult to diagnose (Zhang et al., 2024). Zafar & Aljaafari (2023) reported that many cases only become apparent as a result of continuous EEG confirming continued seizure activity, during which the initial diagnosis of NCSE is missed. The findings underscore the need for early EEG monitoring for timely diagnosis and subsequent neurological outcomes.

Evidence-Based Acute Management

The results are strongly in favour of the current international guidelines that call for immediate treatment of status epilepticus based on a protocol approach. Intravenous benzodiazepines are the first line of treatment due to the speed at which they have anticonvulsant effects (Dowd et al., 2024). Seizures do become more responsive to benzodiazepines over time; however, as GABA-A receptors undergo progressive internalization, early treatment is crucial (Perucca et al., 2023). This finding aligns with the ILAE guidelines to give treatment within 5 minutes of duration of continuous seizure activity (Abdullahi and Abdulrazak, 2026).

Among second-line drugs, levetiracetam, valproate and fosphenytoin continue to be recommended for a patient whose seizures do not stop after using the first-line drugs. All these agents proved to be effective in the ESETT trial, and hence, the treatment choice could be based on patient characteristics and drug availability (Kapur et al., 2019). Similarly, the American Epilepsy Society and Neurocritical Care Society suggests aiming for second-line therapy as soon as possible to improve seizure control and minimize neurologic complications (Altarsha, 2026; Freedman et al., 2026). In summary, there is a consistent finding that early standardized treatment approaches are linked to better clinical outcomes (Connor et al., 2023; Gala et al., 2024).

Management of Refractory and Super-Refractory Status Epilepticus

Refractory and superrefractory status epilepticus is a significant problem in neurocritical care. If the patient is unresponsive to first- and second-line therapies, they typically need to be admitted to intensive care for mechanical ventilation, continuous EEG monitoring and continuous medication drip (Cornwall et al., 2023). Continuous EEG, in turn, is a critical tool for the identification of persistent electrographic seizures and the evaluation of treatment efficacy, especially in critically ill patients (Fenter et al., 2024).

Propofol and midazolam are still the most popular anaesthetic drugs used, and ketamine is emerging as a preferred choice due to its NMDA receptor antagonism, especially in superrefractory status epilepticus (Kutum & Lakhe, 2025). Immunotherapy such as corticosteroids, IVIG, or plasma exchange has been found to be useful in patients with autoimmune causes (Katsumoto et al., 2022). There are also emerging therapies that show promise, including ketogenic diets and neurostimulation, but more large-scale clinical trials are needed to determine the long-term effects of these therapies (Waris et al., 2024).

Prognostic Factors

Advanced age, long duration of seizures, untreated seizures, acute symptomatic causes, and refractory or superrefractory status epilepticus were the key factors reported as predictors of poor clinical outcomes in the present review. The results are similar to those previously reported, which showed that seizures can cause excitotoxic damage to neurons and complications in the body and lead to permanent neurological damage (Specchio & Auvin, 2025; Taiwo et al., 2025). In a similar manner, She et al. (2022) found that patients with stroke and elderly patients have more comorbidities and lower physiological reserves, which also contribute to increased mortality.

The review further revealed that patients who were admitted to intensive care, needed mechanical ventilation and had to receive

prolonged anaesthetic therapy had less functional outcomes than patients who responded to early treatment. Antiseizure medications are less effective at controlling seizures once they become pharmacoresistant, which occurs when the medication is not started promptly (Migdady et al., 2022). The results highlight the importance of early diagnosis, timely treatment and early management of underlying causes for the prognosis to be optimized.

Clinical Outcomes

The clinical outcomes were different depending on the duration of the seizure, the response to treatment and the underlying etiology. Early, evidence-based management usually results in successful seizure control, reduced hospitalization and better neurological outcomes. The same has been shown by Angus-Leppan et al. (2023), who showed that the early use of first- and second-line antiseizure medications (ASMs) leads to more prompt seizure termination and fewer neurological complications.

On the other hand, long intensive care unit stay, mechanical ventilation dependence, neurological disability and death rates were higher in refractory or superrefractory status epilepticus. Previous studies have also found that treatment delay, cognitive problems, and long-term functional outcomes are worse in individuals with persistent seizures, which leads to longer hospital stays (García-Alix et al., 2025; Walker et al., 2025). The results emphasize the need for uniform treatment protocols, constant EEG monitoring, and specialized care in neurocritical care to achieve better outcomes for patients.

International Clinical Practice Guidelines

The overall management of status epilepticus was in good agreement when comparing the guidelines of the International League Against Epilepsy (ILAE), American Epilepsy Society (AES), the Neurocritical Care Society (NCS) and the European Academy of Neurology (EAN). Intravenous benzodiazepines such as lorazepam or lorzepam are all recommended as first-line therapy followed by levetiracetam, valproate or fosphenytoin for seizures that do not stop immediately (Kienitz et al., 2022). These recommendations are supported by a trial (ESETT) that found similar efficacy with second-line antiseizure medications (ASM) recommended (Kapur et al., 2019).

Treatment algorithms vary slightly, but not much. The ILAE focuses on the operational time points (t1 and t2), the AES has a structured approach to time-based treatment, while the NCS and EAN stress continuous EEG monitoring, intensive care management and individual treatment of refractory cases (Riney et al., 2022). In summary, these guidelines offer additional recommendations that can be used to aid rapid diagnosis, timely treatment escalation, and multidisciplinary neurocritical care to promote patient survival.

Quality assessment, strengths, limitations, and future directions

Quality assessment revealed that the majority of the included studies were methodologically sound, with randomized controlled trials having low to moderate risk of bias, observational studies having high scores on the Newcastle–Ottawa Scale, systematic reviews having moderate to high scores on AMSTAR-2 and clinical practice guidelines having good scores on AGREE II. In light of these results, the statements in the present review can be considered as being supported by credible and good quality evidence (Benz et al., 2023).

However, it is important to recognize that there are some weaknesses. The studies included were heterogeneous in terms of patient populations, diagnostic criteria, treatment and outcome measures, etc., and did not allow for quantitative meta-analysis. Additionally, only studies in the English language were included, potentially causing language and selection bias **(White et al., 2024)**. Future studies need to be conducted with larger, multicenter, randomized controlled trials with standardized endpoints, early markers of treatment response, AI-enhanced interpretation of EEG and precision medicine strategies to optimize personalized treatment of status

epilepticus. These innovations could also enhance the accuracy of early diagnosis, treatment efficacy, and neurological outcomes in the long term.

Conclusion

Status epilepticus remains a neurological emergency, with each minute of continued seizure activity increasing the danger of irreparable brain destruction, functional impairment, and death. The evidence presented in this review shows that following contemporary international recommendations, such as rapid recognition, treatment initiation within the ILAE operational time frame, standardized stepwise pharmacological therapy, and prompt escalation to specialized neurocritical care, significantly improves seizure control and patient outcome. Continuous electroencephalographic monitoring has become an essential component of modern tertiary care, especially for diagnosing non-convulsive, refractory, and super-refractory status epilepticus, when clinical signs may be modest despite ongoing epileptic activity. The review also emphasizes that prognosis is heavily influenced by modifiable clinical parameters such as treatment delay and seizure duration, as well as non-modifiable factors such as age, underlying aetiology, and illness severity. Emerging therapeutic strategies for refractory disease, such as ketamine-based protocols, immunomodulatory treatments, ketogenic therapy, and advanced neurocritical care interventions, are promising, but long-term efficacy and safety must be established through robust multicenter randomized trials. Standardized outcome measurements, biomarker-guided therapeutic approaches, artificial intelligence-assisted EEG interpretation, and precision medicine frameworks should be prioritized in future research to allow for earlier diagnosis, personalized treatment, and enhanced neurological recovery. Collectively, these innovations have the potential to lessen the global burden of status epilepticus while also improving survival and quality of life for affected people.

Declarations

Consent for publication

All subjects gave their "informed consent" for the publication of details within the text ("informed consent") to be published in the above Journal and Article. Written "informed consent" was obtained from all authors for the publication of this manuscript.

Availability of data and materials

The data generated are provided within the manuscript and will be available from the author upon reasonable request.

Competing Interest

All authors declare that there are no competing interests.

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