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Research Article

Seizure Management in Prehospital Settings Reducing Time to Definitive Care in Epileptic Emergencies

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Abstract:

Seizure management in prehospital settings plays a critical role in reducing the time to definitive care for patients experiencing epileptic emergencies. Rapid recognition and appropriate intervention by first responders can significantly influence patient outcomes. In such situations, timely administration of anticonvulsant medications, along with proper airway management and monitoring of vital signs, is essential. Training first responders in the identification of different seizure types and their respective management protocols can enhance the efficiency of care provided on-site. Moreover, the integration of advanced communication systems allows paramedics to relay critical patient information to receiving hospitals, ensuring that neurology teams are prepared for immediate intervention upon arrival. Furthermore, the implementation of standardized protocols and guidelines for seizure management in prehospital settings can streamline the response to epileptic emergencies. These protocols should encompass the use of evidence-based practices, such as the administration of benzodiazepines for prolonged seizures, and the establishment of clear pathways for transporting patients to specialized care facilities. Collaboration between emergency medical services (EMS) and hospitals can facilitate continuous education and training, ensuring that all personnel are equipped with the latest knowledge and skills. By prioritizing swift and effective prehospital care, the healthcare system can significantly mitigate the risks.

1. Introduction

Epilepsy is one of the most common and formidable neurological disorders globally, affecting approximately 50 million people worldwide [1]. It is characterized by a persistent predisposition to generate epileptic seizures, which are transient occurrences of signs and/or symptoms due to abnormal, excessive, and synchronous neuronal activity in the brain [2]. For the majority of individuals with epilepsy, seizures can be controlled with antiepileptic medications. However, a significant subset of patients continues to experience seizures that can escalate into medical emergencies, most notably prolonged convulsive seizures and status epilepticus (SE). Status epilepticus is defined as a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms that lead to abnormally prolonged seizures, and it is a time-critical, life-threatening condition [3]. The prehospital phase of such emergencies—the critical window from the onset of the seizure to the patient's arrival at a definitive care facility—represents a pivotal frontier in the chain of survival for these patients.

The management of epileptic emergencies outside the hospital walls is a complex and high-stakes challenge for Emergency Medical Services (EMS) personnel, including paramedics and emergency medical technicians. Their role extends beyond mere transportation; they are the first medically trained responders tasked with immediate assessment, stabilization, and initiation of treatment. The core objective in this setting is unequivocal: to rapidly terminate seizure activity and prevent its deleterious systemic consequences, thereby reducing the time to definitive care. Definitive care, in this context, refers to the comprehensive diagnostic and therapeutic resources of a hospital emergency department, including advanced neurological monitoring, neuroimaging, and access to a broader formulary of medications and specialist consultation. Every minute of ongoing seizure activity increases the risk of permanent neuronal damage, systemic complications, and mortality [4]. Therefore, the efficiency and efficacy of prehospital interventions are not just a matter of patient comfort but are directly correlated with long-term neurological outcomes and survival.

The pathophysiology of prolonged seizures reveals why time is of the essence. Initially, a seizure is characterized by a compensatory phase, where homeostatic mechanisms attempt to maintain cerebral blood flow and energy substrate delivery. However, as the seizure persists beyond approximately 5-10 minutes, transitioning into established status epilepticus, the body enters a decompensatory phase. This phase is marked by systemic hypotension, hypoxia, hyperthermia, and acidosis, which collectively compromise cerebral perfusion and lead to excitotoxic neuronal injury [5]. The longer the seizure continues, the more refractory it becomes to standard benzodiazepine therapy, as internalization of synaptic GABA receptors diminishes their inhibitory efficacy [6]. This self-perpetuating cycle underscores the critical importance of early and effective intervention, ideally before the patient even enters the hospital doors.

The landscape of prehospital seizure management has evolved significantly over the past two decades, largely driven by evidence demonstrating the safety and efficacy of benzodiazepines administered by non-physician personnel. Landmark studies, such as the Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART), conclusively demonstrated that intramuscular midazolam administered by paramedics was at least as safe and effective as intravenous lorazepam for treating status epilepticus in the prehospital setting [7]. This evidence has been instrumental in shaping international guidelines, which now universally recommend benzodiazepines as the first-line treatment for active, generalized convulsive seizures in the community [8, 9]. The widespread adoption of these protocols represents a monumental step forward in bringing definitive care to the patient's location.

Despite these advances, significant challenges and variations in practice persist, creating gaps that can delay time-sensitive care. One major challenge is the accurate identification of the seizure type and its etiology by EMS providers. Distinguishing between a primary epileptic seizure and a seizure mimic—such as syncope, psychogenic non-epileptic seizures (PNES), or metabolic derangements—can be difficult in a chaotic prehospital environment [10]. Misidentification can lead to either the inappropriate administration of benzodiazepines or a dangerous delay in treatment. Furthermore, the "time to medication" clock is influenced by a cascade of logistical factors, including the time for a bystander to recognize an emergency and call for help, the dispatch and response time of the EMS unit, the on-scene assessment time, and the time required to establish a route of drug administration (e.g., obtaining intravenous access versus preparing an intramuscular injection).Significant geographical and systemic variations in EMS protocols further complicate the global picture. There is considerable heterogeneity in the specific benzodiazepine formulary (e.g., diazepam, midazolam, lorazepam), the approved routes of administration (intravenous, intramuscular, intranasal, buccal), and the dosing regimens across different EMS systems and countries [11]. For instance, some systems may restrict the use of certain medications or routes to specific levels of training, potentially creating a treatment delay if a higher-level provider is not available. This lack of standardization means that the quality of prehospital care a patient receives can be a matter of geographic chance, raising important questions about equity and the universal application of best practices.

Another critical, and often underappreciated, component of prehospital management is the role of bystanders and caregivers. As they are the true first responders, their knowledge and actions are foundational. Bystander fear, lack of knowledge about basic first aid (e.g., positioning the patient laterally to prevent aspiration), and hesitation to administer rescue medications if prescribed, can all contribute to a delay in effective management [12]. Moreover, the absence of a clear medical history or an epilepsy action plan at the scene can impede the EMS crew's ability to make rapid, informed decisions. Therefore, effective seizure management is not solely a medical challenge but also an educational and public health one, requiring community engagement and empowerment.

The ultimate measure of success in prehospital seizure management is the reduction of time to definitive care, which is a multi-faceted outcome. It is not merely about faster transport times, but about initiating treatments that alter the clinical course of the emergency before the patient reaches the hospital. When prehospital providers successfully terminate a seizure in the field, they effectively convert a life-threatening neurological emergency into a stabilized post-ictal state for transport. This achievement directly shortens the duration of status epilepticus, mitigates the associated systemic complications, and simplifies the subsequent in-hospital management [13].

2. Pathophysiology of Prolonged Seizures and Status Epilepticus

The management of epileptic emergencies in the prehospital setting is fundamentally a race against time, a concept best understood through the lens of the underlying pathophysiology. A seizure is not a static event but a dynamic neurological process that evolves through distinct phases, each with escalating physiological consequences. The transition from a single, self-terminating seizure to a prolonged seizure and ultimately to status epilepticus (SE) marks a critical shift from a manageable neurological event to a life-threatening medical crisis. The prehospital team's primary mission is to intervene within this narrow therapeutic window to arrest this pathological cascade before irreversible damage occurs. Understanding this cascade is therefore not merely an academic exercise but a clinical imperative that directly informs the urgency and rationale for rapid prehospital treatment [14]. The journey into a medical emergency begins with the initiation of a seizure, characterized by an imbalance between excitatory and inhibitory forces within the neuronal networks of the brain. Normally, glutamate-mediated excitation is carefully balanced by GABA (gamma-aminobutyric acid)-mediated inhibition. In epilepsy, this balance is disrupted, leading to the hypersynchronous, excessive neuronal放电 that manifests as a seizure. A typical generalized tonic-clonic seizure is usually self-limiting, lasting for a few minutes, as the brain's inherent inhibitory mechanisms, primarily via GABA receptors, successfully terminate the episode. However, when these mechanisms fail, or when the excitatory drive is overwhelmingly potent, the seizure persists. By definition, a seizure lasting longer than five minutes is considered prolonged and at high risk of evolving into status epilepticus, necessitating urgent pharmacological intervention [15].This failure of seizure termination marks the entry into the first phase of established status epilepticus, often referred to as the "compensated" or "early" phase. During this period, which typically lasts from 5 to 30 minutes, the body mounts a massive sympathetic response. This results in dramatic physiological changes: surging heart rate and blood pressure to maintain cerebral perfusion, increased cerebral blood flow to meet the brain's heightened metabolic demands, and elevated blood glucose levels. While these are compensatory mechanisms, they come at a cost. The intense muscle activity of a convulsive seizure generates profound lactic acidosis and hyperthermia. Furthermore, the brain's oxygen and glucose consumption can increase by over 200%, creating a state of high metabolic demand that is intrinsically unsustainable [16]. The primary pathological driver in this phase remains the overactivation of glutamate receptors, particularly the NMDA subtype, leading to continuous neuronal firing. From a therapeutic standpoint, this phase is the most responsive to intervention with first-line benzodiazepines, which enhance GABAergic inhibition. The success of prehospital treatment hinges on reaching the patient during this window [17]. If the seizure continues unabated beyond the early phase, the condition progresses to the "refractory" and "super-refractory" stages, accompanied by a fundamental shift in the underlying pathophysiology. This transition, usually beginning after approximately 30 minutes of continuous seizure activity, marks the start of the "decompensated" or "late" phase of status epilepticus. The most critical change at this stage is the internalization of synaptic GABA receptors. With persistent neuronal firing, the postsynaptic neurons undergo rapid biochemical changes, causing GABA receptors to be removed from the cell surface and sequestered inside the neuron. This dramatically reduces the number of available binding sites for benzodiazepines and other GABA-agonists, rendering these first-line medications increasingly ineffective. Simultaneously, there is an upregulation and increased trafficking of NMDA-type glutamate receptors to the synaptic membrane, further amplifying the brain's excitatory drive [18]. This self-reinforcing cycle creates a state of pharmacoresistance, making the seizures significantly harder to terminate and necessitating the use of second-line, and often anesthetic, agents.

The systemic consequences of the decompensated phase are severe and life-threatening. The body's compensatory mechanisms begin to fail, leading to systemic hypotension and a fall in cerebral perfusion pressure. This is compounded by hypoxemia due to impaired ventilation and airway compromise, a common complication in the prehospital setting. The combination of falling oxygen delivery and persistently high metabolic demand pushes the brain into an energy crisis. The initial hyperglycemia is followed by hypoglycemia as glucose stores are depleted. Lactic acidosis worsens, contributing to cardiovascular instability. The hyperthermia can become extreme, directly causing further neuronal injury and promoting cerebral edema. These systemic insults create a vicious cycle where systemic compromise further damages the brain, and the ongoing brain injury exacerbates systemic failure [19]. This is why the clinical picture of a patient in prolonged status epilepticus evolves from one of vigorous convulsions to more subtle, yet equally dangerous, subtle convulsive or even non-convulsive activity, as the brain's energy reserves are exhausted.

At the cellular level, the relentless excitatory activity triggers processes that lead directly to neuronal death, a phenomenon known as excitotoxicity. The constant activation of glutamate receptors, especially NMDA receptors, allows a massive influx of calcium ions ($Ca2+$) into the neurons. This calcium overload acts as a key mediator of cell death, activating a host of destructive enzymes including proteases, lipases, and endonucleases that degrade essential cellular structures. Mitochondria, the cell's power plants, become damaged and can even trigger apoptosis, or programmed cell death. The resulting neuronal necrosis is not limited to the hippocampus, a structure crucial for memory, but can extend to the cortex, thalamus, and cerebellum, leading to widespread and often permanent cognitive and neurological deficits [20]. This excitotoxic injury is the primary reason why the duration of status epilepticus is one of the strongest predictors of long-term functional outcome and mortality.

The concept of the "time window" is thus not a single moment but a continuum of escalating injury. The prehospital provider's encounter with a seizing patient is a snapshot somewhere on this timeline. The overarching goal is to intervene as far to the left of this pathological cascade as possible. Every minute of delay in administering antiseizure medication allows for further GABA receptor internalization, increased excitotoxic damage, and deepening systemic compromise. The transition from a benzodiazepine-responsive to a benzodiazepine-resistant state is a critical threshold that prehospital management aims to prevent [21].

This pathophysiological understanding provides the scientific foundation for every aspect of modern prehospital seizure protocol. The five-minute mark for defining a prolonged seizure and initiating treatment is not arbitrary; it is strategically chosen to intercept the seizure process before the major shift towards pharmacoresistance begins. The preference for rapid-acting, non-intravenous routes of administration, such as intramuscular or intranasal midazolam, is a direct response to the need for speed, overcoming the logistical delay of establishing an intravenous line [22]. The principle is to "treat early and treat adequately" with a sufficient benzodiazepine dose to maximize the chance of termination during the critical window of responsiveness.Furthermore, the systemic complications—hypoxia, hypotension, and hyperthermia—are not secondary concerns but primary targets for prehospital intervention. Effective management, therefore, involves a dual approach: rapid pharmacological termination of the seizure itself and aggressive supportive care to mitigate the systemic consequences. This includes administering supplemental oxygen, ensuring adequate ventilation, monitoring for and treating hypotension with fluids, and managing hyperthermia [23].

3. The Pivotal Role of Bystanders and Caregivers in the Initial Response

In the critical timeline of an epileptic emergency, the period before the arrival of Emergency Medical Services (EMS) is arguably the most vulnerable for the patient. This initial phase is governed not by trained medical professionals, but by bystanders, family members, or caregivers, who become the de facto first responders. Their actions, or lack thereof, set the stage for all subsequent medical interventions and can significantly influence the patient's outcome. While the clinical management by paramedics focuses on pharmacological termination of the seizure, the role of the layperson is foundational, centered on safety, basic life support, and the crucial activation of the emergency response system. Recognizing this group as an integral, though highly variable, component of the prehospital care chain is essential for any comprehensive strategy aimed at reducing time to definitive care [24]. The effectiveness of the entire prehospital system is often determined within the first few minutes of a seizure, long before a paramedic sets foot on the scene.

The most immediate and impactful action a bystander can take is the accurate recognition of a medical emergency and the prompt call for professional help. For generalized tonic-clonic seizures, the signs are often dramatic and unmistakable. However, for other seizure types, such as complex partial seizures or non-convulsive status epilepticus, the presentation can be subtle—characterized by confusion, staring, or automatisms—and may be misinterpreted as intoxication, psychological distress, or simply odd behavior. This delay in recognition directly translates into a delay in EMS activation, effectively pushing back the entire sequence of advanced care. Studies have shown that the median time from seizure onset to EMS arrival can be over 10 minutes, with the bystander's decision-making process constituting a significant portion of this interval [25]. Therefore, public education campaigns that enhance seizure recognition across its diverse manifestations are not merely informational but are a critical public health intervention to shorten the time-to-treatment pipeline.

Once a seizure is recognized, the provision of appropriate first aid is the next critical step. The core tenets of seizure first aid are designed to prevent secondary injury and maintain physiological stability until help arrives. Key actions include: gently guiding the person to the floor if they are not already there; positioning them onto their side into the recovery position to prevent aspiration of saliva or vomit; cushioning their head to prevent traumatic head injury; and removing sharp or hard objects from the immediate vicinity. Perhaps equally important is educating the public on what *not* to do. The persistent and dangerous myths of restraining the person, forcing an object into their mouth to prevent tongue swallowing, or attempting to administer oral medications or water during the active seizure must be continuously dispelled, as these actions can cause significant harm, including dental damage, airway obstruction, or aspiration [26]. The simplicity of correct first aid belies its profound importance in preventing compounding injuries that can complicate the patient's hospital course and recovery.

For individuals with known epilepsy, the role of the caregiver evolves from a reactive bystander to a prepared and empowered first responder. This is particularly true in the context of rescue medication administration. Many patients who are at risk for prolonged seizures or clusters are prescribed benzodiazepines formulated for non-intravenous use, such as buccal or intranasal midazolam or rectal diazepam. These medications are specifically designed for rapid administration by a layperson in the community setting. The timely use of such rescue therapies can abort a prolonged seizure before it escalates into status epilepticus, effectively preventing an EMS call and a hospital visit altogether. This represents the most direct impact a caregiver can have on the patient's clinical trajectory and the healthcare system's burden [27]. However, this potential is only realized if the caregiver is confident, trained, and willing to administer the medication.

Despite the availability of these tools, significant barriers prevent their optimal utilization. Caregiver anxiety and fear of causing harm are potent deterrents. The stress of witnessing a loved one's seizure can be paralyzing, and the responsibility of administering a potent medication can be daunting. Studies have consistently shown that a substantial proportion of caregivers do not administer rescue medications even when indicated, often due to a lack of confidence in their training or fear of potential side effects, such as respiratory depression [28]. Furthermore, the absence of a clear, personalized seizure action plan exacerbates this uncertainty. A seizure action plan is a written document that provides specific, individualized instructions on seizure recognition, first aid steps, when and how to use rescue medications, and when to call EMS. Without this clear guidance, caregivers are left to make critical decisions under extreme duress, which can lead to either inappropriate delays or unnecessary panic.

The psychological and emotional state of the bystander or caregiver is a critical, though often overlooked, variable in the emergency response. A panicked, fearful, or traumatized bystander is less likely to provide effective care or give a coherent history to the arriving EMS crew. The chaotic nature of a seizure can lead to fragmented and unreliable eyewitness accounts, which are nonetheless vital for paramedics trying to determine seizure duration, type, and potential triggers [29]. Bystanders who are themselves distressed may provide inaccurate timing ("it felt like an hour" when it was three minutes) or omit key details, which can impact the initial clinical decisions made by the EMS team. Therefore, interventions that calm the bystander—such as clear, step-by-step instructions from an emergency dispatcher over the phone—not only aid the bystander but indirectly improve the quality of information and care transition to the professionals.

The transition of care from the bystander to the EMS personnel is a critical handoff that can streamline or hinder ongoing management. When the EMS unit arrives, a well-informed bystander or caregiver becomes an invaluable source of information. They can immediately provide a succinct history, including the patient's known epilepsy diagnosis, the time of seizure onset, whether it was a witnessed injury, any prescribed medications, and whether a rescue medication was already administered. This last point is particularly crucial, as it prevents double-dosing of benzodiazepines and alerts the paramedics to the possibility of a refractory seizure [30]. A prepared caregiver who can hand the paramedic the patient's seizure action plan and rescue medication box facilitates a seamless transition and allows for faster, more informed medical decision-making.

To maximize the positive impact of this first link in the chain of survival, targeted educational and support initiatives are essential. Community-based seizure recognition and first aid training programs, such as those offered by epilepsy associations worldwide, are fundamental. These programs should be widely accessible and promoted not only to families of people with epilepsy but also to school staff, workplace safety officers, and the general public [31]. Similarly, healthcare providers have a responsibility to ensure that caregivers are not just prescribed rescue medication but are thoroughly trained in its use through hands-on demonstration and regular refreshers. This training must include clear, unambiguous criteria for when to administer the medication and, just as importantly, when to bypass it and immediately call EMS—for instance, in the case of a first-time seizure, a seizure in water, or if the person is pregnant or has diabetes [32].

Technological advancements offer promising avenues to empower these first responders. Mobile health applications can now provide digital seizure action plans with built-in timers and step-by-step prompts for first aid and rescue medication use. Wearable seizure detection devices can alert caregivers to a seizure they may not have witnessed, enabling a faster response, especially at night [33]. Furthermore, the role of the emergency dispatcher can be enhanced with improved protocols for guiding callers through seizure first aid and gathering essential information before the EMS team is even dispatched, priming the system for an effective response [34].

4. Evidence-Based Pharmacological Management by EMS

Upon the arrival of Emergency Medical Services (EMS), the management of an active epileptic emergency transitions from supportive first aid to targeted pharmacological intervention. This phase represents the most critical and evidence-driven component of prehospital care, where the application of specific protocols directly influences the patient's trajectory toward definitive care. The cornerstone of these protocols is the rapid administration of benzodiazepines, a class of medication that enhances the effect of the brain's primary inhibitory neurotransmitter, GABA. The evolution of these protocols from a "scoop and run" mentality to a "treat and street" or "treat and transport" approach marks a paradigm shift in emergency medicine, firmly rooted in clinical evidence that demonstrates the safety, efficacy, and profound outcome benefits of stopping seizure activity in the field [35]. The execution of these protocols by paramedics is a deliberate, time-sensitive process designed to intercept the pathophysiological cascade of status epilepticus at its most vulnerable point.

The evidence base supporting benzodiazepines as the first-line prehospital treatment is robust and unequivocal. For decades, the goal has been to identify the optimal agent, dose, and route of administration to maximize speed and efficacy while minimizing logistical delays and side effects. The landmark Rapid Anticonvulsant Medication Prior to Arrival Trial (RAMPART) fundamentally changed practice in many EMS systems. This large-scale, randomized, double-blind trial demonstrated that intramuscular (IM) midazolam was at least as effective as intravenous (IV) lorazepam for treating status epilepticus in the prehospital setting, with a comparable safety profile [36]. The key advantage of IM midazolam lies in its rapid and reliable absorption and the elimination of the time-consuming and often difficult process of establishing IV access in a seizing patient. This evidence has made IM midazolam the preferred first-line option in an increasing number of EMS protocols worldwide, as it directly addresses the primary objective of reducing time to drug administration.

However, the pharmacological arsenal in the EMS toolkit is not monolithic, and protocol variations exist based on local guidelines, formulary availability, and provider training levels. While IM midazolam has gained prominence, other benzodiazepines and routes remain in common and effective use. Intravenous lorazepam has a longer duration of anticonvulsant action in the brain than diazepam and is a highly effective agent when IV access is already established or can be rapidly obtained [37]. Intravenous or rectal diazepam is also used, particularly in pediatric protocols. Furthermore, intranasal and buccal mucosal routes for midazolam or diazepam offer non-invasive alternatives that are especially valuable in situations where IM injection is contraindicated or when dealing with very young patients. The choice among these options within a protocol is often structured as an algorithm, guiding the paramedic to the fastest available route based on the clinical scenario and patient characteristics [38]. This flexibility within a standardized framework is essential for adaptable and effective prehospital care.

The practical application of these protocols follows a structured algorithm designed for clarity and speed under pressure. The initial step is always a rapid assessment to confirm the presence of an active, generalized convulsive seizure and to rule out mimics, such as syncope or psychogenic non-epileptic seizures. Once a prolonged seizure (typically >5 minutes) is identified, the protocol is activated. For systems where IM midazolam is first-line, the paramedic will prepare and administer a weight-based dose (commonly 10 mg for adults) into a large muscle mass, such as the deltoid or vastus lateralis. The clock for the "time to medication" stops the moment the injection is complete. If IV access is already present or can be established within a minute or two without delaying care, IV lorazepam (e.g., 4 mg) may be administered instead [39]. The protocol then enters a monitoring phase, observing for seizure cessation and any potential adverse effects, most notably respiratory depression or hypotension.

The administration of the first benzodiazepine dose does not always guarantee seizure termination, leading to the critical protocol component for refractory cases. If the seizure persists after an appropriate interval (usually 4-5 minutes for IV and 5-10 minutes for IM administration), a second, or "repeat," dose of the same benzodiazepine is typically authorized. This step acknowledges that a single dose may be insufficient to break the seizure focus, especially as the duration of the event increases and GABA receptor internalization progresses. The failure of two appropriate doses of a benzodiazepine to terminate convulsive activity effectively defines benzodiazepine-resistant status epilepticus in the prehospital context [40]. At this juncture, the patient's condition is critical, and the focus of the protocol shifts from termination in the field to rapid stabilization and expedited transport, often with consideration of advanced airway management due to the heightened risk of respiratory compromise from cumulative benzodiazepine dosing and the ongoing metabolic crisis.

The safety profile of prehospital benzodiazepine administration is generally favorable, but it is not without risks that paramedics must be trained to anticipate and manage. The most significant adverse effect is dose-related respiratory depression and hypoxia. This risk is amplified when a second dose is required, or if the patient has already been exposed to other respiratory depressants (e.g., alcohol or opioids). Therefore, EMS protocols are inseparable from the equipment and skills for advanced life support. Paramedics must be prepared to provide bag-valve-mask ventilation and, in severe cases, perform rapid sequence intubation to secure the airway [41]. Hypotension is another potential side effect, particularly with IV administration, and can be managed with fluid boluses. Continuous pulse oximetry, cardiac monitoring, and frequent blood pressure checks are standard practice during and after benzodiazepine administration, making the prehospital environment a controlled, albeit mobile, critical care setting.

Despite the strong evidence, the implementation of these evidence-based protocols faces real-world challenges that can create gaps between ideal and actual care. One significant challenge is the persistent variability in protocols across different regions and EMS agencies. The specific benzodiazepine chosen (midazolam vs. lorazepam vs. diazepam), the approved routes, the dosing schedules, and the authority to administer repeat doses can differ substantially, leading to a "postcode lottery" of care [42]. Furthermore, the difficulty of distinguishing true status epilepticus from seizure mimics in the field remains a diagnostic dilemma. Administering benzodiazepines to a patient with psychogenic non-epileptic seizures (PNES) is not only ineffective but also exposes them to unnecessary risk, while withholding treatment from a patient in non-convulsive status epilepticus constitutes a dangerous delay.The training and confidence of the EMS providers are the human factors that bring the written protocol to life. Paramedics require regular, high-fidelity simulation training that goes beyond rote memorization to build clinical judgment. This includes managing the chaotic scene, interacting with distressed bystanders, practicing difficult IV access on seizing patients, and managing the complications of therapy [43]. Reinforcement of the "time is brain" principle is crucial to instill the sense of urgency required to drive rapid protocol execution. Studies have shown that ongoing education and competency assessments directly correlate with higher protocol adherence and better patient outcomes, highlighting that the protocol is only as good as the provider implementing it [44].

5. Identifying and Addressing System Delays

The development of evidence-based clinical guidelines for prehospital seizure management represents a monumental leap forward in emergency care. However, the translation of these protocols from paper to practice is fraught with systemic obstacles that can critically delay intervention. The phrase "time is brain" underscores the urgency, yet the pathway to treatment is often impeded by a cascade of delays embedded within the very systems designed to provide help. Identifying and addressing these barriers is not merely an exercise in efficiency; it is a clinical imperative to prevent the transition of a manageable seizure into refractory status epilepticus with its attendant risks of neuronal injury and mortality. These system delays can be categorized into three critical segments: pre-dispatch and response barriers, on-scene operational barriers, and system-wide infrastructural and educational barriers [45]. A meticulous examination of each segment is essential to fortify the chain of survival for patients experiencing epileptic emergencies.

The first and often most protracted delay occurs before a paramedic even arrives on the scene, rooted in the public's and the dispatch system's response. A fundamental barrier is the bystander's failure to recognize a seizure as a time-sensitive medical emergency. For convulsive seizures, the dramatic presentation may prompt a swift call for help, but for non-convulsive or focal seizures, the symptoms—confusion, staring, or automatisms—can be misinterpreted as psychological distress or intoxication, leading to a dangerous delay in activating the emergency response system [46]. Once a call is placed, the efficiency of the dispatch center becomes the next critical juncture. Dispatchers relying on limited information from often panicked callers may misclassify a "seizure" as a less urgent "sick person" call. This misclassification can determine whether an Advanced Life Support (ALS) unit, equipped with paramedics and necessary medications, or a Basic Life Support (BLS) unit is dispatched, potentially requiring a later and time-consuming upgrade. Geographical and logistical constraints, such as extended rural response times, heavy urban traffic, and limited availability of ALS units, further compound these initial delays, creating a pre-arrival timeline that is largely outside the control of the treating medical team [47].

Upon the arrival of EMS, a new set of on-scene operational barriers emerges, directly impacting the "needle-to-skin" time for medication administration. The most significant of these is the diagnostic challenge faced by paramedics in a chaotic prehospital environment. They must rapidly differentiate true status epilepticus from conditions that mimic it, such as syncope with myoclonic jerks, psychogenic non-epileptic seizures (PNES), or metabolic encephalopathy. This diagnostic uncertainty can lead to hesitation, a period of "watchful waiting," or attempts to gather a more detailed history from distressed bystanders, all of which consume valuable minutes while the seizure continues [48]. Furthermore, the historical reliance on intravenous (IV) routes for benzodiazepines presents a major practical barrier. Establishing peripheral IV access in a seizing, diaphoretic patient is notoriously difficult and time-consuming. Multiple unsuccessful attempts can waste the critical early phase of status epilepticus, directly contributing to treatment refractoriness. This specific barrier provided the primary impetus for the widespread adoption of intramuscular (IM) midazolam, which offers a faster and more reliable route of administration [49].

Beyond the immediate clinical encounter, pervasive system-wide and infrastructural barriers create a patchwork of care quality that is often dependent on a patient's location. A profound lack of standardization in EMS protocols across different regions and countries constitutes a major systemic flaw. There is significant heterogeneity in the choice of first-line benzodiazepine (e.g., midazolam, lorazepam, diazepam), the approved routes of administration (IV, IM, intranasal, buccal), the authorized dosing regimens, and the protocols for administering repeat doses [50]. A paramedic operating across different jurisdictions may be forced to navigate conflicting guidelines, leading to confusion, hesitation, and ultimately, a delay in definitive treatment. This variability creates a "postcode lottery" where a patient's outcome is inadvertently influenced by the specific policies of the local EMS agency rather than by universal best practices.Another critical, yet often overlooked, barrier is the "handoff gap" that occurs during the transition from prehospital to in-hospital care. Even if a seizure is successfully terminated in the field, the process of transport, arrival at the emergency department (ED), triage, and providing a comprehensive handover report to the receiving team can be lengthy. More alarmingly, if the seizure is ongoing upon ED arrival, there can be a significant lag between the end of prehospital care and the administration of the next line of antiseizure medication in the hospital. This gap represents a vulnerable period where the continuity of aggressive seizure management is broken [51]. The problem is exacerbated by a lack of integrated communication systems; without a pre-arrival notification from EMS, the ED team may be unprepared for a critical neurology patient, losing valuable minutes to assemble resources and prepare second-line therapies.

Human factors and knowledge gaps among EMS providers also present significant barriers to rapid intervention. Paramedics may experience "protocol inertia," where a lack of recent training or familiarity with the seizure management algorithm erodes confidence and slows decision-making. Fear of adverse effects, particularly respiratory depression from benzodiazepines, can lead to underdosing or a reluctance to administer a repeat dose, despite overwhelming evidence that the dangers of untreated status epilepticus far exceed the risks of treatment [52]. Additionally, there is frequently a gap in communication regarding medications already administered by caregivers. Failure to quickly ascertain a history of pre-arrival rescue medication (e.g., buccal midazolam) can lead to dangerous double-dosing or an incorrect assumption that benzodiazepines have failed, potentially altering the treatment pathway in a way that is not evidence-based.

Addressing this complex web of barriers requires a multi-faceted and systemic approach targeting each weak link in the chain. To mitigate pre-arrival delays, sustained public education campaigns on seizure recognition and first aid are crucial. Simultaneously, enhancing dispatch protocols with more nuanced medical interrogation scripts can improve the accuracy of call categorization and ensure the appropriate level of response is dispatched immediately [53]. For on-scene barriers, the continued promotion and adoption of IM-first protocols is the most effective strategy to overcome vascular access challenges. Furthermore, incorporating high-fidelity simulation training that focuses on differentiating seizure mimics and managing complications like respiratory depression can build paramedic confidence and reduce hesitation.To tackle system-wide infrastructural barriers, a move toward national or international consensus on core elements of prehospital seizure protocols is essential. Standardizing the first-line drug, route, and dosing would eliminate jurisdictional confusion and ensure equitable care. To bridge the perilous handoff gap, the implementation of structured communication tools like ISBAR (Identification, Situation, Background, Assessment, Recommendation) for handovers and mandatory pre-arrival notification systems for refractory status epilepticus cases are critical. These measures prepare the ED for a seamless transition, effectively creating a "continuum of care" from the community to the hospital bed [54].

6. Technological and Educational Innovations for Faster Care

While systemic barriers to rapid seizure care are significant, the modern era presents unprecedented opportunities to overcome them through a synergistic combination of technological advancement and educational innovation. Moving beyond traditional protocols, a new paradigm is emerging that leverages digital tools and enhanced training methodologies to create a more integrated, intelligent, and responsive prehospital ecosystem. The objective of these innovations is to proactively bridge the critical gaps in the chain of survival—from seizure onset to definitive care—by empowering every stakeholder, from the bystander to the paramedic. This involves deploying technology to accelerate diagnosis and communication, and reinventing educational approaches to build a more confident and competent response network. Together, these strategies form a powerful arsenal in the fight to reduce time-to-treatment and improve outcomes for patients in epileptic emergencies [55].

Technological innovation begins at the very moment a seizure occurs, with the development of sophisticated seizure detection devices. For individuals with known epilepsy, especially those living alone or who experience nocturnal seizures, wearable technology such as smartwatches with accelerometry and photoplethysmography (PPG) sensors can detect the rhythmic movements and physiological changes associated with convulsive seizures. Bedside devices using sonar or mattress sensors can similarly identify nocturnal events. Upon detection, these devices can send automatic alerts to designated caregivers or emergency contacts via smartphone applications, providing the crucial element of early notification that can trigger a rapid response [56]. This technology directly addresses the delay in seizure recognition, effectively creating a "digital first responder" that can summon human help even when the patient is unable to do so themselves, thereby collapsing the previously silent and dangerous period at the start of an emergency.

Beyond detection, mobile health (mHealth) applications are revolutionizing the preparedness and response of both caregivers and EMS providers. For caregivers, dedicated apps can host digital seizure action plans, transforming a static paper document into an interactive guide. These apps can provide step-by-step first aid instructions, activate a timer to accurately track seizure duration, send automated alerts to pre-programmed contacts, and offer clear, situation-specific guidance on when and how to administer rescue medications and when to call for emergency services [57]. This real-time decision support reduces panic and uncertainty, ensuring that the initial response is both swift and correct. For paramedics, companion or integrated apps can provide instant access to drug dosage calculators, institutional protocols, and even video links for procedural guidance, serving as a powerful cognitive aid in the high-stress prehospital environment.

The communication bridge between the scene of the emergency and the receiving hospital is another area ripe for technological transformation. Electronic Patient Care Report (ePCR) systems, when fully integrated with hospital electronic health records (EHRs), can allow for a "digital handoff." Critical information such as the seizure's onset time, medications administered by caregivers or paramedics, dosages, routes, and patient response can be transmitted securely to the emergency department while the ambulance is still en route [58]. This gives the hospital team a vital head start in preparing the next line of therapy, thereby dramatically shrinking the dangerous handoff gap. Furthermore, the emerging field of telemedicine holds promise for prehospital neurology. With the proliferation of high-speed cellular networks, paramedics could potentially use tablet-based systems to establish a live video link with a remote neurologist or a designated hospital consultant. This would allow for real-time expert guidance in complex cases, such as differentiating seizure mimics or managing refractory status epilepticus during prolonged transport, effectively bringing specialist-level support to the patient's side [59].

Parallel to these technological leaps, educational innovations are critical to ensuring that these tools are used effectively and that human expertise remains at the forefront. For EMS providers, the shift from traditional lecture-based training to high-fidelity simulation represents a cornerstone of modern education. Simulation-based training immerses paramedics in realistic scenarios involving manikins that can seize, desaturate, and respond to medications. This allows them to practice the entire sequence of care—from rapid assessment and IM injection to managing respiratory depression—in a zero-risk environment [60]. Repeated simulation builds not only procedural muscle memory but also critical non-technical skills such as team leadership, task delegation, and communication under pressure, directly translating to improved performance and reduced hesitation during actual emergencies.

To combat knowledge decay and protocol drift, continuous micro-learning platforms are becoming an essential educational tool. Instead of relying solely on annual recertification courses, paramedics can engage with short, focused online modules covering specific topics, such as updates in seizure management or a refresher on the use of intranasal benzodiazepines. These micro-lessons, often accessible on mobile devices, facilitate just-in-time learning and can be reinforced with quick quizzes or virtual patient cases [61]. This approach ensures that the latest evidence and protocol changes are consistently reinforced, keeping the knowledge of frontline providers sharp and current. Furthermore, incorporating structured debriefing and video review of real-life calls, where feasible and anonymized, can provide powerful insights for quality improvement and collective learning within an EMS agency.

The ultimate expression of innovation lies in the seamless integration of technology and education to create a cohesive system. For instance, data analytics can be applied to ePCR systems to identify performance gaps. If the data reveals consistent delays in specific parts of the response process—for example, a prolonged time from EMS arrival to medication administration—targeted simulation scenarios and micro-learning modules can be developed to address this precise weakness [62]. This creates a virtuous cycle where technology identifies the problem, and education delivers the tailored solution. Similarly, community-wide initiatives can blend technology and public education. Social media campaigns can drive traffic to interactive web platforms that offer virtual seizure first aid training, using engaging videos and quizzes to improve public knowledge and preparedness on a large scale.

The implementation of these innovations, however, is not without its challenges. Issues of cost, digital literacy, data privacy, and interoperability between different technological systems must be carefully navigated. Ensuring equitable access to these tools is also paramount to prevent a "digital divide" where only certain populations benefit from these advances [63].

7. Outcomes and the Impact of Reduced Prehospital Time on Patient Prognosis

The ultimate validation of any intervention in emergency medicine lies in its demonstrable impact on patient-centered outcomes. For prehospital seizure management, the compelling rationale of "time is brain" must be substantiated by concrete evidence that reducing the time to definitive care translates into tangible improvements in survival, neurological function, and quality of life. Measuring success, therefore, requires moving beyond simple process metrics, such as response times or medication administration rates, to analyze hard clinical endpoints that matter most to patients. The correlation between the duration of status epilepticus (SE) and poor prognosis is unequivocal, establishing the reduction of prehospital time as a primary determinant of clinical success [64]. By examining outcomes across a spectrum—from immediate clinical stability to long-term functional recovery—we can fully appreciate the profound impact of efficient prehospital systems on the trajectory of a patient's life following an epileptic emergency. The most immediate and critical outcome measure is the termination of seizure activity in the field. Success in this domain is a direct precursor to all subsequent positive outcomes. When paramedics successfully administer benzodiazepines and terminate a seizure before or during transport, they achieve the primary objective of halting ongoing neuronal excitation and excitotoxic injury. Studies have consistently shown that prehospital administration of benzodiazepines, particularly intramuscular midazolam, is associated with a significantly higher rate of seizure cessation upon arrival at the emergency department compared to placebo or delayed treatment [65]. This achievement is multifactorial: it directly shortens the total duration of status epilepticus, mitigates the associated systemic complications like hyperthermia and acidosis, and prevents the transition to refractory status epilepticus, a condition that is exponentially more difficult to treat and carries a much higher mortality rate. Thus, the rate of prehospital seizure termination serves as a powerful, proximal indicator of system efficacy. Beyond seizure cessation, the impact on morbidity and mortality is the most significant measure of long-term success. The duration of status epilepticus is one of the strongest independent predictors of mortality. Research has demonstrated that mortality rates can increase from approximately 2.7% for seizures lasting 10-29 minutes to over 19% for those lasting 60-119 minutes, and up to 39% for durations exceeding 120 minutes [66]. By intercepting and terminating seizures in the prehospital phase, EMS systems effectively prevent patients from entering these high-risk duration categories. A reduction in prehospital time directly contributes to a reduction in overall SE duration, which in turn is linked to a lower in-hospital mortality rate. Furthermore, successful early termination reduces the incidence of severe systemic complications that contribute to death, such as cardiac arrhythmias, respiratory failure requiring intubation, and neurogenic pulmonary edema, thereby demonstrating that rapid prehospital care saves lives [67].

While mortality is a stark endpoint, the preservation of neurological function is an equally vital outcome that profoundly affects a survivor's quality of life. Prolonged seizure activity leads to excitotoxic neuronal damage, particularly in vulnerable regions like the hippocampus, which is critical for memory. The resulting cognitive deficits can include problems with short-term memory, executive function, and processing speed. By reducing the total seizure time, effective prehospital management directly limits the extent of this neuronal injury [68]. Patients who receive rapid prehospital benzodiazepines and have their seizures terminated quickly are more likely to be discharged from the hospital with their baseline cognitive function intact. In contrast, those experiencing prolonged SE often face long-term neurological sequelae, which can range from mild cognitive impairment to severe and permanent encephalopathy, necessitating long-term care and support. Therefore, the success of prehospital intervention is measured not only in lives saved but in the quality of those saved lives. The benefits of reduced prehospital time extend significantly into the realm of healthcare resource utilization, which is an important indirect outcome for both the patient and the healthcare system. When a seizure is terminated in the field, the patient's clinical status is often stabilized to the point where they may not require the highest level of hospital care. This can result in a lower likelihood of admission to the intensive care unit (ICU), a shorter overall hospital length of stay, and a decreased need for advanced and costly interventions such as mechanical ventilation and continuous electroencephalographic (cEEG) monitoring [69]. For example, a patient whose seizure is broken by paramedics may be observed in the emergency department and discharged, or admitted to a general ward, whereas a patient in refractory status epilepticus will almost certainly require ICU admission. This reduction in resource intensity translates into lower healthcare costs and frees up critical care resources for other patients, creating a more efficient system overall.Measuring these outcomes requires a robust framework of key performance indicators (KPIs) for prehospital systems. These KPIs move beyond simple response times to capture the entire timeline of care. Critical metrics include: 1) **Time from seizure onset to EMS call**, reflecting public awareness; 2) **Time from EMS arrival to medication administration**, reflecting on-scene efficiency and protocol design; 3) **Rate of successful prehospital seizure termination**; and 4) **Time from EMS call to arrival at a definitive care facility** [70]. By systematically tracking these metrics and correlating them with patient outcomes (e.g., mortality, ICU admission rates, functional status at discharge), EMS agencies can perform continuous quality improvement. This data-driven approach allows for the identification of persistent bottlenecks and the evaluation of new protocols or technologies, ensuring that the system is consistently evolving toward better patient outcomes.The long-term prognosis and functional recovery of a patient are the ultimate testament to the effectiveness of the entire emergency response chain. Functional outcomes are often measured using standardized scales such as the Glasgow Outcome Scale (GOS) or the modified Rankin Scale (mRS) at discharge and during follow-up. A favorable functional outcome (e.g., a return to independent living) is strongly associated with a shorter duration of status epilepticus. Since the prehospital phase constitutes a substantial portion of the total SE duration, any reduction in this time directly increases the probability of a good functional recovery [71]. Patients who experience rapid prehospital intervention are more likely to return to their pre-morbid level of functioning, including their employment and social roles, thereby minimizing the long-term socio-economic impact of the emergency on their lives and families. Finally, the psychological impact on patients and their caregivers must be considered a valid and important outcome. Witnessing or experiencing a prolonged, uncontrolled seizure is a profoundly traumatic event. The knowledge that an efficient system exists—one that can bring rapid, professional help and terminate the terrifying event—provides immense psychological security to individuals living with epilepsy and their families. This sense of security can reduce anxiety and improve overall quality of life, even in the absence of a recurrent event [72].

8. Conclusion

In conclusion, the management of seizure emergencies in the prehospital environment is a complex but critically determinative phase in the patient's care continuum. This research has delineated the compelling pathophysiological rationale for urgent intervention, highlighting the narrow therapeutic window before seizures become self-sustaining and refractory. The effectiveness of the entire system is a chain reliant on its constituent links: the preparedness of bystanders, the flawless execution of evidence-based pharmacological protocols by EMS, and the seamless transition to in-hospital care. While significant barriers—including diagnostic challenges, logistical delays, and protocol variability—persist, they are not insurmountable. The concerted implementation of technological innovations, such seizure detection devices and digital handoff systems, coupled with educational advancements like high-fidelity simulation and continuous micro-learning for providers, presents a robust pathway to overcoming these obstacles. Ultimately, the success of these efforts is unequivocally measured in patient outcomes. Reducing the time to definitive care in the prehospital setting is directly correlated with increased survival, preserved neurological function, and an enhanced quality of life for survivors. Therefore, a sustained commitment to optimizing every facet of the prehospital response system is not just a clinical objective but a moral imperative to safeguard the futures of those affected by these devastating emergencies.

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References

1. Tanigawa K., Tanaka K. Emergency medical service systems in Japan: past, present, and future. Resuscitation. 2006;69(3):365–370. doi: 10.1016/j.resuscitation.2006.04.001.

2. Sh in S.D., Kitamura T., Hwang S.S., Kajino K., Song K.J., Ro Y.S., et al. Association between resuscitation time interval at the scene and neurological outcome after out-of-hospital cardiac arrest in two Asian cities. Resuscitation. 2014;85(2):203–210. doi: 10.1016/j.resuscitation.2013.10.021.
3. Jaffe E., Strugo R., Bin E., Blustein O., Rosenblat I., Alpert E.A., et al. The role of emergency medical services in containing COVID-19. Am J Emerg Med. 2020;38(7):1526–1527. doi: 10.1016/j.ajem.2020.04.023.
4. Kim H.S., Jang T.C., Kim G.M., Lee S.H., Ko S.H., Seo Y.W. Impact of the coronavirus disease 2019 outbreak on the transportation of patients requiring emergency care. Medicine (Baltimore) 2020;99(50):e23446. doi: 10.1097/MD.0000000000023446.
5. Al Amiry A., Maguire B.J. Emergency medical services (EMS) calls during COVID-19: early lessons learned for systems planning (a narrative review) Open Access Emerg Med. 2021;13:407–414. doi: 10.2147/OAEM.S324568.
6. Zachrison KS, Nielsen VM, de la Ossa NP, Madsen TE, Cash RE, Crowe RP, et al. Prehospital stroke care part 1: emergency medical services and the stroke systems of care. Stroke 2022; Epub ahead of print.
7. Morita T., Tsubokura M., Furutani T., Nomura S., Ochi S., Leppold C., et al. Impacts of the 2011 Fukushima nuclear accident on emergency medical service times in Soma District, Japan: a retrospective observational study. BMJ Open. 2016;6(9):e013205. doi: 10.1136/bmjopen-2016-013205.
8. Tanigawa K., Tanaka K. Emergency medical service systems in Japan: past, present, and future. Resuscitation. 2006;69(3):365–370. doi: 10.1016/j.resuscitation.2006.04.001.
9. Gauss T., Ageron F.X., Devaud M.L., Debaty G., Travers S., Garrigue D., et al. Association of prehospital time to in-hospital trauma mortality in a physician-staffed emergency medicine system. JAMA Surg. 2019;154(12):1117–1124. doi: 10.1001/jamasurg.2019.3475.
10. Neshige S., Aoki S., Takebayashi Y., Shishido T., Yamazaki Y., Iida K., et al. A longitudinal seizure outcome following the COVID-19 pandemic in 2020 and 2021: transient exacerbation or sustainable mitigation. J Neurol Sci. 2022;434 doi: 10.1016/j.jns.2021.120100.
11. Fountain N.B., Van Ness P.C., Bennett A., Absher J., Patel A.D., Sheth K.N., et al. Quality improvement in neurology: Epilepsy Update Quality Measurement Set. Neurology. 2015;84(14):1483–1487. doi: 10.1212/WNL.0000000000001448.
12. Jaffe E., Strugo R., Bin E., Blustein O., Rosenblat I., Alpert E.A., et al. The role of emergency medical services in containing COVID-19. Am J Emerg Med. 2020;38(7):1526–1527. doi: 10.1016/j.ajem.2020.04.023.
13. Neshige S., Aoki S., Takebayashi Y., Shishido T., Yamazaki Y., Iida K., et al. A longitudinal seizure outcome following the COVID-19 pandemic in 2020 and 2021: transient exacerbation or sustainable mitigation. J Neurol Sci. 2022;434 doi: 10.1016/j.jns.2021.120100.
14. The 53rd meeting of Novel Coronavirus Response Headquarters. 2021; Available from: https: //www.kantei.go.jp/jp/singi/novel_coronavirus/th_siryou/sidai_r030122.pdf.
15. Beghi E., Carpio A., Forsgren L., Hesdorffer D.C., Malmgren K., Sander J.W., et al. Recommendation for a definition of acute symptomatic seizure. Epilepsia. 2010;51(4):671–675. doi: 10.1111/j.1528-1167.2009.02285.x.
16. The 2nd Meeting of Subcommittee on Novel Coronavirus Disease Control. 2021; Available from: https://www.cas.go.jp/jp/seisaku/ful/taisakusuisin/bunkakai/dai2/kansensaikakudaiboushi_shihyou_teigen.pdf.
17. S ummary of the Hiroshima City Fire Service Bureau. 2022 September 13, 2022; Available from: https://www.city.hiroshima.lg.jp/site/shobo/12062.html.
18. The summary of the declaration of the state of emergency. 2023; Available from: https://corona.go.jp/news/news_20200421_70.html.
19. Keane S., 25 years of advances in the definition, classification and treatment of status epilepticus. Seizure. 2017;44:65–73. doi: 10.1016/j.seizure.2016.11.001.
20. Copeland J., Epidemiological profile of emergency medical services in Japan: a population-based descriptive study in 2016. Acute Med Surg. 2020;7(1):e485. doi: 10.1002/ams2.485.
21. The 103rd Meeting of the Advisory Board on Countermeasures to COVID-19 Infections. 2022; Available from: https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000121431_00395.html.
22. Spaite D.W., Valenzuela T.D., Meislin H.W., Criss E.A., Hinsberg P. Prospective validation of a new model for evaluating emergency medical services systems by in-field observation of specific time intervals in prehospital care. Ann Emerg Med. 1993;22(4):638–645. doi: 10.1016/S0196-0644(05)81840-2.
23. Nakao S., Katayama Y., Kitamura T., Hirose T., Sado J., Ishida K., et al. Epidemiological profile of emergency medical services in Japan: a population-based descriptive study in 2016. Acute Med Surg. 2020;7(1):e485. doi: 10.1002/ams2.485.
24. Summary of the confirmed cases for a patient with COVID-19 in Hiroshima city. 2023 January 10, 2023; Available from: https://www.city.hiroshima.lg.jp/site/shobo/12062.html.
25. Annual review Hiroshima City Fire Service Bureau. 2022 November 1, 2022; Available from: https://www.city.hiroshima.lg.jp/site/shobo/list1809-3710.html.

26. The 103rd Meeting of the Advisory Board on Countermeasures to COVID-19 Infections. 2022; Available from: https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000121431_00395.html.
27. Summary of the Hiroshima City Fire Service Bureau. 2022 September 13, 2022; Available from: https://www.city.hiroshima.lg.jp/site/shobo/12062.html.
28. Trinka E., Cock H., Hesdorffer D. A definition and classification of status epilepticus—Report of the ILAE Task Force on Classification of Status Epilepticus. Epilepsia. 2015;56:1515–1523. doi: 10.1111/epi.13121.
29. Meldrum B., Horton R. Physiology of status epilepticus in primates. Arch. Neurol. 1973;28:1–9. doi: 10.1001/archneur.1973.00490190019001.
30. DeLorenzo R., Hauser W., Towne A. A prospective, population-based epidemiologic study of status epilepticus in Richmond, Virginia. Neurology. 1996;46:1029–1035. doi: 10.1212/WNL.46.4.1029.
31. Jallon P., Coeytaux A., Galobardes B., Morabia A. Incidence and case-fatality rate of status epilepticus in the Canton of Geneva. Lancet. 1999;353:1496. doi: 10.1016/S0140-6736(99)00583-8.
32. Coeytaux A., Jallon P., Galobardes B., Morabia A. Incidence of status epilepticus in french-speaking Switzerland (EPISTAR). Neurology. 2000;55:693–697. doi: 10.1212/WNL.55.5.693.
33. Wu Y., Shek D., Garcia P., Zhao S., Johnston S. Incidence and mortality of generalized convulsive status epilepticus in California. Neurology. 2002;58:1070–1076. doi: 10.1212/WNL.58.7.1070.
34. Hesdorffer D., Logroscino G., Cascino G., Annegers J., Hauser W. Incidence of status epilepticus in Rochester, Minnesota, 1965–1984. Neurology. 1998;50:735–741. doi: 10.1212/WNL.50.3.735.
35. Betjemann J., Josephson S., Lowenstein D., Burke J. Trends in status epilepticus-related hospitalizations and mortality: Redefined in US practice over time. JAMA Neurol. 2015;72:650–655. doi: 10.1001/jamaneurol.2015.0188.
36. Rossetti A., Logroscino G., Milligan T., Michaelides C., Ruffieux C., Bromfield E. Status epilepticus severity score (STESS): A tool to orient early treatment strategy. J. Neurol. 2008;255:1561–1566. doi: 10.1007/s00415-008-0989-1.
37. Sutter R., Kaplan P., Ruegg S. Independent external validation of the status epilepticus severity score. Crit. Care Med. 2013;41:475–484. doi: 10.1097/CCM.0b013e31829eca06.
38. Michael G., O'Connor R. The diagnosis and management of seizures and status epilepticus in the prehospital setting. Emerg. Med. Clin. N. Am. 2011;29:29–39. doi: 10.1016/j.emc.2010.08.003.
39. Silbergleit R., Durkalski V., Lowenstein D. Intramuscular versus intravenous therapy for prehospital status epilepticus. N. Engl. J. Med. 2012;366:591–600. doi: 10.1056/NEJMoa1107494.
40. Delgado-Escueta A., Wasterlain C., Treiman D., Porter R. Current concepts in neurology: Management of status epilepticus. N. Engl. J. Med. 1982;306:1337–1340. doi: 10.1056/NEJM198206033062205.
41. Lowenstein D.H., Alldredge B.K. Status epilepticus. N. Engl. J. Med. 1998;388:970–976. doi: 10.1056/NEJM199804023381407.
42. Labeled item: The epidemology of status epilepticus in the United States. Dham B., Hunter K., Rincon F. Neurocrit. Care. 2014;20:476–483. doi: 10.1007/s12028-013-9935-x.
43. Jallon P., Morabia A. Incidence of status epilepticus in french-speaking Switzerland (EPISTAR). Neurology. 2000;55:693–697. doi: 10.1212/WNL.55.5.693.
44. Roppolo L., Walters K. Airway management in neurological emergencies. Neurocrit. Care. 2004;1:405–414. doi: 10.1385/NCC:1:4:405.
45. Stone B.J., Chantler P.J., Baskett P.J. The incidence of regurgitation during cardiopulmonary resuscitation: A comparison between the bag valve mask and laryngeal mask airway. Resuscitation. 1998;38:3–6. doi: 10.1016/S0300-9572(98)00068-9.
46. Trinka E., Kälviäinen R. 25 years of advances in the definition, classification and treatment of status epilepticus. Seizure. 2017;44:65–73. doi: 10.1016/j.seizure.2016.11.001.
47. Jaffe E., Strugo R., Bin E., Blustein O., Rosenblat I., Alpert E.A., et al. The role of emergency medical services in containing COVID-19. Am J Emerg Med. 2020;38(7):1526–1527. doi: 10.1016/j.ajem.2020.04.023.
48. Al Amiry A., Maguire B.J. Emergency medical services (EMS) calls during COVID-19: early lessons learned for systems planning (a narrative review) Open Access Emerg Med. 2021;13:407–414. doi: 10.2147/OAEM.S324568.
49. The epidemiology of status epilepticus in the United States. Neshige S., Aoki S., Takebayashi Y., Shishido T., Yamazaki Y., Iida K., et al. J Neurol Sci. 2022;434. doi: 10.1016/j.jns.2021.120100.
50. Dham B., Hunter K., Rincon F. The epidemiology of status epilepticus in the United States. Neurocrit. Care. 2014;20:476–483. doi: 10.1007/s12028-013-9935-x.
51. Beghi E., Carpio A., Forsgren L., Hesdorffer D.C., Malmgren K., Sander J.W., et al. Recommendation for a definition of acute symptomatic seizure. Epilepsia. 2010;51(4):671–675. doi: 10.1111/j.1528-1167.2009.02285.x.
52. Treiman DM, Walton NY, Kendrick C. A progressive sequence of electroencephalographic changes during generalized convulsive status epilepticus. Epilepsy Res. 1990 Jan-Feb;5(1):49–60. doi: 10.1016/0920-1211(90)90065-4. PMID: 2303022. [DOI] [PubMed] [Google Scholar]
53. Chin R.F., Neville B.G., Peckham C., Bedford H., Wade A., Scott R.C. Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: prospective population-based study. Lancet. 2006 Jul 15;368(9531):222–229. doi: 10.1016/S0140-6736(06)69043-0. [DOI] [PubMed] [Google Scholar]

54. DeLorenzo R.J., Towne A.R., Pellock J.M., Ko D. Status epilepticus in children, adults, and the elderly. Epilepsia. 1992;33:15–25. doi: 10.1111/j.1528-1157.1992.tb06223.x. [DOI] [PubMed] [Google Scholar]
55. Goldberg E.M., Coulter D.A. Mechanisms of epileptogenesis: a convergence on neural circuit dysfunction. Nat Rev Neurosci. 2013;14(5):337–349. doi: 10.1038/nrn3482. [DOI] [PMC free article] [PubMed] [Google Scholar]
56. Pitkänen A., Lukasiuk K. Mechanisms of epileptogenesis and potential treatment targets. Lancet Neurol. 2011 Feb;10(2):173–186. doi: 10.1016/S1474-4422(10)70310-0. [DOI] [PubMed] [Google Scholar]
57. Nordli D.R., Moshé S.L., Shinnar S., Hesdorffer D.C., Sogawa Y., Pellock J.M., et al. Acute EEG findings in children with febrile status epilepticus: results of the FEBSTAT study. Neurology. 2012 Nov 27;79(22):2180–2186. doi: 10.1212/WNL.0b013e3182759766. [DOI] [PMC free article] [PubMed] [Google Scholar]
58. Elaboration: Sutter R., Kaplan P., Ruegg S. Independent external validation of the status epilepticus severity score. Crit. Care Med. 2013;41:475–484. doi: 10.1097/CCM.0b013e31829eca06. [DOI] [PubMed] [Google Scholar]
59. Shorvon S. Status epilepticus: its clinical features and treatment in children and adults. 1994 Jul 21. Cambridge University Press. [cited 2021 Jul 24]; Available from: https://www.cambridge.org/core/books/status-epilepticus/5D31AA6CC71423D394000ABEBF906CD0
60. Dham B., Hunter K., Rincon F. The epidemiology of status epilepticus in the United States. Neurocrit Care. 2014;20:476–483. doi: 10.1007/s12028-013-9935-x. [DOI] [PubMed] [Google Scholar]
61. Treiman DM, Walton NY, Kendrick C. A progressive sequence of electroencephalographic changes during generalized convulsive status epilepticus. Epilepsy Res. 1990;5(1):49–60. doi: 10.1016/0920-1211(90)90065-4.
62. Kapur J., Elm J., Chamberlain J.M., Barsan W., Cloyd J., Lowenstein D., et al. Randomized trial of three anticonvulsant medications for status epilepticus. N Engl J Med. 2019;381(22). doi: 10.1056/NEJMoa1905795. [DOI] [PMC free article] [PubMed] [Google Scholar]
63. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the international league against epilepsy: position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):522–530. 10.1111/epi.13670 [DOI] [PubMed] [Google Scholar]
64. NICE . Epilepsies: diagnosis and management, Clin Guidel [CG137]. 2016. Available from: https://www.nice.org.uk/guidance/cg137
65. Beghi E, Giussani G, Nichols E, Abd-Allah F, Abdela J, Abdelalim A, et al. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the global burden of disease study 2016. Lancet Neurol. 2019;18(4):357–375. 10.1016/S1474-4422(18)30454-X [DOI] [PMC free article] [PubMed] [Google Scholar]
66. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):512–521. 10.1111/epi.13709 [DOI] [PMC free article] [PubMed] [Google Scholar]
67. Elger CE, Hoppe C. Diagnostic challenges in epilepsy: seizure under-reporting and seizure detection. Lancet Neurol. 2018;17(3):279–288. 10.1016/S1474-4422(18)30038-3 [DOI] [PubMed] [Google Scholar]
68. Mefford HC. Clinical genetic testing in epilepsy. Epilepsy Curr. 2015;15(4):197–201. 10.5698/1535-7511-15.4.197 [DOI] [PMC free article] [PubMed] [Google Scholar]
69. Krumholz A, Wiebe S, Gronseth GS, Gloss DS, Sanchez AM, Kabir AA, et al. Evidence-based guideline: management of an unprovoked first seizure in adults: report of the guideline development Subcommittee of the American Academy of neurology and the American Epilepsy Society. Epilepsy Curr. 2015;15(3):144–152. 10.5698/1535-7597-15.3.144 [DOI] [PMC free article] [PubMed] [Google Scholar]
70. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross JH, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475–482. 10.1111/epi.12550 [DOI] [PubMed] [Google Scholar]
71. Scottish Intercollegiate Guidelines Network , "Guideline 81: diagnosis and management of epilepsies in children and young people," NHS Qual Improv Scotl, pp. 1–48, 2005. Available from: http://www.sign.ac.uk/guidelines/fulltext/81/index.html. [Google Scholar]
72. NICE . Epilepsies in children, young people and adults. NICE guideline. [NG217]. 2022. Available from: https://www.nice.org.uk/guidance/ng217/resources/epilepsies-in-children-young-people-and-adults-pdf-66143780239813