Title	Emergency medical service response for cases of stroke-suspected seizure: A population-based study
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Relation	

Emergency medical service response for cases of stroke-suspected seizure: A population-based study

Abstract

Objectives: We evaluated the on-scene time of emergency medical services (EMS) for cases where discrimination between acute stroke and epileptic seizures at the initial examination was difficult and identified factors linked to delays in such scenarios.

Materials and Methods: A retrospective review of cases with suspected seizure using the EMS database of fire departments across six Japanese cities between 2016 and 2021 was conducted. Patient classification was based on transport codes. We defined cases with stroke-suspected seizure as those in whom epileptic seizure was difficult to differentiate from stroke and evaluated their EMS on-scene time compared to those with epileptic seizures.

Results: Among 30,439 cases with any seizures, 292 cases of stroke-suspected seizure and 8,737 cases of epileptic seizure were included. EMS on-scene time in cases of stroke-suspected seizure was shorter than in those with epileptic seizure after propensity score matching (15.1±7.2 min vs. 17.0±9.0 min; p=0.007). Factors associated with delays included transport during nighttime (odds ratio [OR], 1.73, 95% confidence interval [CI] 1.02–2.93, p=0.041) and transport during the 2020–2021 pandemic (OR, 1.77, 95% CI 1.08–2.90, p=0.022).

Conclusion: This study highlighted the difference between the characteristics in EMS for stroke and epileptic seizure by evaluating the response to cases with stroke-suspected seizure. Facilitating prompt and smooth transfers of such cases to an appropriate medical facility after admission could optimize the operation of specialized medical resources.

Abbreviations:

EMS, emergency medical services; LVO, large vessel occlusion; ER, emergency room; SE, status epilepticus; FSB, Fire Service Bureau; OR, odds ratio; CI, confidence interval; PSC, primary stroke center; n. s., not significant; SD, standard deviation

1. INTRODUCTION

Emergency medical services (EMS) are designed to facilitate the handling of patients requiring emergency treatment and provide rapid transportation to an appropriate medical facility (1). Clinicians are unable to control some of the confounding factors of EMS response. However, clinicians can use triage systems to reduce on-scene time, including the interval between the request for transport to the hospital and departure from the scene (2). Delays in the on-scene time of the EMS response can have detrimental effects on patient outcomes, and sociomedical changes (e.g., the COVID-19 pandemic) accompanied by a surge in EMS demand lead to EMS delays (3-10). Therefore, rapid intervention may not be readily available during periods of high EMS demand, potentially delaying treatment for patients with complex management needs. This delay could be especially critical in cases of neurological emergencies, where timely intervention is crucial.

Optimal transportation of patients is crucial for treating suspected cases of acute large vessel occlusion (LVO) (2,11-13). However, medical conditions that mimic the symptoms of stroke, such as epilepsy, migraine, hypoglycemia, and psychogenic causes, present the challenge of time-critical decision-making in emergency room (ER) settings (14,15). Among these conditions, epileptic seizure resulting in status epilepticus

(SE) is a common neurological emergency that requires prompt intervention (16,17). Therefore, clinicians must be prepared for SE intervention alongside addressing the intervention for LVO when confronted with cases where distinguishing epileptic seizure from stroke is challenging. These clinical issues can be challenges to the EMS in the optimal management of medical resources, and there is limited knowledge on the EMS of these patients with stroke-suspected seizure.

Therefore, we conducted this study to evaluate the difference between EMS for stroke and epileptic seizure by comparing and analyzing the EMS response in cases mimicking stroke symptoms and epileptic seizure. Additionally, we identified factors affecting EMS response to explore the optimal management of medical resources. We made the following hypotheses. First, since ER staff struggle with the management of both acute stroke and epileptic seizure cases, the on-scene time would be longer in cases where there is further difficulty in differentiating epileptic seizure from stroke compared to those with a clear epileptic seizure diagnosis. Second, high EMS demand would be associated with longer on-scene time in these complex cases.

2. MATERIALS & METHODS

Study design

In this retrospective population-based cohort study across six major cities in Western Japan, we examined cases transported by the Fire Service Bureau (FSB) EMS between 2016 and 2021 for seizures in which there was difficulty in the initial differentiation between an epileptic seizure and a stroke. Among these cases, we evaluated the differences between on-scene time in patients with stroke suspected of seizures (hereafter referred to as "stroke-suspected seizure") and those with epileptic seizures. We also aimed to identify factors delaying the on-scene time for those with stroke-suspected seizure. Data were retrieved from each city FSB database individually to assess patient characteristics and the EMS time records. Local government official reports and open data were used to evaluate the impacts at the demographic and societal level. The study protocol was based on our previous investigations (10,18). This study was approved by the Hiroshima University Hospital Ethics Committee (approval no. E2021-2566-01).

Geography and EMS of the study areas

This study included the top six most populated cities in the Chugoku-Shikoku region of

Western Japan (Hiroshima, Okayama, Matsuyama, Kurashiki, Fukuyama, and Takamatsu, each with 500,000-1,000,000 inhabitants). The EMS system in Japan utilizes a uniform nationwide design and is operated throughout the country by local fire departments and emergency medical service personnel, which triage patients for optimal resource utilization (1). The system focuses on pre-hospital triage by emergency medical personnel according to the acuity of the patient, and emergency medical personnel contact a specific hospital to request transportation for patients in need of emergency care. The decision to accept or decline the request is made by hospital doctors. If the hospital declines, the EMS must make a subsequent request to another hospital. This system highlights the significance of the on-scene time in mirroring the challenges faced by ER doctors when deciding on transportation requests. After transportations, ER doctors at the receiving hospital determine diagnoses and assign transport codes for each patient.

Data sources and inclusion criteria

EMS system records are collected using standardized data collection forms that include patient characteristics and the time course of transport (19). We utilized the transport codes in the EMS patient reports to identify cases involving suspected seizures or epilepsy (20). We retrospectively extracted the personal clinical data using the codes from this database (Figure 1). First, we retrieved all cases with suspected seizure or epilepsy due to any causes (transport code of "epileptic seizure," "epilepsy," "convulsive seizure," and "SE," with or without "suspected" and with or without any transport code) diagnosed in the ER from each city's FSB. Since the causes of acute symptomatic seizures can vary leading to differences in emergency facility selection based on the cause, we chose to work with a homogenous patient cohort (21). Therefore, we excluded patients aged <16 years and those with acute symptomatic seizures due to non-stroke etiology (e.g., metabolic, toxic, and infectious) or psychiatric causes (21). Second, we included patients with epileptic seizure (transport code of "epileptic seizure," "epilepsy," "convulsive seizure," or "SE" without the term "suspected") and included them in an "epileptic seizure" group. Conversely, we included in the "stroke-suspected seizure" group those patients for whom there was difficulty in differentiating epileptic seizure from stroke (transport code of "stroke," "cerebral infarction," "cerebral hemorrhage," "subarachnoid hemorrhage," and "transient ischemic attack" with or without "suspected," without any other transport code) (22). Therefore, patients for whom there was a doubt between a diagnosis of epileptic seizure or stroke were defined as having a dual initial diagnosis (i.e., transport code associated with stroke in addition to that associated with suspected epilepsy or seizure). The database used in this study was obtained from the same cohort as in our previous reports (18).

Observational periods

The study period was divided into two observational periods based on temporal spikes in the number of infections during the COVID-19 pandemic in Japan: "pre-period," a 4-year phase before the COVID pandemic (2016–2019); and "pandemic period," a 2-year phase after the World Health Organization Country Office in China was informed of cases of pneumonia of unknown etiology (2020–2021) (23).

Demographic and clinical parameters for EMS response

We evaluated patient-related data such as age, sex, and initial field vital signs (body temperature and level of consciousness). We defined fever as body temperature ≥37.5°C. Patients with impaired consciousness were defined as those who were neither fully awake nor oriented. Additionally, the time-related variables of date and time of transfer were considered. Daytime and nighttime transfers were defined as those that occurred between 08:00 and 19:59 and between 20:00 and 07:59, respectively.

EMS response time

The EMS response time was determined based on the time interval model defined by Spaite et al. (24). On-scene time was defined as the time elapsed between arrival at the scene and departure, comprising access to the patient, initial assessment, on-scene treatment, and patient removal (24).

Confounding factors for EMS response

As EMS transport is influenced by sociomedical factors (9,25), we also evaluated the total EMS call volume occurring in each fire service area per month for all causes (e.g., trauma, psychiatric, and internal medical causes such as COVID-19) during the same month (26). We defined the mean total EMS call volume in each area during the pre-period as the baseline reference for subsequent comparisons.

Data analyses

First, we conducted an overview of the demographic and clinical characteristics and EMS on-scene time for each patient with stroke-suspected seizure and epileptic seizures. Second, our previous report revealed there are some confounding factors associated with on-scene time for cases with epileptic seizure (10,18). Therefore, to address the effect of confounding factors, we conducted mean propensity score matching at a 1:1 ratio to divide the patients into those with stroke-suspected seizure and those with epileptic seizure. We evaluated the differences in each characteristic after matching. We defined the following factors as explanatory variables: age, sex, area of the FSB, and date of transfer (pre- or pandemic period). The propensity score for logit transformation was calculated by setting the caliper width at 0.2. Similarities between the transformed logistic scores and matching variables were confirmed using a distribution map (27). Third, we focused on identifying the factors associated with delaying the on-scene time of the cases with stroke-suspected seizure. Thus, we divided them into two groups: "delayed", with an on-scene time ≥17 min, and "non-delayed", with an on-scene time <17 min. This was based on the median on-scene time recorded in cases with LVO in the same area (2). We subsequently evaluated the difference in each characteristic between the two groups and performed multivariable logistic analysis to identify the factors associated with delaying the on-scene time using the significant variables in the univariate analysis, with the force entry method to estimate the odds ratios (OR) for delayed on-scene time. The parameters for this step were as follows: age, age ≥75 years, sex, impaired consciousness, transport at night, total EMS call volume per month for all causes during the same month above baseline, and transport during the pre or pandemic period. Categorical variables are presented as numbers and percentages. Continuous variables are presented as means with standard deviations or medians and interquartile ranges. The statistical significance of intergroup differences was assessed using $\chi 2$ tests for categorical variables and Student's t-test or the Mann–Whitney U test for continuous variables. If parts of the data were missing, pairwise deletions were used for these analyses. In all analyses, $p > 0.05$ was considered significant. All statistical analyses were performed using the JMP Pro software (version 17; SAS Institute, Cary, NC, USA).

3. RESULTS

Patient characteristics and comparison of cases with stroke-suspected seizure and epileptic seizure

Among the 30,439 cases of seizures for any cause transported by EMS, 21,410 cases involving patients aged <16 years, acute symptomatic seizures due to non-stroke etiology, or psychiatric causes, were excluded. Thus, 292 and 8,737 cases were included in the "stroke-suspected seizure" group and "epileptic seizure" group, respectively (Figure 1). Significant differences in the mean age ($p<0.001$) and mean on-scene time ($p=0.030$) were observed between the stroke-suspected seizure and epileptic seizure groups (Table 1). The propensity score matched 292 cases from each group. We found that the mean on-scene time was significantly shorter in patients with stroke-suspected seizure than in those with epileptic seizure (15.1±7.2 min vs. 17.0±9.0 min; $p=0.007$; Table 2).

Factors associated with on-scene time delay in cases with stroke-suspected seizure

Among 292 cases of stroke-suspected seizure, 104 were included in the delayed group. Significant differences in prevalence of an age of 75 years or older, those being transported during the nighttime, and those being transported during the pandemic were seen in between the "delayed" and "non-delayed" groups. However, total EMS call volume was not associated with delay (Table 3). The multivariable logistic analysis showed that transportation during the nighttime (OR, 1.73, 95% confidence interval [CI] 1.02–2.93, p=0.041) and transportation during the pandemic period (OR, 1.77, 95% CI 1.08–2.90, p=0.022) were associated with delayed on-scene times in cases of stroke-suspected seizure (Table 4).

4. DISCUSSION

This multi-regional study using an EMS database underscored the difference in EMS between patients with suspected stroke and suspected epileptic seizure in Japan. Reasons for this included the observation that, in comparison to the epileptic seizure group, the "stroke-suspected seizure" group tended to elicit quicker responses by clinicians. Additionally, this study highlighted that clinicians faced challenges in providing emergency medicine for these patients during nighttime shifts and sociomedical changes, particularly during the pandemic.

This study revealed that the on-scene time for stroke-suspected seizure was shorter than that for epileptic seizure. Additionally, we focused on the difference in characteristics of the EMS for patients with epileptic seizure and stroke in Japan. The Japan Stroke Society operates specialized stroke centers, such as comprehensive stroke centers and primary stroke centers (PSC), throughout Japan (12,28). As a result, the EMS for stroke-suspected patients is now provided by stroke specialists, mainly at PSCs (12). On the other hand, the EMS for epileptic seizure is provided by emergency and critical care medical centers cooperating with the specialized epilepsy center (10,18). Therefore, while stroke specialists take the lead in handling cases of stroke, epilepsy specialists do not necessarily take the lead in handling cases of suspected epileptic seizures. Although most cases of epileptic seizures recover spontaneously, early detection and intervention of refractory cases should not be ignored. Therefore, it should be recognized that there is a significant burden on EMS for suspected epileptic seizure (20).

Important advances in endovascular thrombectomy for LVO have recently been made, which in turn require medical providers to ensure rapid access, prehospital identification, and triage of these patients (29). To this end, the optimization of pre-admission triage for patient suspected of LVO is currently ongoing (2,12,29,30). Rapid transportation to a specialized stroke center for those with a definite diagnosis of LVO and requiring thrombectomy is ideal. However, strokes arising from a proximal LVO account for approximately 20% of all strokes (12). Indeed, although misdiagnosis of cases with acute ischemic stroke, including epileptic seizure, can occur, clinicians should not preclude potential candidates for thrombolytic therapy considering the efficacy of thrombolysis and its favorable outcomes (15,31-35). Therefore, optimal coordination and interhospital transport become crucial in addressing this issue, with minor cases that do not necessitate thrombectomy being transferred to a non-PSC, while refractory SE cases are transferred to an intensive care unit, where prolonged EEG monitoring is available (16).

This study demonstrated that approximately one-third of the "stroke-suspected seizure" group were transported with a longer on-scene time than the median on-scene time of cases with LVO in the same area (2). Both the time of day and sociomedical changes affected these delays. Although PSCs have been established as integrated emergency response systems by a multidisciplinary team twenty-four seven, arrival during the nighttime or during sociomedical changes delays the time elapsed until treatment even in stroke patients (36-39). However, adapting the workflows to these conditions enabled the resolution of these issues (40). Therefore, clinicians should consider optimal workflows for these patients with stroke-suspected seizure.

This study had several limitations. First, the diagnosis of stroke or epileptic seizures was provided by ER doctors, which affected the accuracy of diagnosis. Second, this study evaluated the on-scene time for cases in which it was difficult to differentiate between epileptic seizures and stroke compared to cases of epileptic seizures but not compared to those with stroke. Instead, we evaluated the median on-scene time of cases of LVO in the same area as reference data (2). Third, we did not evaluate regional differences. Although the EMS system in Japan is well-designed, the characteristics of healthcare systems affect EMS response (1,18). Therefore, population-based data, including large numbers of patients, are needed to confirm the significance and generalizability of the present results. Fourth, this study did not evaluate how differences of the on-scene time in patients with stroke-suspected epilepsy affected their outcomes.

5. CONCLUSION

This study highlighted the difference between the characteristics in EMS for stroke and epileptic seizure by evaluating the response to complex patients for whom a clear diagnosis of epileptic seizure or stroke is not available. There is room for improvement in EMS for suspected epileptic seizure, and the knowledge of EMS for stroke that is being established in Japan will help improve this. Additionally, although EMS for stroke patients is well-established, clinicians struggled to treat these cases upon arrival when there were inadequate medical resources. The optimization of a prompt response in cases with neurological emergencies is a major unmet medical need. Therefore, clinicians should keep this in mind and provide optimal transport in these complex cases. Specifically, facilitating the smooth transfer of patients not requiring thrombectomy or refractory cases to appropriate medical facilities could be important to achieve optimal operation for specialized medical resources such as PSCs.

Declarations

Ethics approval and consent to participate:

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with these guidelines. This was a population-based, observational study. Our study was performed using anonymous clinical data under close supervision, following approval by the Ethics Committee of Hiroshima University Hospital (E2021-2566-01). Informed consent was obtained through an opt-out option on the hospital website. All procedures involving human participants were performed in accordance with the 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards.

Consent for publication:

Patients were provided the option to opt out of the study and be excluded from the analysis; however, none of the patients chose to do so.

Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Declarations of interest: none

Authors' contributions:

• Hidetada Yamada and Shiro Aoki: designed and conceptualized the study; analyzed the data; and drafted the manuscript for intellectual content

• Tomohisa Nezu, Shuichiro Neshige, Atsuko Motoda, and Yu Yamazaki: interpreted the data; and revised the manuscript for intellectual content

• Hirofumi Maruyama: revised the manuscript for intellectual content

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Figure legends

Figure 1. Study flowchart

The identifiable personal data of all 30,439 cases with suspected seizure or epilepsy due to any causes diagnosed between January 1, 2016 and December 31, 2021, were obtained from each city FSB and used in the study. After application of the exclusion criteria, patients were divided into a "stroke-suspected seizure" group (n=292) and an "epileptic seizure" group (n=8,737). Mean propensity score matching at a 1:1 ratio was then performed. The following factors were defined as explanatory variables: age, sex, area of the FSB, and date of transfer (pre-period or pandemic-period). FSB, Fire Service Bureau.