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On-scene time delays for epileptic seizures in emergencies during a social pandemic: a population-based study

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Abstract:	Objectives The on-scene time of Emergency Medical Services (EMS), including time for hospital selection, is critical for people in an emergency. However, the outbreak of the novel coronavirus disease 2019 (COVID-19) led to longer delays in providing immediate care for individuals with non-COVID-19-related emergencies, such as epileptic seizures. This study aimed to examine factors associated with on-scene time delays for people with epilepsy (PWE) with seizures needing immediate amelioration. Materials & Methods We conducted a population-based retrospective cohort study for PWE transported by EMS between 2016 and 2021. We used data from the Hiroshima City Fire Service Bureau database, divided into three study periods: “Pre phase”, the phase before the COVID pandemic (2016–2019); “Early phase”, the early phase of the COVID pandemic (2020); and “Middle phase”, the middle phase of the COVID pandemic (2021). We performed linear regression modeling to identify factors associated with changes in EMS on-scene time for PWE during each period. In addition, we estimated the rate of total EMS call volume required to maintain the same on-scene time for PWE transported by EMS during pandemic expansion. Results Among 2,205 PWE transported by EMS, significant differences in mean age and prevalence of impaired consciousness were found between pandemic phases. Total EMS call volume per month for all causes during the same month <5,000 (-0.55 min, 95% confidence interval [CI] -1.02 – -0.08, p=0.022) and transport during the Early phase (-1.88 min, 95%CI -2.75 – -1.00, p<0.001) decreased on-scene time, whereas transport during the Middle phase (1.58 min, 95%CI 0.70 – 2.46, p<0.001) increased on-scene time for PWE transported by EMS. The rate of total EMS call volume was estimated as 0.81 (95%CI -0.04 – 1.07) during the expansion phase of the pandemic to maintain the same degree of on-scene time for PWE transported by EMS before the

	pandemic. Conclusions On-scene time delays on PWE in critical care settings were observed during the Middle phase. When the pandemic expanded, the EMS system required resource allocation to maintain EMS for time-sensitive illnesses such as epileptic seizures. Timely system changes are critical to meet dramatic social changes.
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Response to Reviewers:	Replies to Reviewer 2 We wish to express our earnest appreciation to Reviewer #2 for providing encouraging comments and insightful suggestions that have helped us to improve the paper. Our responses are presented below. Comment 1: Does the EMS system throughout Japan run in a similar fashion to what the authors outline in Hiroshima, or is it unique to this area of Japan? Reply 1: Thank you for the constructive comment. The emergency medical services (EMS) system in Japan is designed uniformly nationwide and activated by a universal emergency call number anywhere in Japan. Upon receiving an emergency call, the fire department sends the nearest available ambulance to the operational site. There are 733 fire department headquarters and 1,714 fire stations. Although there are some variations in each fire department, the median time from EMS call to EMS arrival on the scene was 8 min, with only a 1-min difference across the regions in Japan. Thus, we have added the relevant texts as follows: p. 9, line 131 to 134 (in Materials & Methods) “The EMS system in Japan is designed uniformly nationwide and operated throughout

the country by local fire departments [1, 19]. In Hiroshima city, EMS is through the Hiroshima City Fire Service Bureau, which responds to emergency requests via a universal emergency call number “

In this relation, we revised the texts in Limitation accordingly:
p. 20, line 313 to 315 p. 21, line 316 to line 320 (in Limitation)
“First, the present study was performed using population-based data from a single region. Thus, there are limitations in generalizing the results of this study. As the EMS system in Japan is operated by local fire departments (733 fire departments in total), regional differences in the EMS system and the distribution of medical facilities were not negligible [19, 35]. However, the EMS system in Japan is well designed. The median time between EMS call to EMS arrival on the scene varies only by less than a minute across different regions in Japan [19].”

Comment 2:
In the Results section, the authors exclude 10,115 cases with "acute symptomatic seizures". Can the authors better define what they mean by this and why these patients were excluded from the study?

Reply 2:
Thank you for the pertinent comment. The present study focused on PWE (who had a seizure chronically); because PWE are at risk to require emergency transport services repetitively in their usual. Thus, we did not include a patient with acute symptomatic seizures. To clarify the reason for inclusion criteria and definition of acute symptomatic seizure, we have added the relevant texts as follows:

p. 11, line 155 to line 160 (in Materials & Methods)
“This study focused on patients who experienced chronically recurrent seizures, particularly those who were expected to require emergency transport services repetitively. Thus, PWE were eligible for inclusion. In contrast, patients with acute symptomatic seizures (seizures occur in close temporal relationship with an acute CNS insult, which may be metabolic, toxic, structural, infectious, or due to inflammation) and psychiatric causes were excluded [21].”

Along with a newly added reference:
p. 27, line 437 to line 438 (in References)
“[21]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): 671–5.”

We also revised the relevant texts in Results accordingly:
p. 16, line 232 to line 233 (in Results)
“Among 12,320 cases with any seizures transported by EMS, 10,115 cases with < 16 years of age, with acute symptomatic seizures, or psychiatric causes were excluded.”

Comment 3:
In the Conclusion section, the authors provide some suggestions but I believe the paper would benefit from a paragraph on the larger implications of the study regarding anticipating and ensuring resources and funding for similar public health emergencies to ensure adequate provision of emergency health care.

Reply 3:
Thank you for the fruitful comments and suggestions. We essentially agree with you. Thus, we have revised the conclusion accordingly:

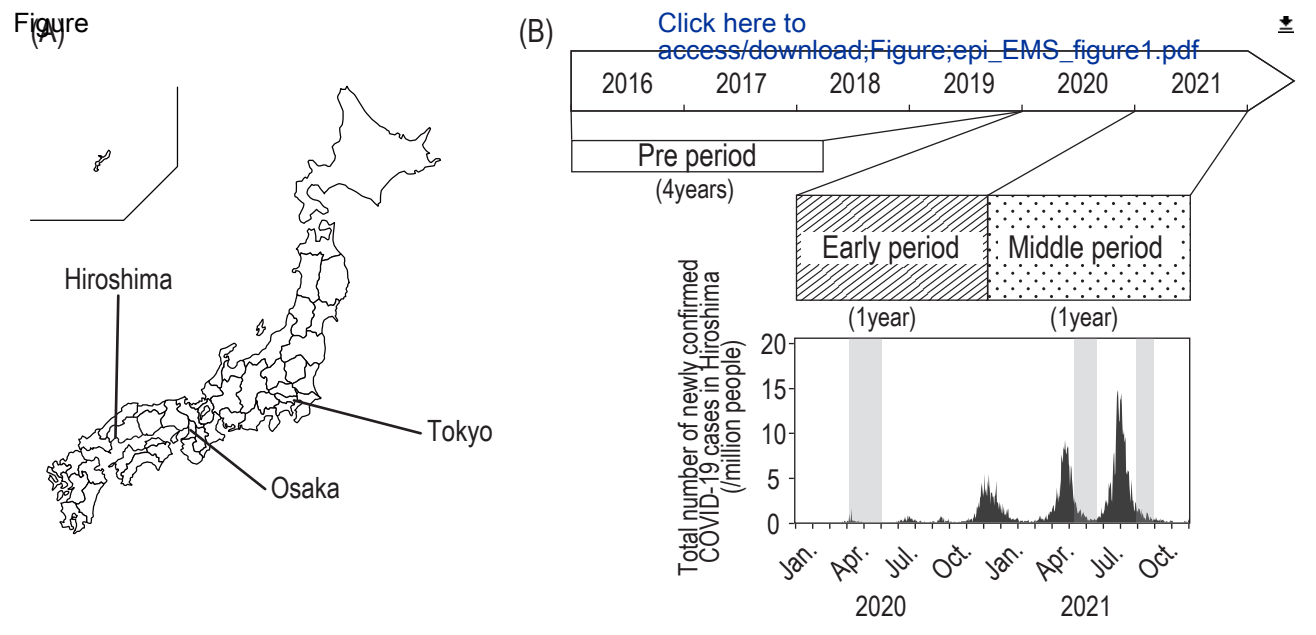
p. 22, line 336 to line 341 (in Conclusions)
“Thus, our study underscores the need for national and local governments to prepare and allocate resources and funding for comparable public health crises, in order to ensure sufficient availability of emergency medical services (EMS) and healthcare.

	Additionally, clinicians should also consider providing intensive follow-up through telemedicine to prevent occasional seizure worsening for PWE during pandemics.”

Highlights

- On-scene time delays for epileptic seizures were prominent during the pandemic.
- Emergency total call volume affected on-scene time for epileptic seizure.
- Resource allocation is required to maintain emergency medicine during a pandemic.

Figure


(A)
Hiroshima
Tokyo
Osaka
(B)
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2016
2017
2018
2019
2020
2021
Pre period
(4years)
Early period
Middle period
(1year)
(1year)
Total number of newly confirmed
COVID-19 cases in Hiroshima
(/million people)
20
15
10
5
0
Jan.
Apr.
Jul.
Oct.
Jan.
Apr.
Jul.
Oct.
2020
2021

Figure

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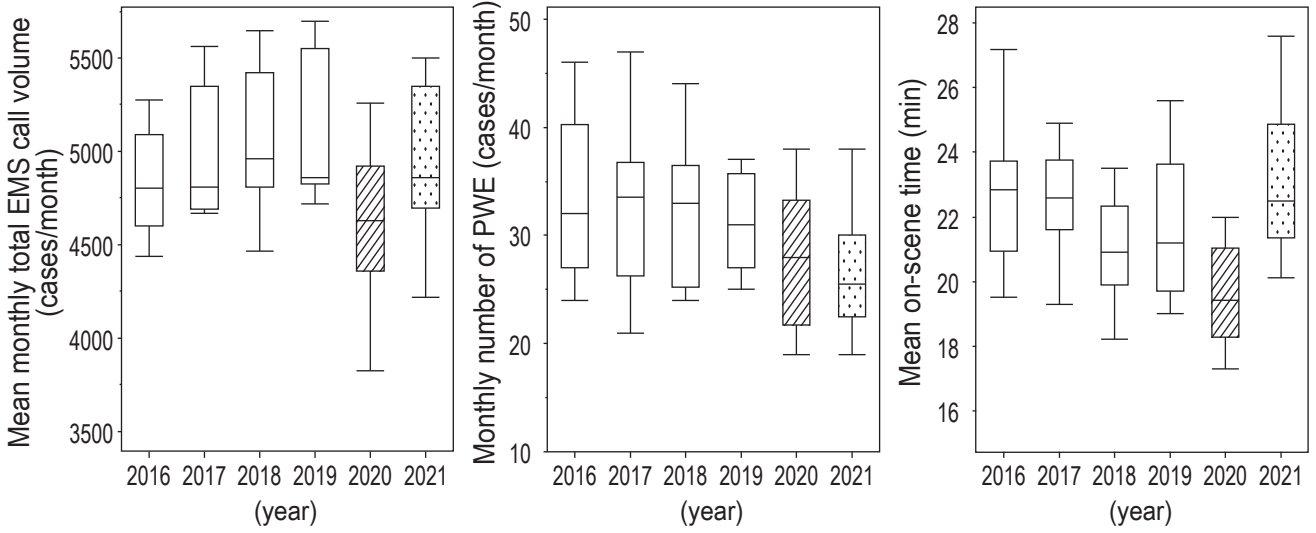

On-scene time delays for epileptic seizures in emergencies during a social pandemic: a population-based study

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Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethics approval statement

This study was approved by the Ethics Committee of Hiroshima University Hospital (approval no. E2021-2566-01).

Patient consent statement

All patients provided informed consent to participate.

Abstract

***Objectives*:** The on-scene time of Emergency Medical Services (EMS), including time for hospital selection, is critical for people in an emergency. However, the outbreak of the novel coronavirus disease 2019 (COVID-19) led to longer delays in providing immediate care for individuals with non-COVID-19-related emergencies, such as epileptic seizures. This study aimed to examine factors associated with on-scene time delays for people with epilepsy (PWE) with seizures needing immediate amelioration.

***Materials & Methods*:** We conducted a population-based retrospective cohort study for PWE transported by EMS between 2016 and 2021. We used data from the Hiroshima City Fire Service Bureau database, divided into three study periods: "Pre phase", the phase before the COVID pandemic (2016–2019); "Early phase", the early phase of the COVID pandemic (2020); and "Middle phase", the middle phase of the COVID pandemic (2021). We performed linear regression modeling to identify factors associated with changes in EMS on-scene time for PWE during each period. In addition, we estimated the rate of total EMS call volume required to maintain the same on-scene time for PWE transported by EMS during pandemic expansion.

***Results*:** Among 2,205 PWE transported by EMS, significant differences in mean age and prevalence of impaired consciousness were found between pandemic phases. Total

EMS call volume per month for all causes during the same month <5,000 (-0.55 min, 95% confidence interval [CI] -1.02 – -0.08, p=0.022) and transport during the Early phase (-1.88 min, 95%CI -2.75 – -1.00, p<0.001) decreased on-scene time, whereas transport during the Middle phase (1.58 min, 95%CI 0.70 – 2.46, p<0.001) increased on-scene time for PWE transported by EMS. The rate of total EMS call volume was estimated as 0.81 (95%CI -0.04 – 1.07) during the expansion phase of the pandemic to maintain the same degree of on-scene time for PWE transported by EMS before the pandemic.

***Conclusions*:** On-scene time delays on PWE in critical care settings were observed during the Middle phase. When the pandemic expanded, the EMS system required resource allocation to maintain EMS for time-sensitive illnesses such as epileptic seizures. Timely system changes are critical to meet dramatic social changes.

Keywords: people with epilepsy; emergency medical service; on-scene time delay; resource allocation; total call volume; non-COVID-19 critical disease

Abbreviations:

EMS, Emergency medical services; PWE, people with epilepsy; COVID-19, coronavirus disease 2019; ANOVA, analysis of variance; SD, standard deviation; CI, confidence interval

1. Introductions

Emergency medical services (EMS) facilitate the categorization of hospital resources to identify hospitals capable of handling emergency patients and enable EMS personnel to rapidly transport patients to appropriate medical facilities [1]. In EMS systems, the on-scene time, including the time required for on-site treatment and the time for selection of a hospital, is critical in life-threatening situations. A delay in definitive treatment can lead to unfavorable outcomes [2-6]. Epileptic seizures resulting in status epilepticus is an emergency disease in which “time is brain”. The prognosis for status epilepticus deteriorates with increasing seizure duration [7]. Thus, extended on-scene time can result in poorer prognosis for people with epilepsy (PWE).

The novel coronavirus disease 2019 (COVID-19) has had a tremendous impact on medical care worldwide [8]. In the EMS setting, various impacts became visible following the outbreak of COVID-19, including a surge in the number of EMS calls, delays in EMS response times, and declines in non-COVID-19 emergency cases [9, 10]. In addition, people who required immediate care for non-COVID-19 causes faced longer delays during the pandemic, which could have critical implications for neurological prognosis [11, 12]. PWE are sensitive to dramatic changes in social situations and seizure exacerbation has been reported in 17.5% of PWE during the

pandemic [13, 14]. However, whether these PWE were transported promptly or experienced delays during the pandemic is uncertain, highlighting the need to examine emergency responses for PWE using EMS.

The factors contributing to on-scene time delays in EMS during unusual circumstances, including pandemics, are numerous and encompass a lack of human and material resources [15]. Identifying the factors associated with on-scene time delays in EMS during a pandemic could shed light on the limitations of the medical care system for PWE during future unusual circumstances. We therefore hypothesized that on-scene time delays in the treatment of PWE would be visible in EMS settings during the pandemic. In addition, such situations may be associated with demand-supply gaps in EMS, as the volume of EMS calls exceeded the availability of local medical resources, regardless of the number of PWE in emergency conditions. To this end, we conducted a longitudinal population-based study to identify factors associated with on-scene time delays in the treatment of PWE in emergencies, and to evaluate the demand-supply gap in EMS.

2. Materials & Methods

2.1. Study design

We conducted this population-based retrospective cohort study for PWE transported by the Hiroshima City Fire Service Bureau EMS between 1 January 2016 and 31 December 2021. Data were retrieved from the Hiroshima City Fire Service Bureau database, including patient characteristics and EMS time records. To evaluate the impacts of demographic and social factors, we used local and national government official reports and EMS provider reports. This study was approved by the Hiroshima University Hospital Ethics Committee (approval no. E-2566).

2.2. Geography and the medical care system in Hiroshima city

Hiroshima city is an ordinance-designated city in western Japan, with an urban and suburban area of 906.69 km^2 and a population of approximately 1.19 million (Figure 1A) [16]. Trends in newly confirmed patients with COVID-19 per million people in this area are summarized in Figure 1B [17, 18]. The EMS system in Japan is designed uniformly nationwide and operated throughout the country by local fire departments [1, 19]. In Hiroshima city, EMS is through the Hiroshima City Fire Service Bureau, which responds to emergency requests via a universal emergency call number.

The total EMS call volume for all causes before the pandemic in this area was about 55,000–60,000 per year and 4,500–5,500 per month [20]. Monthly total EMS call volume trends with all causes in this area are summarized in Figure 2 [20]. EMS for PWE in Hiroshima city have been provided by some emergency and critical care medical centers cooperating with the Epilepsy Center in Hiroshima University Hospital, the largest epilepsy center in Hiroshima prefecture, accredited by the Japanese Epilepsy Society.

2.3. Data sources

EMS system records are collected using standardized data collection forms and include patient characteristics, time of day, and time course of transport [19]. Emergency room doctors at the receiving hospital clinically determine diagnoses for the illness. These data are completed by EMS personnel and then transferred to the information center at the local fire department [19]. In the present study, we used data for all emergency patients with epileptic seizures who required EMS in 2016–2021 obtained from Hiroshima City Fire Service Bureau after removal of all personal identifiers.

2.4. Inclusion and exclusion criteria

We included patients ≥16 years of age who experienced an epileptic seizure and were transported by the Hiroshima City Fire Service Bureau EMS between 1 January 2016 and 31 December 2021. This study focused on patients who experienced chronically recurrent seizures, particularly those who were expected to require emergency transport services repetitively. Thus, PWE were eligible for inclusion. In contrast, patients with acute symptomatic seizures (seizures occur in close temporal relationship with an acute CNS insult, which may be metabolic, toxic, structural, infectious, or due to inflammation) and psychiatric causes were excluded [21].

2.5. Observational periods

This study period was divided into three observational periods based on temporal spikes in infections during the COVID-19 pandemic in Japan: a 4-year phase before the COVID pandemic ("Pre period", January 2016–December 2019, representing baseline data); a 1-year phase early in the COVID pandemic ("Early period", January–December 2020, a year after the World Health Organization Country Office in China was informed of cases of pneumonia of unknown etiology); and a 1-year phase in the middle of the COVID pandemic ("Middle period", January–December 2021, a year after the COVID-19 vaccine started in Japan) (Fig. 1B) [18, 22].

2.6. Demographic and clinical parameters for EMS response

We evaluated patient-associated factors including age, sex, and initial field vital signs (level of consciousness and body temperature). We classified patients with body temperature ≥37.5°C as having fever and patients in states other than fully awake and oriented as having impaired consciousness. We also evaluated clock-associated factors as the date and time of day, divided into daytime (08:00–19:59) and nighttime (20:00–07:59).

2.7. EMS response time

EMS response time was defined as the elapsed time from initiation of an EMS call to arrival at a hospital, and was further divided into three categories: response time; on-scene time; and transport time [15, 23]. On-scene time was defined as the time from arrival at the scene to departure from the scene [15, 23].

2.8. Confounding factors for EMS response

Operations of the EMS were influenced by several social-related factors, particularly during the pandemic [9]. We thus also examined socio-medical conditions concurrent

189 with the transportation of PWE by EMS, including total EMS call volume per month for
190 all causes (such as trauma, internal medical causes, and psychiatric causes) during the
191 same month, total number of newly confirmed COVID-19 cases per week per million
192 people on the same day, occupation rate of hospital beds on the same day, and
193 declaration of a state of emergency. Total EMS call volume per month was typically
194 around 4,500–5,500, and was categorized as decreasing for values ≤5,000 and
195 increasing for values >5,000. In addition, we determined expansion of the pandemic
196 using indicators determined by the government office, i.e., total number of newly
197 confirmed patients with COVID-19 per week per million people >25 and occupation of
198 total hospital beds >50% [24].
199
200 **2.9. Data analyses**
201 To identify factors associated with a change in emergency transporting time for PWE
202 during the COVID-19 pandemic, we performed a three-step analysis. First, we analyzed
203 the demographic characteristics, clinical characteristics, EMS on-scene time, and socio-
204 medical situations of each patient in the study period. We performed analysis of
205 variance (ANOVA) followed by Tukey's post-hoc test for categorical variables, and the
206 chi-square test adding to residual analysis for continuous variables to identify features

of each phase in the pandemic period.

Second, we performed linear regression modeling to identify factors associated with changes in EMS on-scene time for patients with seizures during each period: the whole period, 2016–2021 (Model 1); the pre-pandemic period, 2016–2019 (Model 2); and the pandemic period, 2020–2021 (Model 3). Parameters for each model were: Model 1, age per 1-year increase, impaired consciousness, transport during daytime, total EMS call volume per month for all causes during the same month ≤5,000, and transport during the Pre, Early, or Middle phase of the pandemic. Model 2: age per 1-year increase, impaired consciousness, transport during daytime, and total EMS call volume per month for all causes during the same month ≤5,000. Model 3: age per 1-year increase, impaired consciousness, transport during daytime, total EMS call volume per month for all causes during the same month ≤5,000, total number of newly confirmed COVID-19 cases per week per million people during the same day ≤25, occupancy of total hospital beds during the same day ≤50%, and being under a declaration of a state of emergency [19, 25]. We conducted pairwise deletion for this analysis.

Third, the rate of total EMS call volume per month for all causes was reverse-estimated to maintain the same degree of on-scene time for PWE transported by EMS during the

non-expansion phase of the pandemic (total number of newly confirmed COVID-19 cases per week per million people ≤25, and hospital bed occupancy ≤50%) or expansion phase of the pandemic (total number of new confirmed COVID-19 cases per week per million >25, and hospital bed occupancy >50%). In all analyses, values of $p<0.05$ were considered significant. All statistical analyses were conducted using JMP Pro software (version 16; SAS Institute, Cary, NC, USA).

3. Results

Among 12,320 cases with any seizures transported by EMS, 10,115 cases with < 16 years of age, with acute symptomatic seizures, or psychiatric causes were excluded. Thus, we reviewed the cases of 2,205 PWE transported by EMS (Table 1). Significant differences in mean age and prevalence of impaired consciousness were seen between phases of pandemic period. During the Early phase, mean on-scene time for EMS was 19.6 ± 8.2 min and mean total EMS call volume per month for all causes was 4,665.6 ± 411.0, both of which were lower than those observed during the other phases of the pandemic ($p<0.001$) (Table 1). Trends in mean on-scene time, number of PWE, and mean total EMS call volume per month for all causes during each year and each period are summarized in Figure 2.

Second, during the whole period, in addition to the demographic and clinical characteristics, total EMS call volume per month related to all causes during the same month <5,000 (-0.55 min, 95% confidence interval [CI] -1.02 – -0.08, $p=0.022$), and transport during the Early phase (-1.88 min, 95%CI -2.75 – -1.00, $p<0.001$) showed decreased on-scene time, but patients transported during the Middle phase (1.58 min, 95%CI 0.70 – 2.46, $p<0.001$) showed increased on-scene time for PWE transported by EMS (Model 1). However, in the Pre period, total EMS call volume per month for all

causes during the same month did not affect on-scene time for PWE transported by EMS (Model 2). During the pandemic period, in addition to demographic and clinical characteristics, total EMS call volume per month for all causes during the same month <5,000 (-1.21 min, 95%CI -2.19 – -0.23, p=0.016) decreased on-scene time for PWE transported by EMS. However, the total number of newly confirmed COVID-19 cases, occupancy of total hospital beds, and being under a declaration of a state of emergency did not affect on-scene time for PWE transported by EMS (Model 3) (Table 2).

Third, the rate of total EMS call volume per month for all causes was 1.01 (95%CI 0.95 – 1.22) in the non-expansion phase of the pandemic, but was 0.81 (95%CI -0.04 – 1.07) in the expansion phase of the pandemic to maintain the same degree of on-scene time for PWE transported by EMS (21.8 min; mean on-scene time for the whole period) (Table 3).

4. Discussion

In the present study, on-scene time delays for PWE with seizures in emergencies were observed in the Middle phase, despite the absence of any corresponding increase in number of PWE cases transported by EMS. On-scene time for PWE was unaffected by total EMS call volume during the Pre phase, but was impacted by this factor during the pandemic period, despite a lack of increase in call volume. The estimated rate of total EMS call volume indicated a discrepancy between demand and supply of critical care services in the healthcare system during the expansion phase of the pandemic in our study area. These findings collectively suggest that when total EMS call volume exceeds the availability of local medical resources, EMS on-scene time may occasionally be delayed in unusual circumstances, such as the COVID-19 pandemic, particularly during the expansion phase. Given that prolonged epileptic seizures need to be treated immediately, effecting a transformative adaptation of emergency transport systems in response to substantial alterations in social conditions is imperative.

We confirmed that on-scene time was dramatically affected during the phases of the pandemic. In the Early phase, overall call volumes decreased, similar to outcomes reported in other regions [26]. In the Middle phase, government offices in Japan changed the policy for COVID-19 infections based on perceived immunity in the

population obtained from vaccination or natural infection [27]. The total call volume for EMS in this area recovered to the same degree as seen in the Pre phase [20]. Our findings confirm that demand-supply discrepancies in the critical care system were negligible during the non-expansion phase of the pandemic, but substantial during the expansion phase. The COVID-19 pandemic necessitated the redistribution of various healthcare resources when demand exceeded supply [28]. These results imply that the on-scene time for time-sensitive illnesses, such as epileptic seizures, may be influenced by the availability of EMS resources in unusual circumstances.

Since the onset of the pandemic, despite the worldwide efforts of national and local governments to maintain the quality of healthcare services at the same level as before the pandemic, a decrease in the number of non-COVID-19 emergency cases has been documented globally [9, 27, 29, 30]. In the present study, the incidence of seizures that EMS transported declined during the pandemic. These seizures were associated with higher patient age and a higher prevalence of altered consciousness compared to the pre-pandemic period. During the pandemic period, some societies recommended reducing in-person healthcare facility visits for PWE with stable seizures, which decreased outpatient visits and admissions in epilepsy centers [31]. Our results might indicate that PWE with non-life-threatening status but a need for medication avoided

298 calls to EMS, as in another study on stroke patients [32]. Thus, clinicians should
299 promote intensive follow-up by telemedicine in both new and follow-up patients,
300 especially during pandemics [30].

301 Certain facilities within stroke care units were found to exhibit no significant
302 delay in the interval between hospital arrival and initiation/intervention [32, 33]. These
303 observations suggested that patients in critical care settings can receive adequate
304 treatment even during a pandemic, if prompt transport to appropriate medical facilities
305 is achieved. Patients hospitalized for seizures are often readmitted due to modifiable
306 factors in the care process, such as seizure exacerbation or multiple medical
307 comorbidities [34]. Mitigating readmission rates could alleviate the demand-supply
308 discrepancy in EMS. Home-care support clinics can mitigate the likelihood of
309 rehospitalization in critical care settings, such as in cases of heart failure [35]. These
310 findings collectively suggest that cooperation between professionals in a
311 multidisciplinary team providing emergency care, recovery or chronic care, and
312 epilepsy experts may enhance seizure outcomes and overall health results for PWE.

313 Some limitations to the present study warrant notation. First, the present study
314 was performed using population-based data from a single region. Thus, there are
315 limitations in generalizing the results of this study. As the EMS system in Japan is

316 operated by local fire departments (733 fire departments in total), regional differences in
317 the EMS system and the distribution of medical facilities were not negligible [19, 36].
318 However, the EMS system in Japan is well designed. The median time between EMS
319 call to EMS arrival on the scene varies only by less than a minute across different
320 regions in Japan [19]. Hence, population-based data including multiple regions are
321 needed to confirm the significance and generalizability of the present results. Second, as
322 we were unable to follow-up PWE using EMS after arrival in the hospital, we could not
323 evaluate how the pandemic affected outcomes. Last, multiple potential factors could not
324 be added to our analysis. Total EMS call volume was influenced by health risk
325 messaging by the media and national authorities [30]. Reducing risk factors such as
326 road traffic accidents, falls and injuries, and air-borne infectious diseases could all affect
327 the total call volume to EMS [30]. Our present study could not analyze these multiple
328 potential factors.
329
330

5. Conclusions

In conclusion, on-scene time delays on PWE in critical care settings were noticed during the expansion phase of the pandemic. During the non-expansion phase of the pandemic, the impact of increasing total EMS call volume was inconsequential. However, during pandemic expansion, the EMS system required proper resource allocation to effectively manage time-sensitive illnesses such as epileptic seizures. Thus, our study underscores the need for national and local governments to prepare and allocate resources and funding for comparable public health crises, in order to ensure sufficient availability of emergency medical services (EMS) and healthcare. Additionally, clinicians should also consider providing intensive follow-up through telemedicine to prevent occasional seizure worsening for PWE during pandemics. Timely changes in the system are essential to address significant societal shifts.

Declarations

Ethics approval and consent to participate:

This was a population-based, observational study. Our study was performed with anonymous clinical data under close supervision following approval by the Ethics Committee of the Hiroshima University Hospital (E2021-2566-01). Informed consent was obtained in the form of opt-out 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:

Informed consent was obtained in the form of opt-out on the hospital website. Those who opted-out were to be excluded from analysis. In the present study, no patients opted out.

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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Hiroshima University, for lending their expertise on statistical data analysis.

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We also thank Dr. Megumi Toko, Dr. Hiroyuki Naito, Dr. Takamichi Sugimoto, Dr. Masahiro Nakamori, and Dr. Tomohisa Nezu for their useful contributions.

Declarations of interest:

None.

Funding:

None.

Authors' contributions:

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

• Shiro Aoki and Yu Yamazaki: interpreted the data; and revised the manuscript for intellectual content

• Megumi Nonaka, Yoshiko Takebayashi, Haruka Ishibashi, and Atsuko Motoda: analyzed and interpreted the data

• Hirofumi Maruyama; revised the manuscript for intellectual content

References

[1] Tanigawa K, Tanaka K. Emergency medical service systems in Japan: past, present, and future. Resuscitation 2006;69(3):365–70.

[2] Coute RA, Nathanson BH, Kurz MC, McNally B, Mader TJ; CARES Surveillance Group. The association between scene time interval and neurologic outcome following adult bystander witnessed out-of-hospital cardiac arrest. Am J Emerg Med 2021;46:628–33.

[3] Shin SD, Kitamura T, Hwang SS, Kajino K, Song KJ, Ro YS, 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):203–10.

[4] Ordoobadi AJ, Peters GA, Westfal ML, Kelleher CM, Chang DC. Disparity in prehospital scene time for geriatric trauma patients. Am J Surg 2022;223(6):1200–5.

[5] Alarhayem AQ, Myers JG, Dent D, Liao L, Muir M, Mueller D, et al. Time is the enemy: mortality in trauma patients with hemorrhage from torso injury occurs long before the "golden hour". Am J Surg 2016;212(6):1101–5.

[6] Gauss T, Ageron FX, Devaud ML, 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):1117–24.

[7] Trinka E, Kälviäinen R. 25 years of advances in the definition, classification and treatment of status epilepticus. Seizure 2017;44:65–73.

[8] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20.

[9] Al Amiry A, Maguire BJ. Emergency medical services (EMS) calls during COVID-19: early lessons learned for systems planning (a narrative review). Open Access Emerg Med 2021;13:407–14.

[10] Jaffe E, Strugo R, Bin E, Blustein O, Rosenblat I, Alpert EA, et al. The role of emergency medical services in containing COVID-19. Am J Emerg Med 2020;38(7):1526–7.

[11] Kim HS, Jang TC, Kim GM, Lee SH, Ko SH, Seo YW. Impact of the coronavirus disease 2019 outbreak on the transportation of patients requiring emergency care. Medicine (Baltimore) 2020;99(50):e23446

[12] 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.

[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;434:120100.

[14] Fountain NB, Van Ness PC, Bennett A, Absher J, Patel AD, Sheth KN, et al. Quality improvement in neurology: Epilepsy Update Quality Measurement Set. Neurology 2015;84(14):1483–7.

[15] 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.

[16] Summary of the Hiroshima City Fire Service Bureau. 2022 September 13, 2022; Available from: https://www.city.hiroshima.lg.jp/site/shobo/12062.html. [accessed 10 January 2023]

[17] 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. [accessed 10 January 2023]

[18] COVID-19 TRACKER in Japan. 2022 July 15, 2022; Available from: https://graphics.reuters.com/world-coronavirus-tracker-and-maps/ja/countries-and-territories/japan/. [accessed 10 January 2023]

[19] 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.

[20] Annual review Hiroshima City Fire Service Bureau. 2022 November 1, 2022; Available from: https://www.city.hiroshima.lg.jp/site/shobo/list1809-3710.html. [accessed 10 January 2023]

[21] 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): 671–5.

[22] 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. [accessed 10 January 2023]

[23] Spaite DW, Valenzuela TD, Meislin HW, Criss EA, 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):638–45.

[24] 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. [accessed 10 January 2023]

[25] The summary of the declaration of the state of emergency. 2023; Available from: https://corona.go.jp/news/news_20200421_70.html. [accessed 10 January 2023]

[26] Jasani G, Alemayehu T, Chizmar T, Wilson L. Changes in EMS utilization in the state of Maryland during the first 6 months of the COVID-19 pandemic. Am J Disaster Med 2022;17(1):41–8.

[27] 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. [accessed 10 January 2023]

[28] Ehmann MR, Zink EK, Levin AB, Suarez JI, Belcher HME, Daugherty Biddison EL, et al. Operational recommendations for scarce resource allocation in a public health crisis. Chest 2021;159(3):1076–83.

[29] Tuczyńska M, Matthews-Kozanecka M, Baum E. Accessibility to non-COVID health services in the world during the COVID-19 pandemic: review. Front Public Health 2021;9:760795.

[30] Lastrucci V, Collini F, Forni S, D'Arienzo S, Di Fabrizio V, Buscemi P, et al. The indirect impact of COVID-19 pandemic on the utilization of the emergency medical services during the first pandemic wave: a system-wide study of Tuscany region, Italy. PLoS One 2022;17(7):e0264806.

[31] Kuroda N, Kubota T, Horinouchi T, Ikegaya N, Kitazawa Y, Kodama S, et al. Impact of COVID-19 pandemic on epilepsy care in Japan: a national-level multicenter retrospective cohort study. Epilepsia Open 2022;7(3):431–41.

[32] Siegler JE, Heslin ME, Thau L, Smith A, Jovin TG. Falling stroke rates during COVID-19 pandemic at a comprehensive stroke center. J Stroke Cerebrovasc Dis 2020;29(8):104953.

[33] Mitsuhashi T, Tokugawa J, Mitsuhashi H. Long-term evaluation of the COVID-19 pandemic impact on acute stroke management: an analysis of the 21-month data from a medical facility in Tokyo. Acta Neurol Bell 2022:1–8. Epub ahead of print.

[34] Blank LJ, Crispo JAG, Thibault DP, Davis KA, Litt B, Willis AW. Readmission after seizure discharge in a nationally representative sample. Neurology 2018;92(5):e429–42.

[35] Sun Y, Iwagami M, Komiyama J, Sugiyama T, Inokuchi R, Sakata N, et al. The effect of home care support clinics on hospital readmission in heart failure patients in Japan. J Gen Intern Med 2023; Epub ahead of print.

[36] Matsuyama T, Kitamura T, Katayama Y, Kiyohara K, Hayashida S, Kawamura T, et al. Factors associated with the difficulty in hospital acceptance among elderly emergency patients: a population-based study in Osaka City, Japan. Geriatrics Gerontol Int 2017;17(12):2441–8.

Figure captions

Figure 1. Geography and newly confirmed COVID-19 cases in Hiroshima

A) Geography of Hiroshima.

B) The three observational periods and total number of newly confirmed COVID-19 cases per million people in Hiroshima. Striped meshing area indicated a 1-year phase early in the COVID pandemic as “Early period”. Dot meshing area indicated a 1-year phase middle in the COVID pandemic as “Middle period”. Half-tone dot meshing areas indicate periods under a declaration of a state of emergency.

Figure 2. Annual summary of emergency medical services in this study

Annual trends in mean monthly total emergency medical services (EMS) call volume for all causes in this area, mean monthly number of patients with epilepsy (PWE) transported by EMS, and mean on-scene time for PWE transported by EMS are summarized. Striped meshing area indicated “Early period”. Dot meshing area indicated “Middle period”.

EMS, emergency medical services; PWE, patients with epilepsy.

Table 1. Characteristics of patients with epilepsy transported by emergency medical services per phase of the COVID-19 pandemic

	Total (n = 2,205)	Pre phase (n = 1,546)	Early phase (n = 335)	Middle phase (n = 324)	p
Age, years, mean (SD)	48.2±23.4	47.1±23.2	50.0±23.5	51.6±23.5**	0.002
Female, n (%)	883 (40.0)	618 (40.0)	132 (39.4)	133 (41.1)	0.906
Fever (>37.5℃), n (%)	209 (13.5)	127 (13.9)	38 (11.8)	44 (14.4)	0.569
Impaired consciousness, n (%)	1783 (80.1)	1224 (79.3)	281 (84.1)	278 (85.8)	0.007
Daytime (08:00–19:59), n (%)	1510(68.5)	1066 (69.0)	228 (68.1)	216 (66.7)	0.712

On-scene time, mean (SD)	21.8±10.8	22.0±10.7	19.6±8.2***	23.2±13.1	<0.001
Total EMS call volume per months for all causes during same month, mean (SD)	4,951.9±424.1	5,012.6±414.4	4,665.6±411.0***	4,957.7±358.5	<0.001

*p<0.05; **p<0.01; ***p<0.001.

COVID-19, coronavirus disease 2019; SD, standard deviation; EMS, emergency medical services.

Table 2. Factors associated with on-scene time of patients with epilepsy transported by emergency medical services per phase of COVID-19 pandemic

Variable	Model 1 (whole period)		Model 2 (Pre phase)		Model 3 (pandemic phases)	
	On-scene time (95%CI)	*p*	On-scene time (95%CI)	*p*	On-scene time (95%CI)	p
Age (per 1-year increase)	-0.05 (-0.07 – -0.03)	<0.001	-0.06 (-0.08 – -0.03)	<0.001	-0.04 (-0.08 – -0.01)	0.021
Impaired consciousness	0.93 (0.36 – 1.50)	0.001	0.94 (0.28 – 1.59)	0.005	0.90 (-0.26 – 2.06)	0.127

Daytime (08:00–19:59)	-1.24 (-1.72 – -0.76)	<0.001	-0.88 (-1.45 – -031)	0.003	-2.02 (-2.91 – -1.13)	<0.001
Total EMS call volume per month for all causes during same month (<5,000/month)	-0.55 (-1.02 – -0.08)	0.022	-0.40 (-0.95 – 0.14)	0.15	-1.21 (-2.19 – -0.23)	0.016
Phase (Early phase)	-1.88 (-2.75 – -1.00)	<0.001				
Phase (Middle phase)	1.58 (0.70 – 2.46)	<0.001				
Total number of newly confirmed COVID-19 cases per week per million people during same day (<25/million people)					-1.39 (-3.15 – 0.37)	0.121

Occupation of total hospital beds during same day (<50%)	-0.40 (-1.79 – 0.99)	0.568
Under declaration of state of emergency	0.07 (-1.08 – 1.21)	0.908

Model 1: age per 1-year increase, impaired consciousness, transported during daytime, total EMS call volume per month for all causes during same month ≤5,000, transported during Pre, Early, or Middle phase

Model 2: age per 1-year increase, impaired consciousness, transported during daytime, total EMS call volume per month for all causes during same month ≤5,000

Model 3: age per 1-year increase, impaired consciousness, transported during daytime, total EMS call volume per month for all causes during same month ≤5,000, total number of newly confirmed COVID-19 cases per week per million people during same day ≤25, occupancy of total hospital beds during same day ≤50%, under declaration of state of emergency

COVID-19, coronavirus disease 2019; EMS, emergency medical services; CI, confidence interval

Table 3. Estimated rate of total EMS call volume per month for all causes during same month to maintain the same degree of on-scene time for PWE transported by EMS in the pandemic period

On-scene time (min)	Variable		Estimated rate of total EMS call volume per month for all causes during same month (95%CI)
	Total number of newly confirmed COVID-19 cases per week per million people during same day (/ million people)	Hospital bed occupancy during same day (%)	
21.8	≤25	≤50	1.01 (0.95 – 1.22)
21.8	≤25	>50	0.98 (0.65 – 1.16)
21.8	>25	≤50	0.85 (0.35 – 1.05)
21.8	>25	>50	0.81 (-0.04 – 1.07)

EMS, emergency medical services; PWE, people with epilepsy; COVID-19, coronavirus disease 2019; CI, confidence interval.

Declarations

Ethics approval and consent to participate:

This was a population-based, observational study. Our study was performed with anonymous clinical data under close supervision following approval by the Ethics Committee of the Hiroshima University Hospital (E2021-2566-01). Informed consent was obtained in the form of opt-out 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:

Informed consent was obtained in the form of opt-out on the hospital website. Those who opted-out were to be excluded from analysis. In the present study, no patients opted out.

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:

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Authors' contributions:

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

• Shiro Aoki and Yu Yamazaki: interpreted the data; and revised the manuscript for intellectual content

• Megumi Nonaka, Yoshiko Takebayashi, Haruka Ishibashi, and Atsuko Motoda: analyzed and interpreted the data

• Hirofumi Maruyama; revised the manuscript for intellectual content