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## Case study

## Clinical characteristics of patients seizure following the 2016 Kumamoto earthquake

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## ABSTRACT

**Purpose:** To investigate the clinical characteristics of patients with seizure following the 2016 Kumamoto earthquake.**Methods:** We retrospectively studied patients with seizure admitted to our hospital for 12 weeks following the earthquake. We compared the clinical backgrounds and characteristics of the patients: before (the same period from the previous 3 years) and after the earthquake; and the early (first 2 weeks) and late (subsequent 10 weeks) phases.**Results:** A total of 60 patients with seizure were admitted to the emergency room after the earthquake, and 175 (58.3/year) patients were admitted before the earthquake. Of them, 35 patients with seizure were hospitalized in the Department of Neurology after the earthquake, and 96 (32/year) patients were hospitalized before the earthquake. In patients after the earthquake, males and non-cerebrovascular diseases as an epileptogenic disease were seen more frequently than before the earthquake. During the early phase after the earthquake, female, first-attack, and non-focal-type patients were seen more frequently than during the late phase after the earthquake.**Conclusions:** These characteristics of patients with seizure during the early phase after the earthquake suggest that many patients had non-epileptic seizures. To prevent seizures following earthquakes, mental stress and physical status of evacuees must be assessed.

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## 1. Introduction

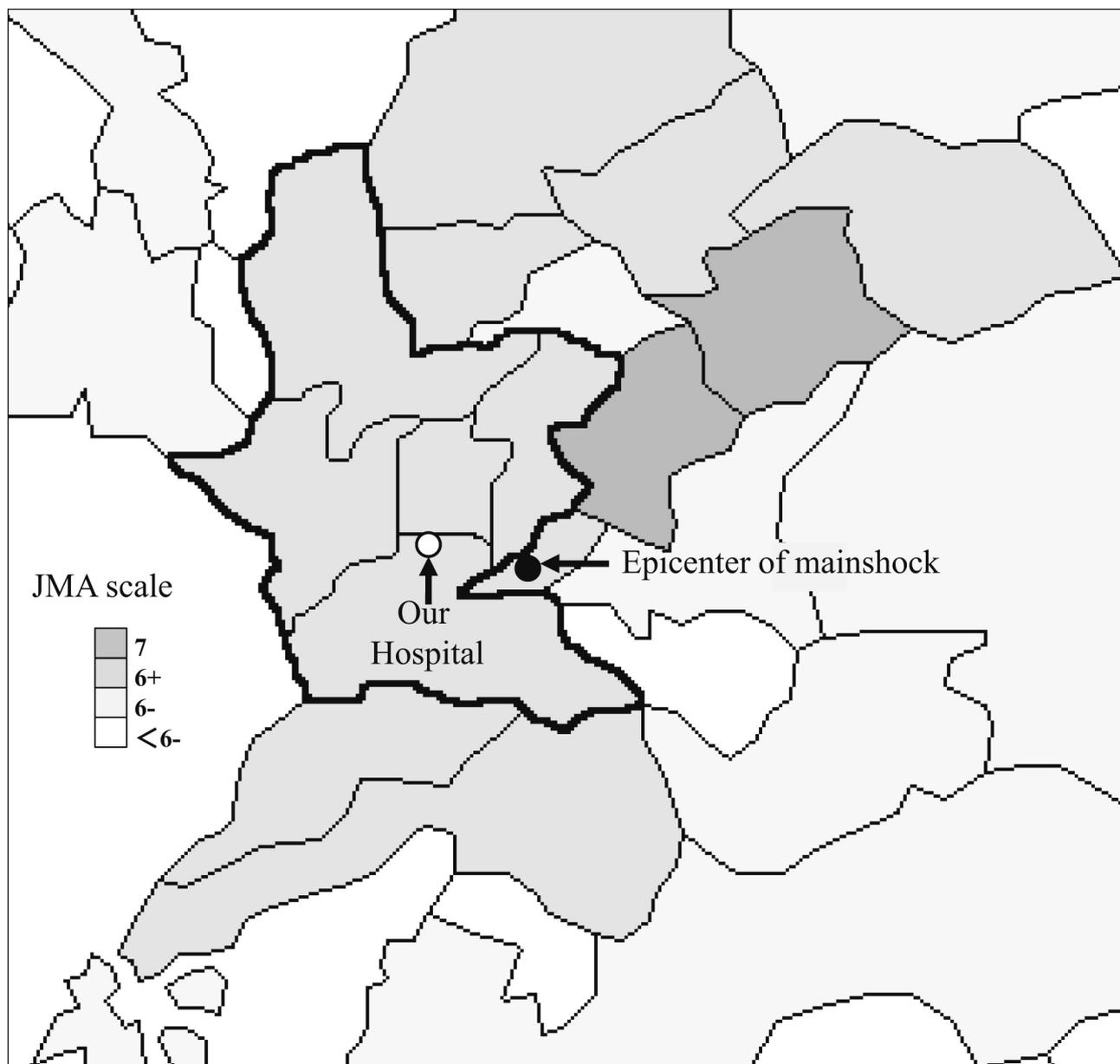
Analyzing the clinical characteristics of diseases following earthquake is useful to help establish protocols for prevention and treatment of those diseases. Following earthquakes, an increased incidence of hypertension [1,2], arrhythmia [3,4], cardiac arrest or sudden death [5,6], acute coronary disease [7–11], heart failure [6,10], takotsubo cardiomyopathy [12], deep venous thrombosis [13,14], pulmonary thromboembolism [13], stroke [7–11,14–17], and pneumonia [6,18] was reported previously. To the best of our knowledge, however, there are only a few studies [19–21] in which the frequency or clinical characteristics of patients with seizure following earthquakes were analyzed. Therefore, the clinical characteristics of patients with seizure following earthquakes remain unclear.

The 2016 Kumamoto earthquake [22,23] and its aftershocks began on April 14, 2016 (Fig. 1). This event was a series of earthquakes beneath Kumamoto City of the Kumamoto Prefecture in the Kyushu Region, Japan, including a foreshock earthquake on April 14, 2016, with magnitude of 6.2 on the Richter scale, and an epicenter of 32°45' N, 130°49' E, at a hypocenter depth of approximately 12 km. The mainshock occurred on April 16 (Coordinated Universal Time on April 15), 2016, with a magnitude of 7.3 on the Richter scale, and an epicenter of 32°45' N, 130°45' E, at a hypocenter depth of approximately 11 km. During the foreshock and main shock of the earthquake, the maximum of the Japan Meteorological Agency's (JMA) seismic coefficient scale was 7°, which corresponded to XIII degrees on the Mercalli intensity scale. The earthquakes killed 50 people, and 7417 buildings were severely damaged.

The Saiseikai Kumamoto Hospital is located in Kumamoto city, and was situated 6 km west of the epicenter of the mainshock of the earthquake (Fig. 1). Fortunately, we were able to provide medical care the day after the mainshock, despite being in a disaster-stricken area (the JMA seismic scale was 6+ at the mainshock site). Here, we present a study in which the backgrounds and clinical

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**Fig. 1.** Seismic coefficients and proximity of our hospital to the epicenter. Japan Meteorological Agency's seismic coefficient scale of the mainshock of 2016 Kumamoto earthquake in each administrative division [22].

characteristics of patients with seizure following the earthquake were evaluated. Our aim was to establish the frequency and clinical characteristics of patients with seizure of following the earthquake.

## 2. Methods

This was a retrospective study in consecutive patients with seizure who were admitted to the emergency room of our hospital. The study protocol followed the principles outlined in the Declaration of Helsinki and were approved by the ethics committee of our hospital. All patients provided written informed consent for the use of their medical data.

### 2.1. Management of patients with seizure in our hospital

Before and after the 2016 Kumamoto earthquake, patients with seizure or loss of consciousness that came to the emergency room

were examined by emergency physicians and then evaluated with brain computed tomography (CT) scan, laboratory tests, electrocardiogram monitoring, and were also subsequently examined by the neurologist or neurosurgeon on duty. Patients experiencing an initial attack, repeated seizures, status epilepticus, or residual neurological deficits caused by the attack were hospitalized at our facility, except for individuals who declined this option. The following rules were distributed by the administration. Patients with seizure caused by: a current brain tumor, hemorrhagic stroke, or trauma were hospitalized in the Department of Neurosurgery; cardiac disease, including arrhythmia and valvular disease, were hospitalized in the Department of Cardiology; systemic disease, including metabolic or toxic disease, were hospitalized in the Emergency Department; other diseases, including ischemic stroke and previously diagnosed brain tumor, hemorrhage and trauma were hospitalized in the Department of Neurology. In the patients hospitalized in the Department of Neurology, magnetic resonance brain imaging (MRI) was carried out immediately and electroen-

cephalography (EEG; 30 min in the daytime) was performed the first business day after their admission.

## 2.2. Inclusion criteria

We enrolled all patients admitted to the emergency room of our hospital between April 15 to July 9, 2016 as the “after earthquake” group. Patients with seizure around the corresponding period from 2013 to 2015 were used as a reference (i.e., the “before earthquake” group). Patients with seizure enrolled in this study satisfied the following criteria: those who (1) experienced a seizure within 24 h before admission to the emergency room of our hospital; and (2) could be diagnosed with seizure due to obvious non-epileptic diseases, including syncope or shivering, were excluded. Additionally, patients with acute symptomatic seizures as well as unprovoked seizures [24] were included as subjects because distinguishing these conditions was quite difficult in the emergency room without longitudinal observation after their discharge.

## 2.3. Data collection

Medical data, including age, sex, past history of seizure, type of seizure, and epileptogenic disease, were collected prospectively from all of the seizure patients admitted to the emergency room of our hospital. If the patients were hospitalized in the Department of Neurology of our hospital, additional data, including past history, premorbid modified Rankin scale, history of evacuation, medication status after the earthquake, vital sign on admission, and laboratory tests were collected. A history of evacuation, including sleeping in a small vehicle and/or shelter, was considered to be positive if the patient reported at least 1 day of staying somewhat other than their home. Type of seizure, including generalized, myoclonic, focal, and focal with secondary generalized, were diagnosed by neurologists or neurosurgeons following patient interviews and consultation with bystanders and medical staff. Status epilepticus-related abnormal findings, such as hyperintense lesions in the cerebral cortex or thalamic pulvinar nuclei on diffusion-weighted MR images were observed, and ruled out as being due to stroke, encephalitis, or traumatic disease [25]. Neurologists evaluated EEG epileptic abnormalities, including spike and wave, spike complex, periodic synchronized discharges, and periodic lateralized epileptic discharge. Epileptogenic diseases were diagnosed by neurologists according to the patient’s past history, characteristics and laterality of the seizure, and the lesions site as revealed by neuroimaging and EEG.

## 2.4. Statistical analysis

In the present study, the following two groups of patients were statistically analyzed: (1) those admitted to the emergency room in our hospital, and (2) those hospitalized in the Department of Neurology in our hospital. We performed a two-step analysis. First, we divided the patients into two subgroups: the before earthquake group and the after earthquake group. Second, we divided the patients in the after earthquake group into two subgroups: the early-phase group, in which patients were admitted within 1–2 weeks after the earthquake; and the late-phase group, in which patients were admitted 3–12 weeks after the earthquake.

The Mann–Whitney U test was used to compare the ages, vital sign parameters, the modified Rankin scale, and the laboratory test results between the two groups. Other clinical characteristics of the patients were compared between the two groups using the chi-square test. The statistical analyses were performed using a commercially available software package (JMP, version 12; SAS Institute Inc., Cary, NC, USA).  $p$  values  $< 0.05$  were considered statistically significant.

## 3. Results

### 3.1. Frequency of patient admission

In total, 60 patients with seizure were admitted to the emergency room in our hospital during the 12-week period after the earthquake; 175 (59 in 2013; 55 in 2014; 61 in 2015; 58.3/year) patients were admitted during the corresponding period before the earthquake. The number of patients after the earthquake increased by 1.03-fold compared with that before the earthquake ( $p = 0.655$ ). Further 35 patients with seizure were hospitalized in the Department of Neurology after the earthquake; 96 (34 in 2013; 30 in 2014; 32 in 2015; 32/year) patients were hospitalized before the earthquake. The number of patients after the earthquake slightly increased by 1.09-fold compared with that before the earthquake ( $p = 0.371$ ).

Fig. 2 shows the time course of the weekly aftershock counts and the number of evacuees (panel A) as well as weekly number of patients admitted to the emergency room, and hospitalized in the Department of Neurology (panel B) in our hospital. In the first week after the earthquake, patients hospitalized in the Department of Neurology increased by 2-fold compared with the corresponding period before the earthquake. However, after then there were no subsequent marked differences in the weekly number of patients with seizure either admitted to the emergency room or hospitalized in the Department of Neurology between before and after the earthquake.

### 3.2. History of evacuation

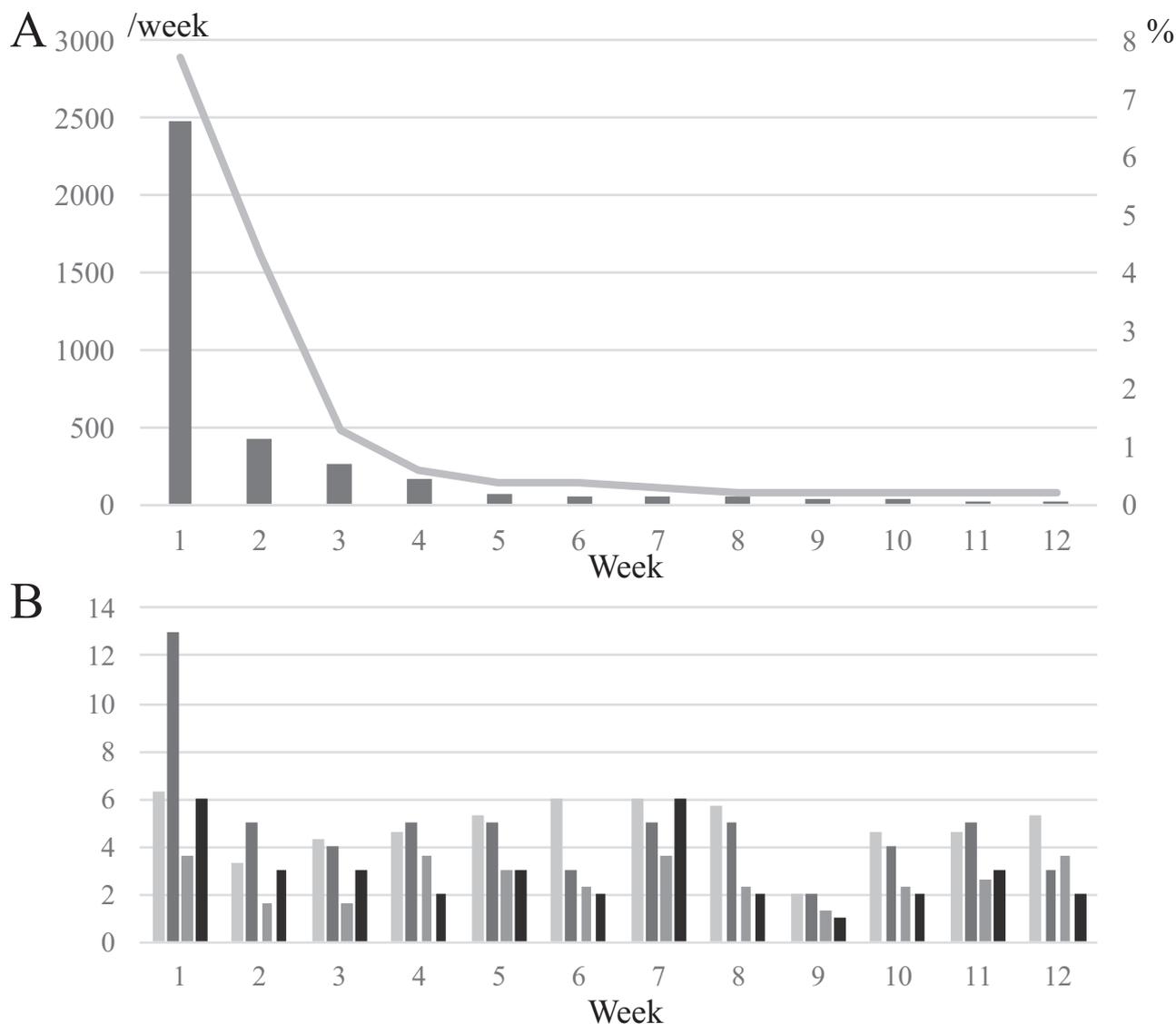
Of the 35 patients hospitalized in the Department of Neurology after the earthquake, 6 had a past history of sleeping in a shelter; 3 had slept at a shelter the night before, 2 were in a shelter at the onset, 7 had a past history of sleeping in a small vehicle, 1 had slept in a small vehicle the night before, and 0 were in a small vehicle at the onset. In the 35 patients hospitalized in the Department of Neurology after the earthquake, 16 patients were taking antiepileptic agents before the earthquake; all of them continued the medication after the earthquake.

### 3.3. Clinical characteristics of patients after the earthquake

Table 1 shows the clinical characteristics of patients hospitalized in the Department of Neurology before or after the earthquake. Table 2 shows the clinical characteristics of patients admitted to the emergency room in our hospital before or after the earthquake. Males and patients with non-cerebrovascular diseases as epileptogenic diseases were observed significantly more frequently in the after earthquake group than in the before earthquake group (Table 2). The laboratory examinations revealed a significantly lower brain natriuretic peptide in the after earthquake group compared with the before earthquake group. However, no differences between the two groups were detected for other background factors, vital sign parameters, seizure type, other laboratory findings, frequency of epileptic findings on EEG, or hyperintense lesions in the diffusion-weighted images.

### 3.4. Clinical characteristics of patients during the early phase after the earthquake

Table 1 also shows the clinical characteristics of patients hospitalized in the Department of Neurology during the early and late phases after the earthquake. Table 2 also shows the clinical characteristics of the patients admitted to the emergency room during the early and late phases after the earthquake. Male sex, past his-



**Fig. 2.** Weekly frequency of aftershocks, percentage of evacuees, and number of patients. The horizontal line means indicates the number of weeks after earthquake. A: The bar graph (scale: left vertical line) shows the frequency of aftershocks [22]. The line graph (scale: right vertical line) shows the percentage of evacuees (per population) from Kumamoto City, Uto City, and Uki City, which are the regions from which more than 75% of admitted patients resided [23]. B: Number of patients with seizure admitted to our hospital. Light gray bar: admission to the emergency room before the earthquake. Dark gray bar: admission to the emergency room after the earthquake. Middle-light gray bar: hospitalization in the Department of Neurology before the earthquake. Black bar: hospitalization in the Department of Neurology after the earthquake.

tory of seizure, sleeping in a small vehicle, and focal seizure were observed significantly less frequently in the early phase group compared with the late phase group. Among the laboratory examinations, the hematocrit level was significantly lower in the early phase group compared with the late phase group. However, no differences between the two groups were detected for other background factors, vital sign parameters, epileptogenic diseases, other laboratory findings, frequency of epileptic findings on EEG, or hyperintense lesions on diffusion-weighted images.

#### 4. Discussion

We examined the clinical characteristics of patients with seizure admitted after the 2016 Kumamoto earthquake to our hospital, which was located near the epicenter. The present study had three major findings. At first, the number of patients admitted with seizure was similar before and after the earthquake for both the

emergency room and the Department of Neurology. Second, males were admitted more frequently after the earthquake compared with before the earthquake. Finally, females, first attack, generalized seizure, and unknown epileptogenic disease were observed more frequently in the early phase compared with the late phase after the earthquake. To the best of our knowledge, this is the first report of comparing clinical characteristics and including laboratory findings of the patients with seizure between before and after the earthquake and early and late phases after the earthquake.

The present study found only a slight increase in the number of patients with seizure after the earthquake compared with that before the earthquake. Conversely, Itabashi and colleagues reported a 4-fold increase in the number of patients with seizure after the Great East-Japan Earthquake compared with before the earthquake [14]. In the previous large earthquakes, neuro-hormonal activation [26] and an increase in post-traumatic stress disorder [27] were reported. Itabashi and colleagues also suggested that stress associated with a life-threatening situations may

**Table 1**  
Clinical characteristics of patients with seizure hospitalized in the Department of Neurology.

	Before earthquake n = 96	After earthquake n = 35	p value	After earthquake		p value
				Early phase n = 9	Late phase n = 26	
Age, year, mean ± SD	68 ± 19	66 ± 19	0.527	74 ± 18	63 ± 18	0.141
Sex, male, (%)	<b>46 (48)</b>	<b>26 (74)</b>	<b>0.006</b>	<b>4 (44)</b>	<b>22 (85)</b>	<b>0.022</b>
Past history, (%)						
Hypertension	56 (58)	18 (51)	0.482	5 (56)	13 (50)	0.774
Diabetes mellitus	17 (18)	5 (14)	0.638	2 (22)	3 (12)	0.448
Dyslipidemia	30 (31)	8 (23)	0.342	2 (22)	6 (23)	0.958
Current smoking	14 (15)	8 (23)	0.274	3 (33)	5 (19)	0.398
Atrial fibrillation	21 (22)	5 (14)	0.322	1 (11)	4 (15)	0.747
Ischemic heart disease	10 (10)	3 (9)	0.751	0 (0)	3 (12)	0.171
Cerebrovascular disease	22 (23)	7 (20)	0.720	1 (11)	6 (23)	0.417
Seizure	39 (41)	17 (49)	0.417	<b>1 (11)</b>	<b>16 (62)</b>	<b>0.006</b>
Premorbid modified Rankin scale, mean ± SD	1.8 ± 1.8	1.5 ± 1.9	0.340	2.3 ± 2.4	1.2 ± 1.7	
History of evacuation (%)						
Sleeping in a shelter		6 (17)		2 (22)	4 (15)	0.646
Sleeping in a small vehicle		7 (20)		<b>0 (0)</b>	<b>7 (27)</b>	<b>0.030</b>
Vital sign, mean ± SD						
Systolic blood pressure, mmHg	146 ± 29	140 ± 29	0.227	145 ± 20	139 ± 31	0.282
Diastolic blood pressure, mmHg	79 ± 16	80 ± 15	0.761	80 ± 8	80 ± 16	0.821
Heart rate, /min	96 ± 23	90 ± 21	0.128	89 ± 15	91 ± 23	0.910
Body temperature, °C	36.8 ± 0.8	36.8 ± 0.8	0.847	36.7 ± 0.6	36.9 ± 0.8	0.663
Type of seizure (%)						
Focal	74 (77)	27 (77)	0.994	<b>4 (44)</b>	<b>23 (88)</b>	<b>0.015</b>
Focal, secondary generalized	41	14		2	12	
Generalized	13 (14)	6 (17)		4 (44)	2 (8)	
Myoclonic	9 (9)	2 (6)		1 (11)	1 (4)	
Epileptogenic diseases (%)						
Cerebrovascular disease	<b>53 (55)</b>	<b>10 (29)</b>	<b>0.006</b>	1 (11)	9 (35)	0.235
Brain trauma	5 (5)	8 (23)		1 (11)	7 (27)	
Brain tumor	2 (2)	1 (3)		0 (0)	1 (4)	
Dementia	7 (7)	2 (6)		2 (22)	0 (0)	
Other	7 (7)	4 (11)		1 (11)	3 (12)	
Unknown	22 (23)	10 (28)	0.510	4 (44)	6 (23)	0.393
Laboratory examinations						
White cell count, 10 <sup>3</sup> /mm <sup>3</sup> , mean ± SD	9.3 ± 4.3	8.4 ± 3.4	0.347	8.8 ± 3.7	8.3 ± 3.4	0.700
Hematocrit, %, mean ± SD	39.1 ± 5.3	39.8 ± 5.2	0.735	<b>35.2 ± 2.6</b>	<b>41.2 ± 4.9</b>	<b>0.003</b>
Platelets, 10 <sup>3</sup> /mm <sup>3</sup> , mean ± SD	213 ± 68	187 ± 63	0.063	203 ± 59	182 ± 65	0.405
Blood sugar, mg/dL, mean ± SD	146 ± 57	151 ± 61	0.457	167 ± 91	146 ± 50	0.807
Blood urea nitrogen, mg/dL, mean ± SD	16.0 ± 8.6	14.7 ± 5.9	0.701	13.7 ± 7.5	15.0 ± 5.4	0.503
Creatinine, mg/dL, mean ± SD	0.89 ± 1.03	0.77 ± 0.28	0.962	0.72 ± 0.36	0.79 ± 0.26	0.187
Myoglobin, ng/dL, mean ± SD	165 ± 267	194 ± 215	0.148	236 ± 143	186 ± 510	0.507
Creatine kinase, U/L, mean ± SD	188 ± 336	439 ± 1350	0.113	143 ± 111	510 ± 1,500	0.438
C-reactive protein, mg/dL, mean ± SD	0.78 ± 2.15	0.93 ± 2.10	0.062	1.89 ± 3.83	0.64 ± 1.15	0.428
Hemoglobin A1c, (%), mean ± SD	6.0 ± 1.4	5.8 ± 1.1	0.541	6.4 ± 1.9	5.7 ± 0.7	0.658
LDL-cholesterol, mg/dL, mean ± SD	108 ± 37	112 ± 41	0.827	119 ± 58	110 ± 38	0.979
Albumin, g/dL, mean ± SD	3.9 ± 0.6	4.0 ± 0.7	0.217	<b>3.7 ± 0.5</b>	<b>4.1 ± 0.7</b>	<b>0.032</b>
Brain natriuretic peptide, pg/mL, median (25–75th percentiles)	<b>50.1 (18.5–95.8)</b>	<b>17.2 (9.4–32.7)</b>	<b>0.001</b>	30.7 (16.2–167.4)	15.9 (8.5–109.9)	0.116
D-dimer, µg/mL, median (25–75th percentiles)	1.1 (0.8–2.5)	1.1 (0.7–2.1)	0.711	1.8 (1.0–3.5)	1 (0.6–2.1)	0.308
Abnormal findings on EEG, (%)	17/91 (19)	7/32 (22)	0.698	1/7 (14)	6/25 (24)	0.569
Hyperintense lesions on DWI, (%)	14/81 (17)	4/28 (14)	0.709	1/5 (20)	3/23 (13)	0.698

EEG: electroencephalography, DWI: diffusion-weighted imaging.

enhance seizure generation [28,29]. However, Itabashi and colleagues conducted a single-institution, retrospective study. Further, they had fewer subjects compared with our study, and they studied patients that experienced the Great East-Japan Earthquake, a much larger earthquake than the 2016 Kumamoto earthquake. Therefore, the stress induced by these two life-threatening situations may have differed. Moreover, Itabashi and colleagues included unprovoked seizures but not acute symptomatic seizures, potentially leading to different change.

A past history of seizure and focal seizure were observed significantly less frequently in the early phase group than in the late phase group. The earthquake may have had a physical and mental impact sufficient to elicit the first attack in patients predisposed to epilepsy who had never experienced a seizure. However, Watson

and colleagues reported that that non-epileptic seizures increased as well as epileptic seizures after earthquake and suggested that stress associated with a life-threatening situation might enhance seizure generation [19]. Both a higher incidence of initial attacks and non-focal seizures after the earthquake indicate that these attacks were non-epileptic in nature in our study. Patients with non-cerebrovascular diseases were also observed more frequently in the after earthquake group compared with the before earthquake group as well as in the early phase group compared with the late phase group, indicating non-epileptic seizures induced by psychogenic stress.

The effects of sex differed by earthquake phase in the current study. During the early phase, females were observed significantly more frequently than in the late phase; males were observed more

**Table 2**  
Clinical characteristics of patients with seizure admitted to the emergency room.

	Before earthquake n = 175	After earthquake n = 60	p value	After earthquake		
				Early phase n = 18	Late phase n = 42	p value
Age, year, mean $\pm$ SD	63 $\pm$ 20	61 $\pm$ 21	0.550	68 $\pm$ 20	58 $\pm$ 21	0.090
Sex, male (%)	<b>89 (51)</b>	<b>40 (67)</b>	<b>0.032</b>	<b>8 (44)</b>	<b>32 (76)</b>	<b>0.019</b>
Past history of seizure	93 (53)	29 (48)	0.520	<b>3 (17)</b>	<b>26 (62)</b>	<b>0.001</b>
Type of seizure (%)						
Focal	104 (59)	36 (60)	0.938	<b>5 (28)</b>	<b>31 (74)</b>	<b>0.001</b>
Focal, secondary generalized	55	18		2	16	
Generalized	50 (29)	19 (32)		10 (56)	9 (21)	
Myoclonic	21 (12)	5 (8)		3 (17)	2 (5)	
Epileptogenic diseases (%)						
Cerebrovascular disease	<b>68 (39)</b>	<b>12 (20)</b>	<b>0.006</b>	2 (11)	10 (24)	0.317
Brain trauma	12 (7)	10 (17)		1 (6)	9 (21)	
Brain tumor	9 (5)	3 (5)		0 (0)	3 (7)	
Dementia	9 (5)	4 (7)		2 (11)	2 (5)	
Other	14 (8)	5 (8)		2 (11)	3 (7)	
Unknown	63 (36)	26 (43)		11 (61)	15 (36)	

frequently after the earthquake than before the earthquake. Shibahara and colleagues also reported that males were observed more frequently for 8 weeks after an earthquake than in the same period before an earthquake [20]. One possible reason for the inter-sexual difference is that women may feel more stress during the early phase compared with the late phase and men may feel more stress during late phase compared with the early phase.

The laboratory tests revealed that brain natriuretic peptide was significantly lower in the after earthquake group compared with the before earthquake group. The reason for this is unclear. In the early phase group, hematocrit and albumin were significantly lower than that in the late phase group. Hypoproteinemia in patients with seizure after an earthquake was reported previously [21]. Malnutrition in evacuees induced by carbohydrate-heavy meals may contribute to seizure, particularly during the early phase after an earthquake.

On the other hand, the laboratory examinations showed that biomarkers of hypercoagulation, hyperviscosity and dehydration (i.e., D-dimer, hematocrit, and blood urea nitrogen) did not increase after the earthquake. We did not conduct some of laboratory examinations useful to evaluate hyper-coagulation, including plasmin activator inhibitor-1 and fibrinogen which were evaluated by previous study [1]. Moreover, examinations of biomarkers of seizure severity, including myoglobin and creatine kinase, and frequency of epileptic EEG findings and hyperintense lesions on diffusion-weighted images did not increase after the earthquake. Another possible reason for these negative findings is that the earthquake was relatively small and thus may not have impacted patients' physical condition as much as a larger earthquake. In addition, health care for the evacuees in the disaster-stricken area of the earthquake might have been more effective at preventing hypercoagulation, dehydration, and severe epilepsy than in the previous earthquakes of similar magnitude.

These characteristics of patients with seizure after the earthquake and during the early phase after the earthquake suggest that many had non-epileptic seizure induced by psychogenic stress. Mental health assessments and care for evacuees in disaster-stricken areas may prevent such non-epileptic seizures. Therefore, patients that present to the hospital soon after a disaster with seizures should be examined by physicians who explain that their seizure may be caused by non-epileptic pathophysiology. A thorough examination that results in a diagnosis of epilepsy should be followed by the introduction of anti-epileptic agents.

The main limitation of the present study was that we employed a single-center design. However, many physicians in disaster-stricken areas are unable to provide clinical information for further

surveillance. We believe that single-center studies with detailed analyses as well as community-based exhaustive surveillances are important for appropriate analysis of diseases following disasters. The present study had the other limitations. First, the EEG was performed intermittently and for a short period. Second, we did not perform a psychiatric examination, which may be useful for analyzing the seizure mechanism [19,27].

In summary, we studied the clinical characteristics of patients with seizure after the 2016 Kumamoto earthquake. After the earthquake, male and non-cerebrovascular diseases as epileptogenic disease were seen more frequently. Moreover, during the early phase, females, the first attack, and non-focal seizure were observed more frequently. These characteristics of patients with seizure during the early phase after the earthquake suggest that many patients had non-epileptic seizures. Careful evaluation of the mental stress and physical status of evacuees may help to prevent seizures following earthquakes.

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### Conflict of interest

The authors have no conflicts of interest to declare.

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