



Long-Term Impact of the Kumamoto Earthquake on Out-of-Hospital Cardiac Arrest With Cardiac and Non-Cardiac Origins

— An Interrupted Time Series Analysis —

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Background: Possible etiologies of out-of-hospital cardiac arrest (OHCA), including aortic dissection, ruptured aortic aneurysms, and pulmonary embolism, may be classified as non-cardiac causes. We investigated whether cardiac and non-cardiac OHCA increased following the Kumamoto earthquake and whether the impact on OHCA extended to regions far from the epicenter.

Methods and Results: We prospectively analyzed a nationwide registry of patients who experienced OHCA between January 2013 and December 2019. Data from cases registered in 7 prefectures, including Kumamoto (Kyushu region; n=82,060), in the All-Japan Utstein Registry were analyzed for OHCA of cardiac and non-cardiac origin. The numbers of OHCA before and after the Kumamoto earthquake were compared using an interrupted time series analysis. The incidence of both cardiac (rate ratio [RR] 1.22) and non-cardiac (RR 1.27) OHCA in Kumamoto Prefecture increased after the earthquake. The difference disappeared when the analysis was limited to patients with non-cardiac OHCA with a clear cause of cardiac arrest. The number of cardiac and non-cardiac OHCA did not increase in other prefectures within the Kyushu region.

Conclusions: The Kumamoto earthquake led to an increase in the incidence of cardiac and non-cardiac OHCA. However, this was attenuated by increasing distance from the epicenter. Except for cardiac causes, cases complicated by earthquake-related events may include non-cardiac OHCA due to vascular diseases that might be overlooked.

Key Words: Cardiac origin; Cardiovascular event; Earthquake; Non-cardiac origin; Out-of-hospital cardiac arrest

Earthquakes are sudden-onset natural phenomena that simultaneously impose extreme physical, psychological, and emotional stress on many people over a wide area. Japan comprises only 0.25% of the world's total land area; nevertheless, it is one of the foremost countries to experience earthquakes, with an approximate 23% probability of the occurrence of a large-scale earthquake (magnitude of 6.0 or greater).¹ The Kumamoto earthquake was characterized by 2 magnitude 7 earthquakes occurring in the same area within 28 h, with approximately 3,000 seismic intensity 1 or higher events in the first 2 weeks after the earthquake and more than 4,000 aftershocks in the first 8 months after the earthquake.²

Therefore, cardiac events leading to out-of-hospital cardiac arrests (OHCA) may have increased not only immediately after the Kumamoto earthquake, but also continuously compared with the pre-earthquake period.

Vascular diseases, such as acute aortic dissection (AAD) or ruptured aortic aneurysms, are considered causes of OHCA, along with pulmonary embolism (PE). However, these diseases are not of cardiac origin, and there is no separate category for their classification in the current Utstein Registry; hence, they are classified as "other OHCA of non-cardiac origin". Therefore, it is unclear whether OHCA of non-cardiac origin increased after the Kumamoto earthquake.

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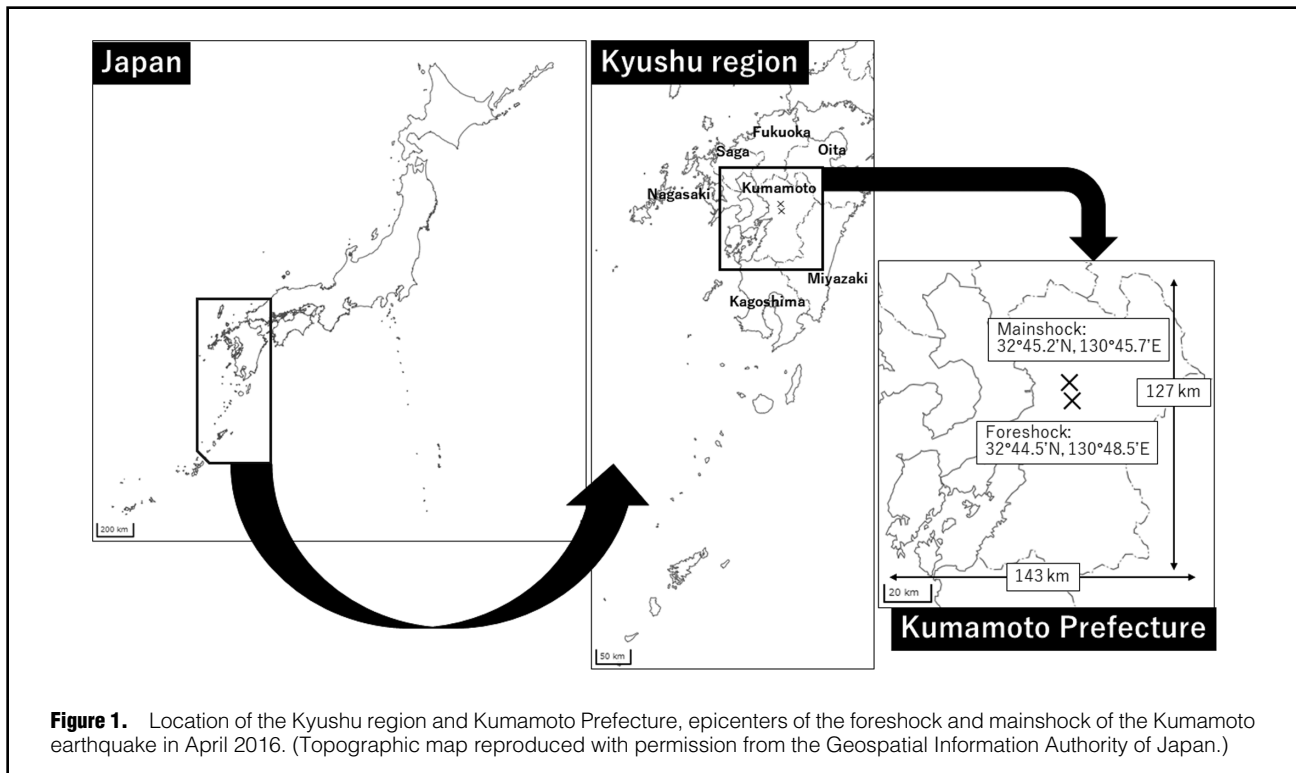
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More OHCA are expected to have occurred close to the epicenter; however, it is unclear whether this effect was also observed in the prefectures surrounding Kumamoto.

In an interrupted time series (ITS) design, data are measured at multiple time points before and after the introduction of an intervention to examine the effect of the intervention. This “quasi-experimental” design is superior to many other observational study designs (e.g., before and after) in that it avoids threats to internal validity, such as short-term fluctuations, secular trends, and regression to the mean. ITS analyses are used to examine the effects of public health system-wide policy interventions where using a randomized trial is impracticable or infeasible. In addition, ITS analyses can be used to examine the impacts of exposures such as earthquakes.³

In this study we hypothesized that the incidence of OHCA of cardiac and non-cardiac origins after the Kumamoto earthquake differed from the underlying trend before the earthquake. We also examined whether the Kumamoto earthquake affected the incidence of OHCA outside of Kumamoto Prefecture, far from the epicenter, using an ITS analysis.

Methods

Data Source, Study Area, and Emergency Medical Service System

This study is a retrospective analysis based on data from the All-Japan Utstein Registry, which is a prospective nationwide population-based registry system for OHCA with Utstein-style data collection⁴ that was established on January 1, 2005, by the Fire and Disaster Management Agency (FDMA), as described in detail previously.⁵ All fire stations with dispatch centers and collaborating medi-

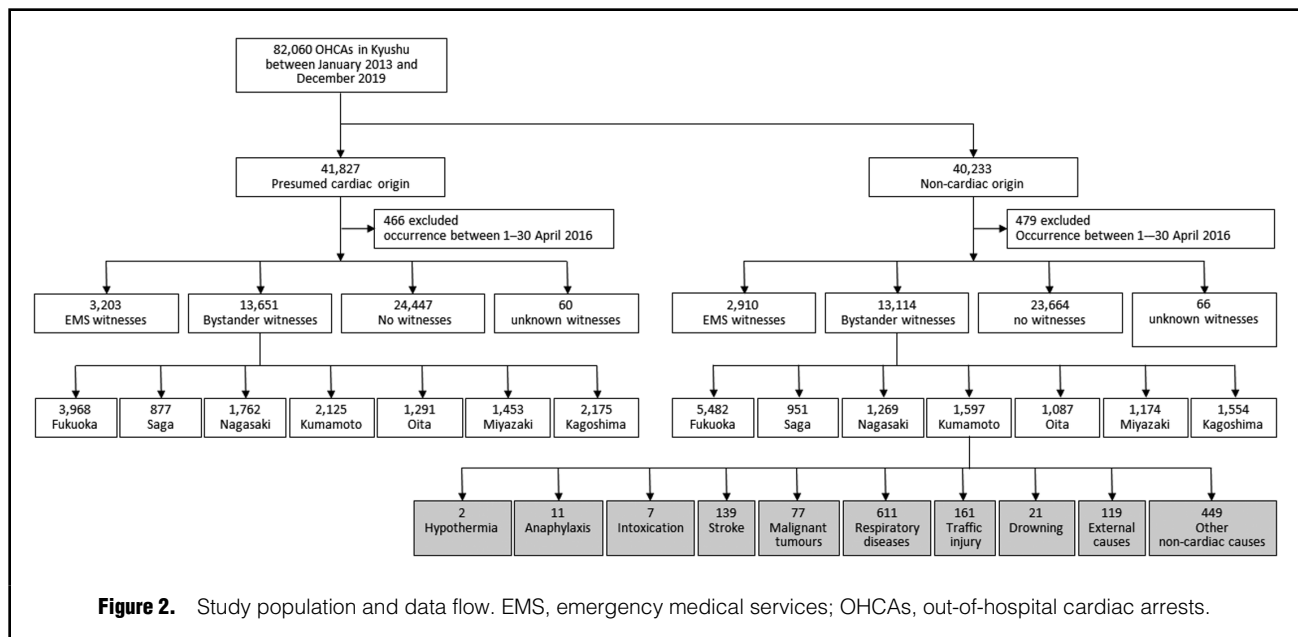
cal institutions contribute to the registry. Registry data are provided to a subcommittee on resuscitation science in the Japanese Circulation Society, following prescribed governmental legal procedures.

This study was approved by the Ethics Committee of Kawasaki Medical School (Approval no. 3383) and was conducted in accordance with the Declaration of Helsinki. The requirement for written informed consent was waived.

The Kyushu region is located in the southwest of Japan and has an area of approximately 42,300 km², including both urban and rural communities across 7 prefectures (Fukuoka, Saga, Nagasaki, Kumamoto, Oita, Miyazaki, and Kagoshima).⁶ In 2019 it has a total population of approximately 12.8 million,⁷ and it has 95 municipally governed fire stations with dispatch centers following uniform guideline-based resuscitation protocols.^{8,9} Kumamoto Prefecture covers an area of 7,400 km² (~127 km from north to south and 143 km from east to west). It has a stable population of approximately 1.7 million, according to the Kumamoto Prefectural Government Office records,¹⁰ and has 12 municipally governed fire stations with dispatch centers (Figure 1).⁸ Japanese emergency medical service (EMS) providers are not authorized to terminate resuscitation efforts, and most patients who experience OHCA are transported to the nearest hospital, and were therefore included in the present study; cases of decapitation, incineration, decomposition, rigor mortis, or dependent cyanosis were excluded.^{5,11}

Kumamoto Earthquake and Study Population

A foreshock of a 6.5 magnitude earthquake (seismic scale: 7) occurred on April 14, 2016, in Kumamoto (32°44.5'N, 130°48.5'E), and a subsequent mainshock of magnitude 7.3 (seismic scale: 7) occurred on April 16, 2016 (32°45.2'N,



130°45.7'E; **Figure 1**). Thereafter, 22 of the 25 following earthquakes (88%) during April 2016 measured 5 or greater on the 7-stage seismic scale.¹² Therefore, we defined April 2016 as the exposure period and excluded from the statistical analyses patients who developed OHCA between April 1 and April 30, 2016. We compared the incidence and subsequent event rates of OHCA before and after the Kumamoto earthquake in April 2016. Data on the monthly total incidence of OHCA in the Kyushu region, including Kumamoto, between 2013 and 2019 were extracted from the All-Japan Utstein Registry database. Data from patients who experienced bystander-witnessed OHCA and for whom EMS responders initiated resuscitation prior to hospital transfer were included in the study. Patients with cardiac arrests occurring after the arrival of EMS responders, unwitnessed OHCA, or those with an unidentified witness status were excluded. Cardiac arrest was defined as the end of cardiac mechanical activity as determined by the absence of signs of circulation.⁴ An arrest was presumed to be of cardiac origin unless evidence suggested stroke, respiratory diseases, malignant tumors, intoxication, drowning, traffic injury, hypothermia, external causes, anaphylaxis, or other non-cardiac causes. The physicians in charge who interacted with the EMS personnel were responsible for determining the etiology.^{5,11}

OHCA Data Collection and Quality Control

Data were collected prospectively according to the Utstein guidelines.⁴ The OHCA registry data included only the prefecture's name as the place of onset for personal information security. All event times were synchronized according to the dispatch center clock.^{5,11} The time of collapse was determined through an interview that EMS personnel conducted with a bystander before the EMS personnel left the scene.^{5,11} Data forms were completed by the EMS personnel in cooperation with the patients' physician-in-charge, and the information was subsequently entered into the registry system on the FDMA database server. The forms were logically checked using a computerized system

and verified by an implementation working group. If the data form was incomplete, the FDMA returned it to the respective fire station for completion.^{5,11} Non-cardiac causes of OHCA are often obvious and easy to determine because the specific subcategories include hypothermia, anaphylaxis, intoxication, stroke, malignant tumors, respiratory diseases, traffic injury, drowning, and external causes. In this study, we defined "patients with non-cardiac OHCA in the diagnostic category" as patients with non-cardiogenic cardiac arrest in which the diagnosis was unambiguous. OHCA of presumed cardiac etiology are based on available information, such as autopsy data and hospital records; however, this frequently becomes a diagnosis of exclusion. Patients who do not fit in the more readily defined category of cardiac arrest of non-cardiac etiology are included in this category.¹³

Statistical Analyses

An ITS design is an observational design for investigating population-level exposure, such as natural disasters, or interventions, such as enforcement of laws related to public health.³ When exposure occurs at a known time, postexposure trends can be examined for distinct changes from pre-existing trends, thus serving as a counterfactual.³ Therefore, it seems appropriate to use ITS analysis on the incidence of OHCA before and after the earthquake. We used a generalized linear model based on the Poisson distribution of cardiac and non-cardiac OHCA monthly counts and explored whether the OHCA trend after the earthquake differed from that before the earthquake after adjusting for seasonality and long-term trends³ in the Kyushu region and each prefecture in Kyushu. We included Fourier terms up to the second harmonic¹⁴ to adjust for seasonal variations in OHCA. We checked the plot of the model residuals and partial autocorrelation function and confirmed little evidence of autocorrelation.

Various effect metrics may be calculated in the circumstance where a simple segmented linear model is fitted. The effect of the earthquake on the outcome can be calculated

Table 1. Number of Patients With OHCA of Cardiac Origin Before (January 2013–March 2016) and After (May 2016–December 2019) the Kumamoto Earthquake in the Kyushu Region and Each Prefecture

Prefecture	Cardiac origin OHCA			Non-cardiac origin OHCA		
	Total (n=13,651)	Jan. 2013–Mar. 2016 (n=6,263)	May 2016–Dec. 2019 (n=7,338)	Total (n=13,114)	Jan. 2013–Mar. 2016 (n=5,968)	May 2016–Dec. 2019 (n=7,146)
Fukuoka	3,968	1,774	2,194	5,482	2,371	3,111
Saga	877	414	463	951	454	497
Nagasaki	1,762	789	973	1,269	646	623
Kumamoto	2,125	1,004	1,121	1,597	719	878
Oita	1,291	571	720	1,087	539	548
Miyazaki	1,453	673	780	1,174	531	643
Kagoshima	2,175	1,038	1,137	1,554	708	846

OHCA, out-of-hospital cardiac arrests.

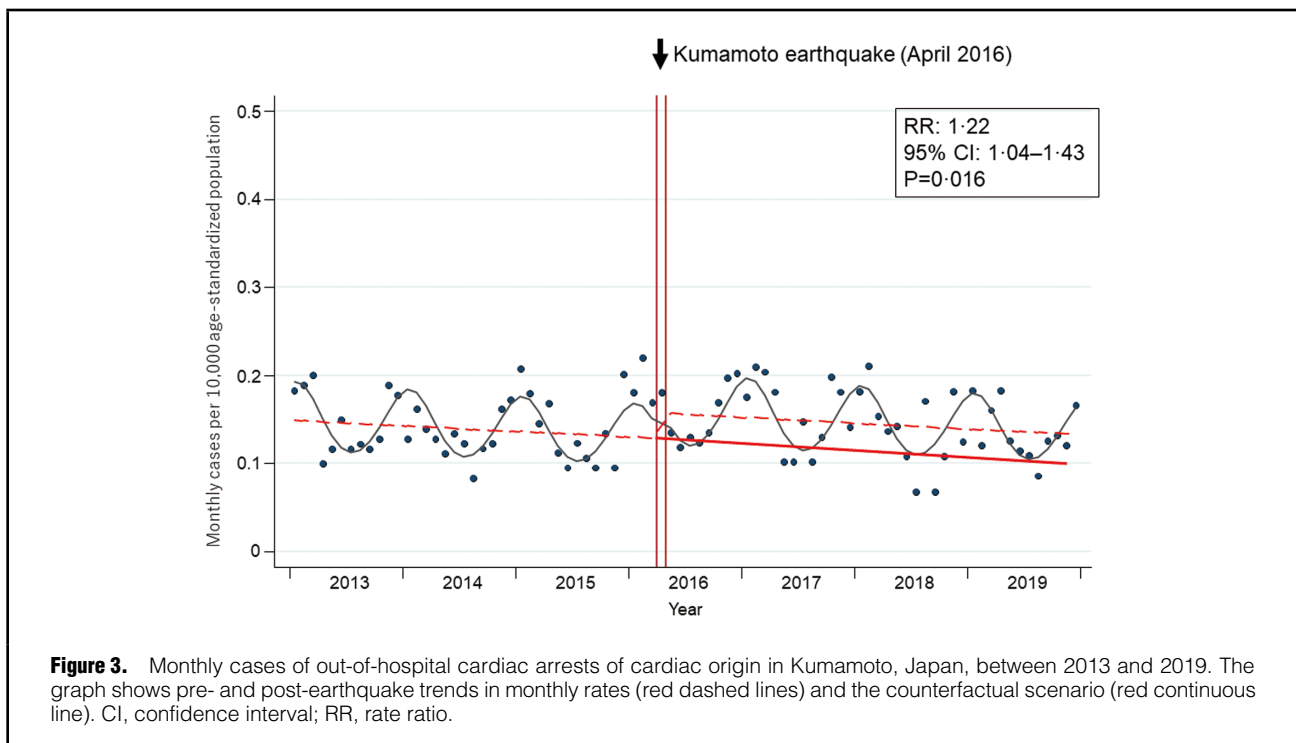


Figure 3. Monthly cases of out-of-hospital cardiac arrests of cardiac origin in Kumamoto, Japan, between 2013 and 2019. The graph shows pre- and post-earthquake trends in monthly rates (red dashed lines) and the counterfactual scenario (red continuous line). CI, confidence interval; RR, rate ratio.

by estimating the change in level or the change in the slope of the pre- and post-earthquake trends, or both. By combining the 2, we estimated the rate ratio (RR) of the earthquake effect at a specified time after the earthquake based on the predicted counterfactual, that is, using the trend in the pre-earthquake period to predict what would have occurred in the post-earthquake period, in the absence of the earthquake. Stratified analyses were conducted to investigate whether the Kumamoto earthquake may have had a differential effect according to patient background, including age group (<75 vs. ≥75 years) and sex.

Data were analyzed using STATA version 16 (StataCorp, College Station, TX, USA). All tests were 2-sided and performed at a 5% level of statistical significance.

Results

Study Population

A total of 82,060 consecutive patients developed OHCA

of cardiac and non-cardiac origin between January 1, 2013 and December 31, 2019 in the Kyushu region. Of these, 945 patients who developed OHCA from April 1 to April 30, 2016 (466 with presumed cardiac origin and 479 with non-cardiac origin) were excluded from the statistical analyses. Finally, the study included 26,765 patients (cardiac origin, n=13,651 [≥75 years: 61.6%; male sex: 60.0%]; non-cardiac origin, n=13,114 [≥75 years: 62.9%; male sex: 54.8%]) whose OHCA were witnessed by bystanders (**Figure 2**). The numbers of patients with OHCA of cardiac and non-cardiac origins before (January 2013–March 2016) and after (May 2016–December 2019) the Kumamoto earthquake in the Kyushu region and each prefecture are presented in **Table 1**.

OHCA of Cardiac Origin

The age-standardized onset rates and predicted regression curve for OHCA of cardiac origin in Kumamoto Prefecture are shown in **Figure 3**. The mean (±SD) number of

Table 2. Monthly Cases and RR of OHCA of Cardiac Origin After the Earthquake Compared With Before the Earthquake

Prefecture	Before the earthquake (Jan. 2013–Mar. 2016)	After the earthquake (May 2016–Dec. 2019)	P value
Fukuoka			
Mean ($\pm$ SD) no. cases monthly ^A	0.10 $\pm$ 0.02	0.10 $\pm$ 0.03	
RR (95% CI)	Ref.	1.02 (0.88–1.19)	0.792
Saga			
Mean ($\pm$ SD) no. cases monthly ^A	0.13 $\pm$ 0.05	0.13 $\pm$ 0.05	
RR (95% CI)	Ref.	1.21 (0.89–1.63)	0.224
Nagasaki			
Mean ($\pm$ SD) no. cases monthly ^A	0.15 $\pm$ 0.06	0.17 $\pm$ 0.05	
RR (95% CI)	Ref.	1.25 (0.98–1.59)	0.072
Kumamoto			
Mean ($\pm$ SD) no. cases monthly ^A	0.14 $\pm$ 0.04	0.15 $\pm$ 0.04	
RR (95% CI)	Ref.	1.22 (1.04–1.43)	0.016
Oita			
Mean ($\pm$ SD) no. cases monthly ^A	0.13 $\pm$ 0.04	0.14 $\pm$ 0.04	
RR (95% CI)	Ref.	1.15 (0.90–1.47)	0.251
Miyazaki			
Mean ($\pm$ SD) no. cases monthly ^A	0.16 $\pm$ 0.05	0.17 $\pm$ 0.05	
RR (95% CI)	Ref.	0.88 (0.71–1.09)	0.235
Kagoshima			
Mean ($\pm$ SD) no. cases monthly ^A	0.16 $\pm$ 0.05	0.16 $\pm$ 0.05	
RR (95% CI)	Ref.	1.11 (0.92–1.34)	0.282
All prefectures except Kumamoto			
Mean ($\pm$ SD) no. cases monthly ^A	0.12 $\pm$ 0.03	0.13 $\pm$ 0.03	
RR (95% CI)	Ref.	1.08 (0.97–1.19)	0.144

^APer 10,000 age-standardized population. CI, confidence interval; RR, rate ratio. Other abbreviations as in Table 1.

cardiac OHCA cases before and after the earthquake were 0.14 $\pm$ 0.04 and 0.15 $\pm$ 0.04 per 10,000 age-standardized population per month, respectively. **Figure 3** shows a significant increase in the number of cardiac OHCA after the earthquake compared with the predicted incidences (RR 1.22; 95% confidence interval [CI] 1.04–1.43; $P=0.016$). Of the 2,125 patients with cardiac OHCA in Kumamoto Prefecture, 1,402 were aged ≥ 75 years (66.0%) and 1,281 were men (60.3%). Stratified analyses were performed to explore the factors influencing the incidence of OHCA of cardiac origin. The RR for age ≥ 75 years (RR 1.30; 95% CI 1.06–1.59; $P=0.012$) and male sex (RR 1.26; 95% CI 1.03–1.54; $P=0.026$) showed significant increases after the earthquake.

Table 2 shows the monthly cases and the RR of OHCA of cardiac origin in each prefecture of the Kyushu region. Compared with the pre-earthquake period, the number of cases of cardiac OHCA increased significantly in Kumamoto Prefecture after the earthquake. However, no significant increase in incidence after the earthquake was noted in any other prefecture of the Kyushu region compared with before the earthquake.

OHCA of Non-Cardiac Origin

The age-standardized onset rates and predicted regression curve for OHCA of non-cardiac origin in Kumamoto Prefecture are shown in **Figure 4**. The mean ($\pm$ SD) numbers of OHCA cases before and after the earthquake were 0.10 $\pm$ 0.04 and 0.11 $\pm$ 0.03 per 10,000 age-standardized population per month, respectively. **Figure 4** shows a signifi-

cant increase in the number of non-cardiac OHCA after the earthquake compared with the predicted incidences (RR 1.27; 95% CI 1.04–1.55; $P=0.018$) after the earthquake. In 1,597 patients with OHCA of non-cardiac origin in Kumamoto Prefecture, the diagnostic categories of non-cardiac origins were respiratory diseases ($n=611$; 38.3%), traffic injuries ($n=161$; 10.1%), stroke ($n=139$; 8.7%), external causes ($n=119$; 7.5%), malignant tumors ($n=77$; 4.8%), drowning ($n=21$; 1.3%), intoxication ($n=7$; 0.4%), hypothermia ($n=2$; 0.1%), and anaphylaxis ($n=11$; 0.7%). A total of 449 (28.1%) patients had other non-cardiac causes (**Figure 2**). **Figure 5A** shows no significant differences in the number of non-cardiac OHCA with diagnostic categories after the earthquake compared with the predicted incidences (RR 1.09; 95% CI 0.86–1.38; $P=0.483$). Even when restricted to respiratory diseases, which was the most common diagnostic category, the number of OHCA cases did not increase (RR 1.07; 95% CI 0.79–1.45; $P=0.676$). **Figure 5B** shows a significant increase in the number of non-cardiac OHCA after the earthquake compared with the predicted incidences in patients limited to non-cardiac OHCA without diagnostic category. The increase in the number of OHCA cases after the earthquake almost doubled compared with the pre-earthquake period (RR 1.93; 95% CI 1.25–2.97; $P=0.003$).

Table 3 shows the monthly cases and RR of OHCA of non-cardiac origin in each prefecture of the Kyushu region. Compared with the pre-earthquake period, the number of cases of OHCA increased significantly in Kumamoto Prefecture after the earthquake. However, there were no

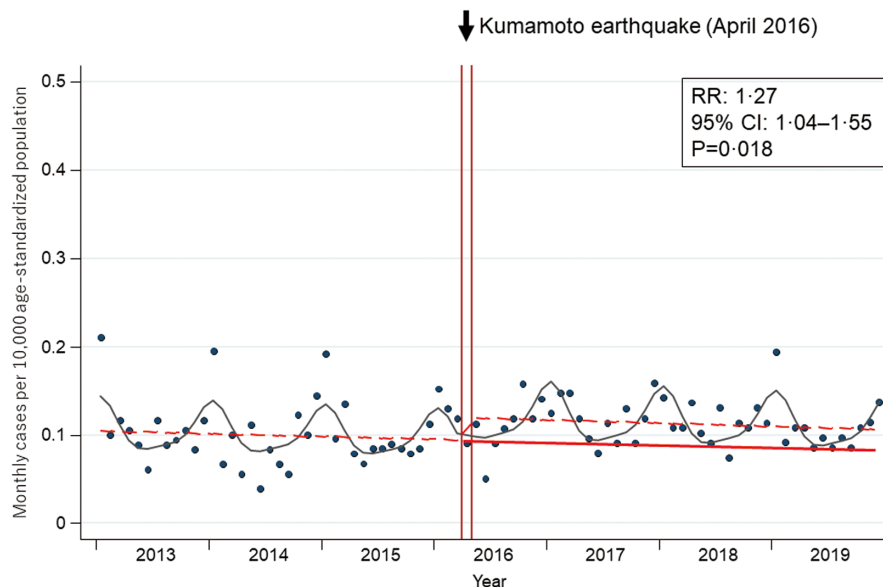


Figure 4. Monthly cases of out-of-hospital cardiac arrests of non-cardiac origin in Kumamoto, Japan, between 2013 and 2019. The graph shows the pre- and post-earthquake trends in monthly rates (red dashed lines) and the counterfactual scenario (red continuous line). CI, confidence interval; RR, rate ratio.

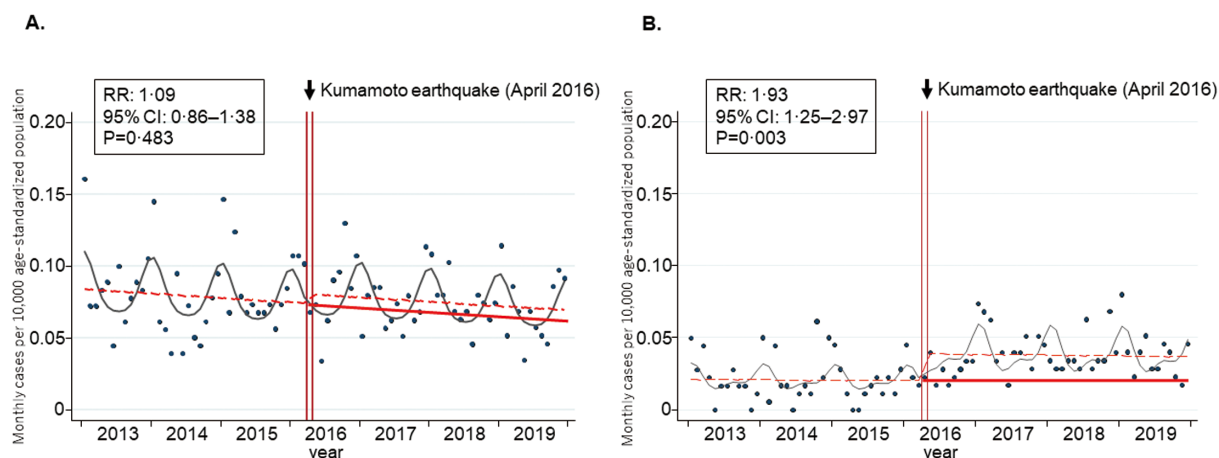


Figure 5. Monthly cases of out-of-hospital cardiac arrests of non-cardiac origin according to causes in Kumamoto, Japan, between 2013 and 2019. **(A)** Composite of diagnostic categories (respiratory diseases, traffic injuries, stroke, external causes, malignant tumors, drowning, intoxication, hypothermia, and anaphylaxis). **(B)** Other non-cardiac causes. The graphs show pre- and post-earthquake trends in monthly rates (red dashed lines) and the counterfactual scenario (red continuous line). CI, confidence interval; RR, rate ratio.

significant increases in the number of cases of OHCA after the earthquake in any prefecture, except Kumamoto, compared with the pre-earthquake period.

Discussion

The number of patients with OHCA of cardiac origin increased significantly after the Kumamoto earthquake in Kumamoto Prefecture, with the monthly incidence increas-

ing by 22%. However, in the surrounding prefectures far from Kumamoto, the number of OHCA of cardiac origin did not increase significantly after the earthquake compared with the pre-earthquake period. The number of cases of OHCA of non-cardiac origin also increased after the earthquake in Kumamoto Prefecture. However, the definitive causes of non-cardiac OHCA responsible for this increase could not be determined.

Increased cardiac events were reported after earth-

Table 3. Monthly Cases and RR of OHCA of Non-Cardiac Origin After the Earthquake Compared With Before the Earthquake

Prefecture	Before the earthquake (Jan. 2013–Mar. 2016)	After the earthquake (May 2016–Dec. 2019)	P value
Fukuoka			
Mean ($\pm$ SD) no. cases monthly ^A	0.12 $\pm$ 0.03	0.14 $\pm$ 0.03	
RR (95% CI)	Ref.	0.97 (0.85–1.12)	0.709
Saga			
Mean ($\pm$ SD) no. cases monthly ^A	0.14 $\pm$ 0.05	0.14 $\pm$ 0.05	
RR (95% CI)	Ref.	0.97 (0.76–1.25)	0.842
Nagasaki			
Mean ($\pm$ SD) no. cases monthly ^A	0.12 $\pm$ 0.05	0.11 $\pm$ 0.04	
RR (95% CI)	Ref.	0.98 (0.73–1.30)	0.884
Kumamoto			
Mean ($\pm$ SD) no. cases monthly ^A	0.10 $\pm$ 0.04	0.11 $\pm$ 0.03	
RR (95% CI)	Ref.	1.27 (1.04–1.55)	0.018
Oita			
Mean ($\pm$ SD) no. cases monthly ^A	0.12 $\pm$ 0.04	0.11 $\pm$ 0.04	
RR (95% CI)	Ref.	1.01 (0.78–1.31)	0.941
Miyazaki			
Mean ($\pm$ SD) no. cases monthly ^A	0.12 $\pm$ 0.03	0.14 $\pm$ 0.05	
RR (95% CI)	Ref.	1.12 (0.87–1.43)	0.377
Kagoshima			
Mean ($\pm$ SD) no. cases monthly ^A	0.11 $\pm$ 0.03	0.12 $\pm$ 0.02	
RR (95% CI)	Ref.	1.11 (0.90–1.37)	0.316
All prefectures except Kumamoto			
Mean ($\pm$ SD) no. cases monthly ^A	0.12 $\pm$ 0.03	0.13 $\pm$ 0.02	
RR (95% CI)	Ref.	1.01 (0.91–1.12)	0.873

^APer 10,000 age-standardized population. Abbreviations as in Tables 1,2.

quakes, and most were associated with earthquakes of magnitude 6.0 or greater.¹⁵ The Kumamoto earthquake not only caused 2 consecutive magnitude 7 foreshocks and mainshocks in the same area, but also more than 4,000 aftershocks that persisted for 8 months, which led to forced evacuation for a long period. Therefore, cardiac events caused by earthquake-related stress may be long lasting. We excluded cases of OHCA in April 2016, when the stress in the hyperacute phase immediately after the Kumamoto earthquake was considered to be particularly likely to be involved in the occurrence of cardiovascular-related OHCA. Therefore, this study included cases of OHCA during the acute and chronic phases of earthquakes. Previously, we reported an increase in cases of acute myocardial infarction after the Kumamoto earthquake over a 3-year follow-up using an ITS design and the same methodology used in the present study.¹⁶ Prolonged stress may trigger coronary spasms and rupture of atherosclerotic plaques, and increase the propensity to develop thrombi, leading to myocardial ischemia and myocardial infarction. An imbalance in the oxygen supply–demand equation may contribute to lethal ventricular arrhythmias.^{15,17} Coronary artery disease remains the predominant cause of OHCA, and it may be logical to consider that OHCA of cardiac origin increased after the Kumamoto earthquake.

There was a significant increase in the number of cases of cardiac OHCA in Kumamoto Prefecture but not in other prefectures in the Kyushu region. Cardiac events were more likely to occur closer to the epicenter. During the Great East Japan Earthquake, the increase in the num-

ber of cardiac OHCA persisted for several weeks in the disaster area, whereas their incidence increased only during the first week immediately after the earthquake in the non-disaster area.^{18,19} The difference in the duration of the risk increment could be due to the disparity in psychological stress levels between the areas, as well as long-term physical stress from the breakdown of lifelines, evacuations, and cold temperatures in disaster areas. In the Northridge earthquake, the increase in admissions for acute myocardial infarction after the earthquake was greater at hospitals within 15 miles (24km) of the epicenter than at hospitals more than 15 miles from the epicenter.²⁰ However, few reports have been made about the distance from the epicenter and events. Although stress is likely to depend on the magnitude of the earthquake and the subsequent damage, countermeasures, such as cardiovascular care, cardiopulmonary resuscitation training, and supply of automated external defibrillators, should be employed immediately after earthquakes, especially in areas within a few dozen kilometers of the epicenter.

Notably, there was a significant increase in the number of non-cardiac OHCA after the Kumamoto earthquake in Kumamoto Prefecture. However, no significant increase was observed in the number of non-cardiac OHCA in the diagnostic category. There was also no significant increase in the incidence of respiratory etiology, which was the most common cause. Meanwhile, the incidence of other non-cardiac causes in cases of non-cardiac OHCA almost doubled after the earthquake. Other non-cardiac causes accounted for 12% of all OHCA cases of cardiac and non-

cardiac origins. Diseases assigned to other non-cardiac causes may include AAD and ruptured aortic aneurysms. According to previous reports, the incidence of other non-cardiac OHCA was approximately 8–12% when limited to studies where all patients who experienced OHCA underwent computed tomography and/or echocardiography as diagnostic examinations.^{21,22} However, aortic aneurysm rupture may be a less common cause of all OHCA, at approximately 0.3–0.4%.^{23,24} Earthquake-related stress and environmental changes may increase sympathetic activation and salt sensitivity in evacuees, which, combined with salt intake, may result in the development of hypertension, leading to AAD and aneurysm rupture.^{25,26} PE generally represents 2–5% of all causes of OHCA.²⁷ We reported that 10.6% of examinees at various evacuation centers around the epicenter in the first month after the Kumamoto earthquake had deep vein thrombosis.²⁸ It is not surprising that there were a certain number of cases of OHCA due to PE after the Kumamoto earthquake. Vascular diseases such as AAD, ruptured aortic aneurysms, and PE, which can be reliably diagnosed, are classified in the category of other non-cardiac causes in the case of OHCA of non-cardiac origin because there is no equivalent category for these diseases in the Utstein Registry form. However, in the current Japanese form, “aortic diseases” corresponding to AAD and ruptured aortic aneurysms and “internal causes” corresponding to PE have been added as non-cardiac categories since 2021. Few studies have been conducted on the development of vascular diseases after earthquakes; thus, this should be examined in the future.

Study Limitations

This study has some limitations. First, in comparing the incidence of OHCA, differences in the potential risk of the local population should be considered. However, the current Utstein Registry lacks information on risk factors for the development of OHCA, such as medical history and socioeconomic factors. This makes accurate adjustment difficult. Therefore, our results should be interpreted with caution. Second, the causes of non-cardiac OHCA are obvious; hence, cases of OHCA that do not fall into the non-cardiac category were entered into the cardiac category in an exclusionary diagnostic manner.¹³ However, the actual cause of OHCA may be rarely diagnosed because of the unstable condition of the patient after transportation to hospital. Cases of OHCA due to AAD, ruptured aortic aneurysms, and PE may still be classified as cardiac unless the cause of the OHCA is accurately diagnosed. In cases of non-traumatic sudden death, the discrepancy in the cause of death between autopsy and imaging with computed tomography was 30%, with PE being the most common imaging error in the identification of the cause of death.²⁹ Therefore, the number of cases of other non-cardiac causes may be underestimated. Third, stress caused by the earthquake could not be assessed due to the lack of available data. However, there is an enormous amount of literature on the relationship between psychological stress and cardiovascular diseases.³⁰ Various stresses, including physical, psychological, social, and environmental, after the Kumamoto earthquake, may have significantly affected the onset of OHCA, because many buildings and houses collapsed and people in the affected areas were forced to live as evacuees in temporary housing. Conversely, there may be other factors aside from the different stresses caused by earthquakes, which could be difficult to assess.

Fourth, the ITS design lacks control over other environmental exposures that may affect the natural trend of OHCA onset. Several large-seismic-scale earthquakes occurred in Japan during the study period (2013–2019). In September 2018, Hokkaido experienced a seismic scale 7 earthquake (Hokkaido Eastern Iburi earthquake) equivalent to the Kumamoto earthquake. A previous report showed a positive relationship between the disaster area near the epicenter and cardiovascular mortality.³¹ However, because Kumamoto and Hokkaido are approximately 1,400 km apart, and the Hokkaido Eastern Iburi earthquake did not directly cause any damage in Kumamoto Prefecture, it is unlikely that this earthquake had a significant effect on the results of the present study. At the end of 2019, the novel coronavirus first appeared in Wuhan, China; however, it was not identified in Japan until January 2020.³² Because the COVID-19 pandemic could have affected the incidences of OHCA, data up to December 2019 from the Utstein Registry were used in the present study.

Conclusions

In conclusion, the Kumamoto earthquake had an impact on and increased the incidence of OHCA of cardiac and non-cardiac origins in Kumamoto Prefecture. However, the incidence decreased with increasing distance from the epicenter. The number of cases classified as OHCA of non-cardiac origin in the diagnostic category did not increase with earthquakes; nevertheless, OHCA with other non-cardiac causes that may represent vascular diseases should be investigated in future studies. Along with modifying the current Utstein data form to include a category of OHCA due to vascular disease, training for basic life support that can be administered by the general public and advanced life support administered by medical staff should be continuously provided and encouraged in order to prepare for the increase in OHCA of cardiovascular origin that may occur after major earthquakes in the future.

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Author Contributions

S.K. and T.M.: study design, data analysis, interpretation of results, manuscript - revision and writing the final version; K.T.: manuscript - revision; N.Y., Y.T., and T.I.: principal investigators, conceptualization of the All-Japan Utstein Registry, study design and completion, data collection and management, interpretation of results, manuscript - revision. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

IRB Information

This study was approved by the Ethics Committee of Kawasaki Medical School (Approval no. 3383). The requirement for written informed consent was waived.

Data Availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

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Supplementary Files

Please find supplementary file(s);
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