

[ ORIGINAL ARTICLE ]

## Peptic Ulcers in Fukushima Prefecture Related to the Great East Japan Earthquake, Tsunami and Nuclear Accident

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### Abstract:

**Objective** Due to the Great East Japan Earthquake, which occurred in March 2011, many residents of Fukushima Prefecture were affected by a radiation accident in addition to suffering loss or damage from the earthquake and the subsequent tsunami. The aim of this study was to evaluate the actual condition of patients with peptic ulcers related to the disaster.

**Methods** Patients with peptic ulcers at six hospitals in three different regions of Fukushima Prefecture during the two months following the disaster and the corresponding period of the year before and the year after the disaster were enrolled in this study. Changes by period and region in the number of esophagogastroduodenoscopy (EGD) examinations and the number of peptic ulcer patients were evaluated as the primary endpoints. Changes in the frequencies of hemorrhagic ulcers were evaluated by period and by region as secondary endpoints.

**Results** The numbers of EGDs and peptic ulcer cases compared to the previous year decreased in 2011 and then increased in 2012. However, the ratio of hemorrhagic ulcers to peptic ulcers was higher in 2011 (51.9%) than in 2010 (38.1%) and 2012 (31.1%), and the 2011 hemorrhagic ulcer ratio was the highest at 63.6% in the coastal area. Regarding bleeding cases during 2011, the rate at 1 month after the disaster (64.1%) was higher than the rate at 2 months after the disaster (40.5%) ( $p=0.033$ ).

**Conclusion** The number of patients with peptic ulcers did not increase immediately following the disaster in Fukushima Prefecture. However, the rate of bleeding patients increased soon after the disaster, especially in the coastal area.

**Key words:** endoscopy, Fukushima, disaster, gastric ulcer, *Helicobacter pylori*, radiation

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### Introduction

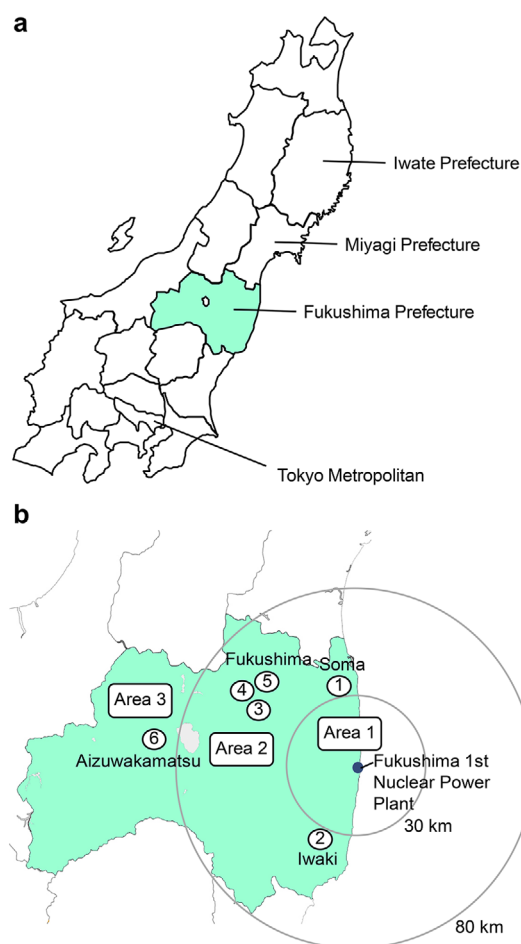
The Great East Japan Earthquake occurred on March 11, 2011. With its epicenter in the Pacific Ocean and a maximum magnitude of 9.0, the quake was recorded as the

strongest that had ever occurred around Japan. Its maximum seismic intensity was 7, and the great tsunami that followed caused a tremendous amount of damage along a wide range of Japan's Pacific coastal area in the Tohoku and Kanto districts. The quake disaster caused more than 400,000 people to become evacuees, and it killed approximately 20,000 (in-

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**Figure 1.** Fukushima Prefecture during the Great East Japan Earthquake. (a) Fukushima Prefecture, lying to the north-east of Tokyo, and Miyagi and Iwate Prefectures, located to the north of Fukushima, were severely damaged by the quake and tsunami caused by the Great East Japan Earthquake. (b) Locations and geographical area classifications of the six study hospitals. 1. Public Soma General Hospital (Soma City), 2. Fukushima Rosai Hospital (Iwaki City) in Area 1, 3. Fukushima Medical University Hospital (Fukushima City), 4. Ohara General Hospital (Fukushima City), 5. Japanese Red Cross Fukushima Hospital (Fukushima City) in Area 2, 6. Fukushima Prefectural Aizu General Hospital (Aizuwakamatsu City) in Area 3.

cluding missing persons), with particularly severe damage in Fukushima, Miyagi, and Iwate Prefectures in the Tohoku District (Fig. 1a).

The Great Hanshin-Awaji Earthquake, which was another major quake in Japan, occurred in west Japan on January 17, 1995. Aoyama et al. (1-3) reported an increased number of patients with hemorrhagic gastric ulcers compared to the number at one year earlier. The Great East Japan Earthquake occurred 16 years after the Great Hanshin-Awaji Earthquake. Over that period, there were remarkable changes in medical practices in Japan, including the new coverage of *Helicobacter pylori* eradication by health insurance and an increase in the use of antithrombotic drugs and non-steroidal anti-inflammatory drugs (NSAIDs). In addition, unlike the Great

Hanshin-Awaji Earthquake, which occurred in a localized area involving large cities, the Great East Japan Earthquake affected a wide geographical area, including the coastal zones of the Tohoku district.

The residents of Fukushima Prefecture were strongly affected by the quake and tsunami. In addition, a serious problem of radiation exposure arose due to the accident at the Fukushima Daiichi Nuclear Power Plant complex. The radiation exposure issue forced the residents in the coastal area of Fukushima Prefecture within a radius of 30 km from the power plant to evacuate to distant places (Fig. 1b). In addition, the residents living in the inland area of Fukushima Prefecture who were not included in the forced evacuation program, mainly those with children, moved to other prefectures out of fear of radiation exposure. As a result, Fukushima residents suffered a broad range of diseases and mental stress (4-9).

We therefore conducted this retrospective study of peptic ulcer patients at one year before the disaster, just after the disaster, and one year after the disaster in order to characterize the peptic ulcers observed in Fukushima Prefecture following the Great East Japan Earthquake.

## Materials and Methods

### Patients

Six core hospitals in Fukushima Prefecture participated in this study: Soma General Hospital, Fukushima Rosai Hospital, Fukushima Medical University Hospital, Ohara General Hospital, Japanese Red Cross Fukushima Hospital, and Fukushima Prefectural Aizu General Hospital (currently Fukushima Medical University Aizu Medical Center). Patients who were newly diagnosed with peptic ulcers at any of these six facilities during the two-month period after the Great East Japan Earthquake (March 11 to May 10, 2011), during the same period one year before the earthquake (March 11 to May 10, 2010) and during the same period one year after the earthquake (March 11 to May 10, 2012) were enrolled in the study. A peptic ulcer was defined as a mucosal injury with a distinct depth and an endoscopically determined size of  $\geq 5$  mm, excluding cancerous ulcers (10). A hemorrhagic gastric ulcer was defined as an endoscopically noted ulcer in a patient with hematemesis and/or melena. Both outpatients and inpatients were included.

Furthermore, similar to a report on the Great Hanshin-Awaji Earthquake (1) and in view of the quake damage, the six facilities were classified into three geographical areas according to their distance from the nuclear power plant (Fig. 1b). Area 1 was defined as 2 facilities close to the nuclear power plant and located in the Pacific coastal area (Soma General Hospital in Soma City and Fukushima Rosai Hospital in Iwaki City); Area 2 encompassed 3 facilities that were approximately 60 km from the nuclear power plant and located inland (Fukushima Medical University Hospital, Ohara General Hospital, and Japanese Red Cross Fukushima

Hospital, all located in Fukushima City); and Area 3 included 1 facility approximately 100 km from the nuclear power plant located further inland (Fukushima Prefectural Aizu General Hospital in Aizuwakamatsu City). Area 1 was strongly affected by the quake, tsunami, and radiation exposure. Although Area 2 was not inundated by the tsunami because of its inland location, it was exposed to higher levels of radiation than the cities of Soma and Iwaki (where the two hospitals in Area 1 were located) due to the influence of wind direction following the nuclear power plant accident; some residents suffered mental stress from radiation exposure and evacuated from Fukushima Prefecture at their own discretion. Area 3 was also strongly affected by the quake, and Fukushima Prefectural Aizu General Hospital was partially destroyed (11). However, this area was minimally affected by radiation exposure.

### Data collection and analyses

One (T.H.) of the authors sent a patient data report to his coauthors at the six facilities (M.S., Y.E., R.I., A.I., Y.T., and H.S.) by e-mail between May and June 2011. After retrospectively documenting the data for the years 2010 and 2011 at each facility, case report forms (CRFs) were recovered by October 2011. The data for 2012 were also sent by T.H. to the coauthors in March 2012, and CRFs were recovered by October 2012. The data that were collected were analyzed by T.H. at Fukushima Medical University Hospital.

The compiled data included the day and time of the diagnosis of peptic ulcers, patient age and sex, ulcer location (stomach and/or duodenum), hemorrhagic symptoms (hematemesis and melena), the presence/absence of *H. pylori* infection and the method of its diagnosis, oral drugs in use at the time of the diagnosis (NSAIDs and antithrombotic drugs), and residence at the time of the diagnosis (hospital, home, shelter facility, etc.). *H. pylori* infection was diagnosed mainly based on the serum *H. pylori* IgG antibody content. In addition, if patients tested positive in a microscopy test, rapid urease test, or urea breath test, they were identified as being infected with *H. pylori*. Serum *H. pylori* antibody titers were measured using an enzyme immunoassay, with a titer of  $\geq 10$  U/mL considered to indicate positivity. Low-dose aspirin was not included in the category of NSAIDs, but it was handled as an antithrombotic drug. Data on the number of esophagogastroduodenoscopy (EGD) examinations performed at each facility during the study period were also collected.

This study conformed to the ethical guidelines of the 1975 Declaration of Helsinki. It was conducted with the approval of the Ethics Committee of Fukushima Medical University (approval No. 1234).

### Outcomes

Changes by period and geographical area in the number of EGD examinations and the number of peptic ulcer patients were compared and evaluated as primary endpoints. As secondary endpoints, the ratio of peptic ulcer patients per

EGD examination, characteristics of ulcer patients [sex, age, gastric ulcer/duodenal ulcer ratio (GU/DU ratio)], frequency of hemorrhagic ulcers, causal factors for ulcers, and residence at the time of the diagnosis of ulcers were compared and evaluated by period and geographical area. Note that temporary shelters, private housing used for temporary evacuation, and new addresses from dwellings in which patients were living at the time of the quake were all considered to be evacuation facilities. The number of hemorrhagic peptic ulcer patients in 2011 was compared and evaluated within one month after the quake (March 11 to April 10) and between one and two months after the quake (April 11 to May 10). Patients with both GU and DU were excluded from the discussion on the GU/DU ratio.

### Statistical analyses

When comparing and evaluating data among the various periods, continuous variables were expressed as the mean  $\pm$  standard deviation, and a *t*-test was used. Discrete variables were expressed with actual numbers and percentages, and a chi-square test was used. A *p* value of  $<0.05$  was considered to indicate statistical significance. Statistical analyses were conducted using the Statcel 2 software program (OMS Publishing, Tokorozawa, Japan).

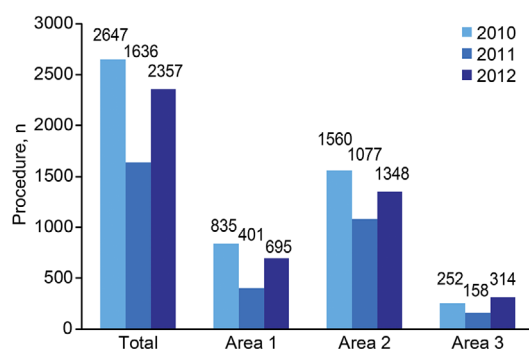
## Results

### Changes over time in the number of endoscopic examinations and peptic ulcers

The number of EGDs performed during the 2-month period just after the onset of the quake in 2011 was 1,636, accounting for 61.8% of the 2,647 EGDs performed during the same period in 2010 (Fig. 2, Table). However, in the same period of 2012, at 1 year after the restoration of the hospital function, the number of EGDs performed was 2,357, which represented an improvement to 89.0% of the 2010 level. Trends for this endpoint were similar across all areas. The number of peptic ulcer patients decreased to 81 soon after the quake in 2011 from the previous year's total of 126 (64.3% compared with 2010) and increased to 103 in 2012 compared to 2011 (127.2% compared with 2011) (Fig. 3a). Trends for this endpoint were similar between Areas 1 and 2 but not in Area 3, where fewer peptic ulcer patients were found in 2010 than in later years. However, the ratio of peptic ulcer patients to the number of EGDs did not differ significantly among the three periods, and there were no significant differences by geographical area in each period (Fig. 3b).

### Characteristics of the peptic ulcer patients

The mean age of the study population was approximately 65 years. The number of male patients was approximately twice that of female patients, and the incidence of GU was approximately twice the incidence of DU; these aspects did not differ among the three periods (Table). However, the ra-



**Figure 2.** Numbers of EGD examinations during the corresponding periods (Mar. 11-May 10) in 2010, 2011, and 2012. The number of EGD examinations performed during the 2-month period just following the quake in 2011 was 1,636, which accounted for 61.8% of the 2,647 examinations performed during the same period one year earlier in 2010. In the same period of 2012, one year after the quake, the number was 2,357, which represented an improvement to 89.0% of the 2010 level. EGD: esophagogastroduodenoscopy

tio of hemorrhagic ulcers to peptic ulcers was higher in 2011 (51.9%) than in 2010 (38.1%) and 2012 (31.1%), and the 2011 hemorrhagic ulcer ratio was the highest at 63.6% in Area 1 (Fig. 4a). In Area 2, the prevalence of hemorrhagic ulcer decreased from 43.9% in 2011 to 24.5% in 2012. When analyzing monthly data on hemorrhagic ulcers in 2011, the prevalence was 64.1% (25/39) up to 1 month after the onset of the quake and over 40.5% (17/42) during the month that followed ( $p=0.033$ ) (Fig. 4b).

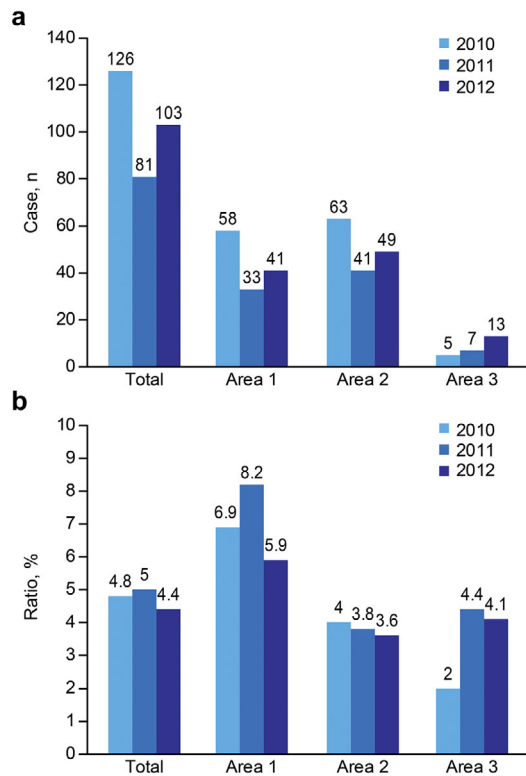
### Causal factors for peptic ulcers

Diagnostic examinations for *H. pylori* infection were performed in 53.2% of patients in 2010, 56.8% in 2011, and 55.3% in 2012 (Table). The *H. pylori* infection rate was 63.8% in 2010, 60.9% in 2011, and 56.5% in 2012 with no significant differences among the three periods. The oral NSAID medication rate was 18.3% in 2010, 22.2% in 2011, and 22.3% in 2012 with no significant differences among the three periods. The annual oral antithrombotic drug medication rates were 18.3%, 18.5%, and 14.6% with no significant differences among the three periods. During the three

**Table.** Patient Characteristics of Peptic Ulcer Patients during the Corresponding Periods (Mar. 11 - May 10) for 2010, 2011, and 2012.

	2010	2011	2012	p value
Number of EGD, n	2,647	1,636	2,357	
Number of patients with PU, n	126	81	103	
Number of patients with hemorrhagic ulcer, n (%)	48 (38.1%)	42 (51.9%)	32 (31.1%)	0.015
Area 1	21 (36.2%)	21 (63.6%)	12 (36.6%)	0.007
Area 2	27 (42.9%)	18 (43.9%)	15 (24.5%)	ns
Area 3	0 (0%)	3 (42.9%)	5 (38.5%)	ns
Age, year: mean ( $\pm$ SD)	64.7 (16.9)	65.1 (13.7)	64.8 (16.6)	ns
Male/female ratio	2.3 (88/38)	2.1 (55/26)	1.6 (63/40)	ns
GU/DU ratio	2.2 (81/31)	2.3 (54/24)	2.3 (70/30)	ns
HP infection				
Diagnosis rate, %	53.2% (67/126)	56.8% (46/81)	55.3% (57/103)	ns
Infection rate, %	64.2% (43/67)	60.9% (28/46)	61.4% (35/57)	ns
Positive	43	28	35	
Negative	24	18	22	
Post eradication	2	1	5	
NSAID intake	23 (18.3%)	18 (22.2%)	23 (22.3%)	ns
Antithrombotic drug intake	23 (18.3%)	15 (18.5%)	15 (14.6%)	ns
HP negative plus no NSAID plus no antithrombotic drug	14 (11.1%)	10 (12.3%)	14 (13.6%)	ns
Patient's resident				
Refugee shelter	0	6	6	
Hospital	Not examined	17	9	
Home	Not examined	58	88	
Number of patients with hemorrhagic ulcer living in refugee shelter, n (%)	-	3 (50%)	5 (83.3%)	

ns: not significant, SD: standard deviation, EGD: esophagogastroduodenoscopy, PU: peptic ulcer, GU: gastric ulcer, DU: duodenal ulcer, HP: *Helicobacter pylori*, NSAID: non-steroidal anti-inflammatory drug



**Figure 3.** Numbers and rates of peptic ulcer patients in the three areas during the corresponding period (Mar. 11-May 10) between 2010, 2011, and 2012. (a) The number of peptic ulcer patients in 2011 was 81, a decrease from the previous year's number of 126, and the number increased to 103 in 2012 compared to 2011. Trends were similar between Areas 1 and 2. (b) However, the ratio of peptic ulcer patients to the number of EGD examinations did not differ markedly among the three periods, and there were no significant differences by area among the periods. EGD: esophagogastroduodenoscopy

periods, the proportion of *H. pylori* infection-negative patients who did not receive either NSAIDs or antithrombotic drugs was 13.6%, 12.3%, and 13.6%, respectively, and there were no significant differences among the three periods.

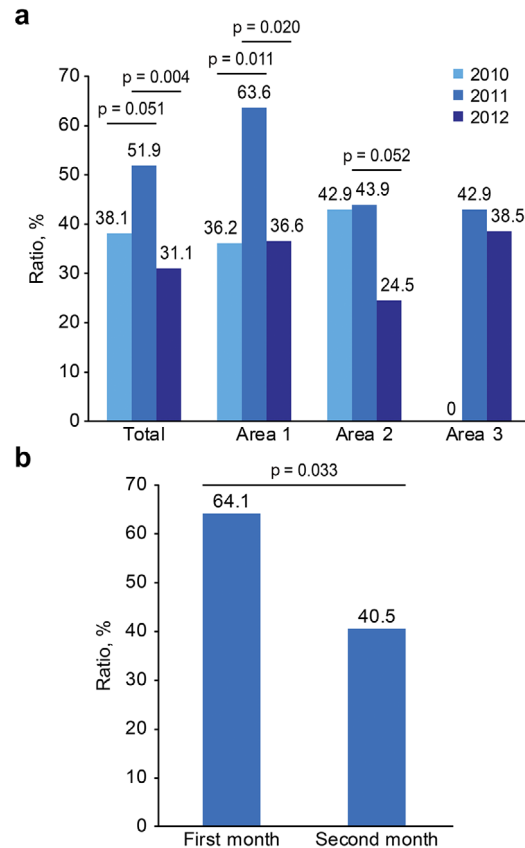
### Residency at the time of ulcers onset

In both 2011 and 2012, six patients were living in evacuation facilities at the time of the ulcer onset. More specifically, their residences were mainly temporary shelters in 2011 and temporary dwellings and new addresses in 2012 (Table). The patients' hemorrhagic ulcers accounted for 50% (3/6) of ulcers in 2011 and 83.3% (5/6) in 2012.

## Discussion

In this study, the number of patients with peptic ulcers did not increase immediately after the Great East Japan Earthquake, tsunami, and nuclear accident in Fukushima Prefecture. However, the rate of bleeding patients increased soon after the disaster, especially in the coastal area.

Kanno et al. (10, 12, 13) conducted a survey to character-



**Figure 4.** Bleeding event ratios of peptic ulcer patients. (a) Within the entire study population, the ratio increased in 2011 compared to 2010 and decreased in 2012 compared to 2011. Similar trends were found in Area 1, with the ratio being 63.6% in 2011. In Area 2, the ratio decreased in 2012 compared to 2011, although no differences were found between 2010 and 2011. (b) The ratio of patients experiencing hemorrhagic ulcers during the first month following the quake (Mar. 11-Apr. 10, 2011) was higher at 64.1% than the 40.5% ratio obtained during the following month (Apr. 11-May 10, 2011).

ize cases of peptic ulcers found at seven facilities in Miyagi Prefecture during the three-month period just following the quake. In that study, peptic ulcers and hemorrhagic ulcers increased 1.5- and 2.2-fold, respectively, compared with the rates reported one year earlier. However, the opinion of the Kanno study differed from that of the Aoyama study (1) on the Great Hanshin-Awaji Earthquake as follows: given that the frequency of *H. pylori*-negative non-NSAID-induced ulcers increased significantly from 13% at one year previous to 24%, mental stress (particularly daily life in refugee shelter (13) may be an independent causal factor for peptic ulcers during large disasters.

The number of EGDs performed in all areas in this study decreased after the Great East Japan Earthquake because of difficulties providing typical endoscopic practice due to blackouts, water supply suspensions, lack of medical material supplies, and other quake-related factors (10). However, in Area 3 (approximately 20-50 km from the epicenter), defined by the Aoyama study (1), the number of EGDs was

92.3% compared to the previous year, which showed only a small reduction. In Area 3 as defined in this study, the number of EGDs decreased to 62.7% compared to the previous year, despite being located at a greater distance from the epicenter than the Area 3 defined in the Aoyama study. This finding underscores the severe impact of the Great East Japan Earthquake. In addition, the number of EGDs performed in 2012, which was the year following the quake, increased to a level close to or higher than the 2010 level in each area, indicating that hospital functions normalized after the quake.

The number of peptic ulcer patients in this study was expected to increase, yet there was an unexpected decrease just after the quake. This finding differed from the results of the Kanno study (10). One reason for this decrease may be that many tsunami-injured individuals in the vicinity of the nuclear power plant under the influence of the radiation accident could not be saved. Therefore, some tsunami-injured patients who experienced peptic ulcers might not have been included in the analysis. In addition, many residents who escaped damage from the quake and tsunami were evacuated from Fukushima Prefecture due to fear of radiation exposure (8). This group likely included many residents who experienced ulcers from mental stress, but they were not included in this study. In addition, many patients with mild symptoms might not have been able to visit a doctor due to traffic congestion and general confusion after the quake and tsunami. Furthermore, in 2012, the year following the quake, the number of peptic ulcer patients increased compared to the 2011 level, but it was smaller than in 2010. This outcome suggests that residents who were relatively resistant to mental stress stayed in Fukushima Prefecture in 2012. In addition, the number of ulcer patients in Area 3 was very small compared to the other areas, and the trend in ulcer patients across the study periods in Area 3 also differed from the trends in other areas. Area 3 is the Aizu region in Fukushima Prefecture. Due to issues immediately after the earthquake, data were collected from only one hospital. Therefore, the sample size was small. Furthermore, at this hospital, since the number of specialists in the gastrointestinal endoscopy increased from the previous year, the number of ulcer patients immediately after the quake increased compared to other areas, and ulcer patients showed a conspicuous increase the following year.

The ratio of hemorrhagic ulcers to peptic ulcer patients increased after the quake, just as previous studies reported (1, 10, 12, 13). Other similarities were noted with regard to higher ratios observed in Area 1 (close to the epicenter) and during the first month after the onset of the quake. Aoyama et al. (1) reported increased numbers of hemorrhagic gastric ulcers with *H. pylori* infection. However, our study found an *H. pylori* infection rate of 60.9% in 2011. This is attributable to the decrease in the rate of *H. pylori* infection in Japan (14, 15). Regarding the two causal factors for peptic ulcers (3, 16-18) of *H. pylori* infection and oral NSAID medication, no marked differences were found

among the study periods, and there were no marked differences in the oral antithrombotic drug medication rate either. Across all periods examined, 12% to 13% of the patients were *H. pylori*-negative recipients of oral non-NSAID non-antithrombotic medications. Therefore, we concluded that mental stress was not the only factor influencing the development of peptic ulcers but was one factor inducing severe ulcers, such as hemorrhagic ulcer. In addition, the decrease in the ratio of hemorrhagic ulcers in 2012, the year following the quake, seemed to be associated with a decreasing intensity of stress. Kanno et al. (13) found that 76 (87.4%) of 87 peptic ulcer patients living in refugee shelter had hemorrhagic ulcers, which demonstrates that living in a refugee shelter was a risk factor for hemorrhagic ulcer. In this study, a hemorrhagic ulcer developed in 50% of peptic ulcer patients living in a refugee shelter in 2011 and in 83.3% in 2012. A particularly interesting finding in 2012 was the high hemorrhage rate observed among patients living in shelter facilities, for which some daily living data were available, rather than in temporary shelters. Those patients seem to have been intensely affected by mental stress due to anxiety concerning radiation exposure, as Yabe et al. (8) reported that the nuclear accident after the Great East Japan Earthquake and tsunami caused psychological distress among residents in Fukushima Prefecture throughout the survey.

Several limitations associated with the present study warrant mention. First, the study was a retrospective cohort observational study. Second, only six facilities were involved in the study, and the overall sample size was small. Third, it was not possible to accurately investigate the movement of residents who evacuated. As such, the proportion of recipients of diagnostic examinations for *H. pylori* infection was low, at 50%. Finally, the data on the presence/absence of oral treatment with proton pump inhibitors and histamine 2 receptor antagonists were unable to be discussed because no adequate records were available at the individual facilities during the emergency.

In conclusion, after the Great East Japan Earthquake, the incidence of peptic ulcers did not increase in Fukushima Prefecture. This seems to be related mainly to the radiation disaster. However, the ratio of hemorrhagic ulcers increased, particularly in areas close to the epicenter and within one month after the quake. One novel aspect of this study was that it characterized peptic ulcers one year after the onset of the Great East Japan Earthquake.

**The authors state that they have no Conflict of Interest (COI).**

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