研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Aoki T, Takahashi J, Fukumoto Y, Yasuda S, Ito K, Miyata S, Shinozaki T, Inoue K, Yagi T, Komaru T, Katahira Y, Obata A, Hiramoto T, Sukegawa H, Ogata K, Shimokawa H.	Effect of the Great East Japan Earthquake on Cardiovascular Diseases -Report From the 10 Hospitals in the Disaster Area-.	Circ J.	77	490-493	2013
Aoki T, Fukumoto Y, Yasuda S, Sakata Y, Ito K, Takahashi J, Miyata S, Tsuji I, Shimokawa H.	The Great East Japan Earthquake Disaster and cardiovascular diseases.	Eur Heart J.	33	2796-2803	2012
Nakano M, Kondo M, Wakayama Y, Kawana A, Hasebe Y, Shafee MA, Fukuda K, Shimokawa H.	Increased Incidence of Tachyarrhythmias and Heart Failure Hospitalization in Patients With Implanted Cardiac Devices After the Great East Japan Earthquake Disaster.	Circ J.	76	1283-1285	2012
Nihei T, Takahashi J, Kikuchi Y, Takagi Y, Hao K, Tsuburaya R, Shiroto T, Ito Y, Matsumoto Y, Nakayama M, Ito K, Yasuda S, Shimokawa H.	Enhanced Rho-kinase activity in patients with vasospastic angina after the Great East Japan Earthquake.	Circ J.	76	2892-2894	2012

肥田頼彦、中島悟史、 森野禎浩、中村元行	【災害時における循環器診療-どう立ち向かうか-】識る 震災時における発症増加の機序を識る 震災と心不全(解説/特集)	Heart View	16	708-713	2012
竹石恭知他	福島県急性心筋梗塞発症登録調査2011年集計	福島県医師会報	74	506-514	2012
中里和彦、竹石恭知	大震災と循環器・呼吸器疾患　大震災と急性冠症候群	呼吸と循環	60	903-909	2012
Nakamura M, Tanaka F, Takahashi T, Makita S, Ishisone T, Onodera M, Ishibashi Y, Itai K, Onoda T, Ohsawa M, Tanno K, Sakata K, Shinichi O, Ogasawara K, Ogawa A, Kuribayashi T, Okayama A.	Sex-specific threshold levels of plasma B-type natriuretic peptide for prediction of cardiovascular event risk in a Japanese population initially free of cardiovascular disease.	Am J Cardiol	108	1564-1569	2011

Ⅳ．研究成果の刊行物・別刷

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

RAPID COMMUNICATION

Effect of the Great East Japan Earthquake on Cardiovascular Diseases

– Report From the 10 Hospitals in the Disaster Area –

Tatsuo Aoki, MD, PhD; Jun Takahashi, MD, PhD; Yoshihiro Fukumoto, MD, PhD; Satoshi Yasuda, MD, PhD; Kenta Ito, MD, PhD; Satoshi Miyata, PhD; Tsuyoshi Shinozaki, MD, PhD; Kanichi Inoue, MD, PhD; Tetsuo Yagi, MD, PhD; Tatsuya Komaru, MD, PhD; Yoshiaki Katahira, MD, PhD; Atsushi Obata, MD; Tetsuya Hiramoto, MD, PhD; Hiroyasu Sukegawa, MD, PhD; Kazunori Ogata, MD, PhD; Hiroaki Shimokawa, MD, PhD

Background: We reported an increased occurrence of cardiovascular diseases (CVDs) after the Great East Japan Earthquake by examining ambulance records, but it had to be confirmed by cardiologists.

Methods and Results: We enrolled patients admitted to the cardiology department of the 10 hospitals in the disaster area from 4 weeks prior to 15 weeks after March 11 in the years 2008–2011 (n=14,078). The weekly occurrence of several CVDs, including heart failure (HF), pulmonary thromboembolism (PTE) and infectious endocarditis (IE), was sharply and significantly increased after the Earthquake.

Conclusions: The Disaster caused significantly increases in the occurrence of HF, PTE and IE. (*Circ J* 2013; **77:** 490–493)

Key Words: Cardiovascular disease; Disasters; Great East Japan Earthquake

We examined ambulance records from Miyagi prefecture and reported that the occurrence of cardiovascular diseases (CVDs), including heart failure (HF), acute coronary syndrome (ACS), stroke, and cardiopulmonary arrest, had increased after the Great East Japan Earthquake (magnitude 9.0 on March 11, 2011).[1] However, because the ambulance records were made in the emergency rooms by doctors who were not always cardiologists, our findings had to be confirmed by cardiologists in the disaster area. Furthermore, we did not examine the incidence of pulmonary thromboembolism (PTE), infectious endocarditis (IE) or takotsubo cardiomyopathy in that previous study because those diagnoses require a professional approach.[1]

In this study, we examined the medical records made by cardiologists to determine whether the occurrence of CVDs, including HF, acute myocardial infarction (AMI), PTE, IE and takotsubo cardiomyopathy, had increased after the Earthquake.

Methods

The ethical committees of Tohoku University Hospital and participating hospitals approved the protocol of the present study.

Study Population and Participating Hospitals

We enrolled all patients admitted to the cardiology department of the 10 hospitals in Miyagi prefecture from 4 weeks prior to 15 weeks after the Earthquake in 2011 and in the corresponding periods in 2008, 2009 and 2010 (n=14,078). We also col-

Received December 24, 2012; revised manuscript received January 5, 2013; accepted January 7, 2013; released online January 18, 2013 Time for primary review: 3 days

Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai (T.A., J.T., Y.F., K. Ito, S.M., H. Shimokawa); Department of Cardiovascular Medicine, National Cerebral and Cardiovascular Center Hospital, Suita (S.Y.); Department of Cardiovascular Medicine, Sendai Medical Center, Sendai (T.S.); Department of Cardiovascular Medicine, South Miyagi Medical Center, Okawara (K. Inoue); Department of Cardiovascular Medicine, Sendai City Hospital, Sendai (T.Y.); Division of Cardiology, Tohoku Rosai Hospital, Sendai (T.K.); Cardiovascular Center, Tohoku Kouseinenkin Hospital, Sendai (Y.K.); Department of Cardiovascular Medicine, Saka General Hospital, Shiogama (A.O.); Department of Cardiovascular Medicine, Osaki Citizen Hospital, Osaki (T.H.); Department of Cardiovascular Medicine, Japanese Red Cross Ishinomaki Hospital, Ishinomaki (H. Sukegawa); and Department of Cardiovascular Medicine, Kesennuma City Hospital, Kesennuma (K.O.), Japan

The Guest Editor for this article was Hiroshi Ito, MD.

Mailing address: Hiroaki Shimokawa, MD, PhD, Professor and Chairman, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan. E-mail: shimo@cardio.med.tohoku.ac.jp

ISSN-1346-9843 doi:10.1253/circj.CJ-12-1594

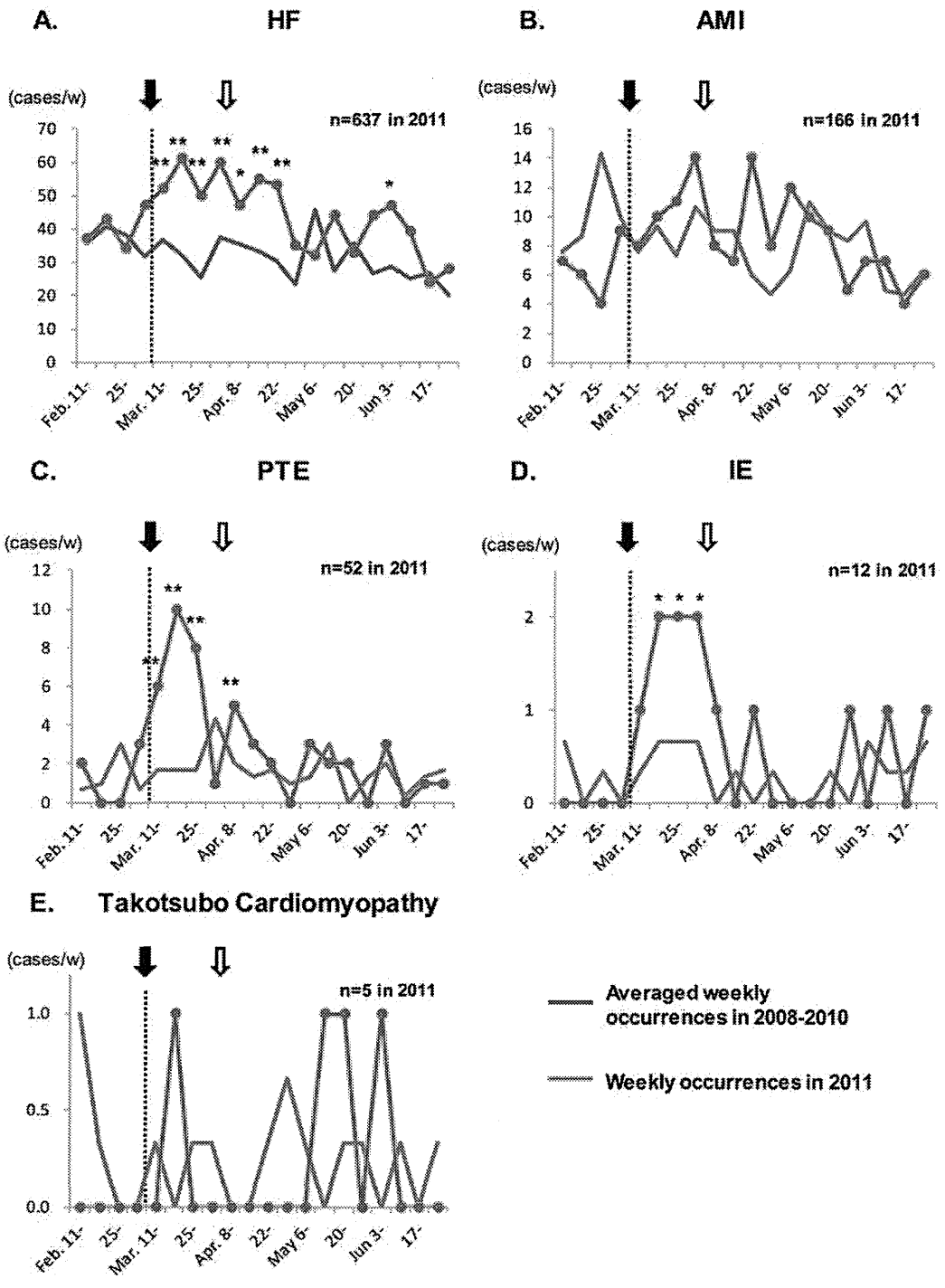

Figure 1. Weekly occurrence of cardiovascular diseases: (**A**) heart failure (HF), (**B**) acute myocardial infarction, (**C**) pulmonary thromboembolism (PTE), (**D**) infectious endocarditis (IE) and (**E**) takotsubo cardiomyopathy. HF, PTE and IE were significantly increased after the Earthquake. *P<0.05, **P<0.01. Black arrows indicate the occurrence of the Great East Japan Earthquake (magnitude 9.0, March 11, 2011), and white arrows indicate the largest aftershock (magnitude 7.2, April 7, 2011).

lected additional information about the date of admission, sex and age of the patients from the medical insurance database. We defined the 3 hospitals facing the Pacific Ocean as those in the seacoast area with direct assault by the tsunamis, and the remaining 7 hospitals as those in the inland (remote) area.

Definition of the Diseases

All definitive diagnoses of the patients were confirmed at discharge by cardiologists and classified according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10). We also collected the diag-

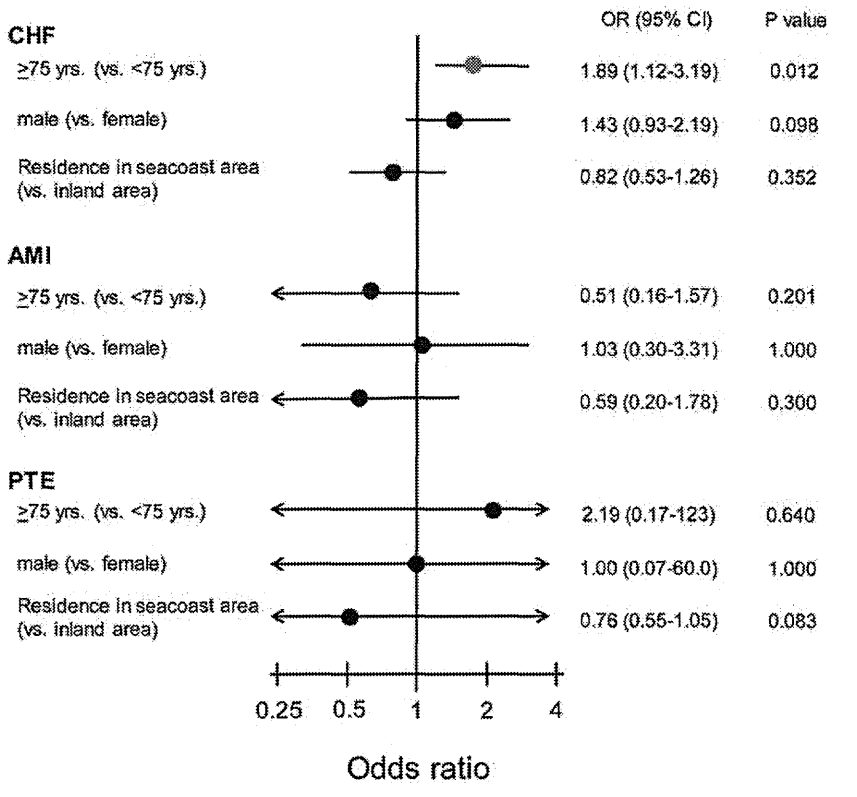

Figure 2. Effect of age, sex and area of residence on increased occurrence of cardiovascular diseases. We first counted the occurrence of each variable in the 4 weeks before and after the Earthquake in 2011, and subsequently calculated the odds ratio. No significant influence of age, sex or residence area was noted, except for the influence of high age on the occurrence of HF. Because there was no patient with IE or takotsubo cardiomyopathy before the Earthquake in 2011, we were unable to calculate the odds ratio of these 2 diseases. *P<0.05. AMI, acute myocardial infarction; HF, heart failure; PTE, pulmonary thromboembolism; OR, odds ratio; 95% CI, 95% confidence interval.

nosis at discharge from the medical insurance database as the ICD-10 code, comprising I-50.0 (HF), I-21.0–I-21.9 (AMI), I-26.0–I-26.9 (PTE), I-33.0–I-33.9 (IE) and takotsubo cardiomyopathy (I-51.8).

Statistical Analysis

We used a Poisson regression model to assess differences in the variables between 2011 and the previous 3 years.[1] Furthermore, as previously reported,[1] we calculated the odds ratio with the 4-week occurrence in 2011 before and after the Earthquake in terms of age (<75 or ≥75 years), sex, and area of residence (inland vs. seacoast). Continuous variables are expressed as mean±SD. All statistical analyses were performed using R 2.15.0 (www.r-project.org/). All P values were 2-sided, and P<0.05 was considered to be statistically significant.

Results

The number of patients enrolled in the study for 2008, 2009, 2010 and 2011 was 3,190, 3,582, 3,752 and 3,554, respectively. In 2011, the prevalence of male sex was significantly lower (62.2%, 61.75, 59.95 and 58.8% in 2008, 2009, 2010 and 2011, respectively, P=0.014) and age (years) was significantly higher (68.8±13.9, 69.5±13.9, 70.4±14.2, and 71.2±14.2 in 2008, 2009, 2010 and 2011, respectively, P<0.05).

The weekly occurrence of each of HF, PTE and IE was significantly increased after the Earthquake (Figures 1A,C,D). We also noted a mild but insignificant peak of the weekly occurrence of AMI after the Earthquake (Figure 1B). There were very few cases of takotsubo cardiomyopathy, even after the Earthquake (Figure 1E). The significant increase in the weekly occurrence of HF was prolonged for 7 weeks after the Earthquake in 2011 (Figure 1A), whereas the time course of PTE showed a second peak at the largest aftershock (magnitude 7.2 on April 7, 2011).

The subgroup analyses showed that among the 3 factors examined (age, sex, and area of residence), only higher age (>75 years) significantly influenced the occurrence of HF but not that of AMI or PTE (Figure 2). Because there was no patient with IE or takotsubo cardiomyopathy for 4 weeks before the Earthquake in 2011, we were unable to calculate the odds ratio of either disease.

Discussion

In the present study of cardiologists records, as compared with our recent study using ambulance records,[1] we were able to demonstrate the following: (1) a sharp and sustained (over 7 weeks) increase in the occurrence of HF after the Earthquake, (2) a sharp but transiently increased occurrence of both PTE and IE after the Earthquake, and (3) a tendency for the occurrence of AMI to be increased, but not that of takotsubo cardiomyopathy, after the Earthquake.

Increased Occurrences of CVD

The present study demonstrated a significant increase in the occurrence of both HF and PTE, consistent with the findings of our recent study[1] and another study,[2] and of IE, which was a novel finding not reported previously.[3–8]

The Earthquake forced many people in the Miyagi prefecture to take shelter and/or to live without daily necessities, services, and medicines. Disaster situations can increase the occurrence of CVDs through physical and mental stresses.[9] Furthermore, a prolonged stressful situation can suppress the immune sys-

tem,[10] leading to increased rates of infectious diseases, such as IE.

Activation of the sympathetic nervous system of people involved in the present disaster would have elevated both blood pressure and heart rate, as previously reported.[9,11] The report by Satoh et al has also demonstrated that self-monitored blood pressure significantly increased after the Earthquake.[12] Furthermore, we recently reported that the Earthquake increased the occurrence of ventricular tachyarrhythmias among patients with an implantable cardiac defibrillator.[13] Thus, we consider that an activated sympathetic nervous system, elevated blood pressure, and increased occurrence of tachyarrhythmias were all involved in the increased occurrence of HF during and after the Great East Japan Earthquake.

Although people in temporary accommodation were supplied with information and compression stockings, the increased occurrence of PTE after the Earthquake was not prevented.[3] The occurrence of severe PTE, with resultant improved mortality from PTE, may have been decreased; however, further studies regarding the effects of preventive practice for PTE are needed.

In the present study, the occurrence of AMI also tended to increase after the Earthquake, and in our recent study there was a significant increase in the occurrence of ACS (AMI plus unstable angina).[1] Unlike in a previous report,[3] we did not observe an increased occurrence of takotsubo cardiomyopathy. The reasons for the discrepancy remains to be examined in future studies.

Effects of Age, Sex and Location of Hospitals on CVDs

In the present study, no significant influence of age, sex or area of residence was noted for CVDs, except for the influence of higher age on the occurrence of HF, which suggested that the Earthquake had a greater effect on elderly people.

Although the tsunami directly and seriously affected the seacoast area, the increased occurrence of CVDs after the Earthquake was comparable between the seacoast and inland areas. Similar indirect effects of a disaster on CVD occurrence were reported after the World Trade Center Disaster in 2001, whereby the blood pressure of people in Mississippi was equally elevated as in those in New York City.[14] These results indicate that life-threatening events, such as a great earthquake, can trigger CVDs even in remote areas.

The limitations of this study include the lack of detailed patient data, such as clinical characteristics and underlying heart disease. In order to prospectively observe the long-term prognosis of the patients, we are following the HF patients in a cohort in the Tohoku area,[15] which had been established 2.5 years before the Earthquake.

Conclusions

The Great East Japan Earthquake Disaster significantly increased the occurrence of CVDs, including HF, PTE and IE. Elderly patients with HF were significantly more affected by the Earthquake.

Acknowledgments

This work was supported by the contribution of the Japanese Circulation Society.

Disclosures

None.

References

1. Aoki T, Fukumoto Y, Yasuda S, Sakata Y, Ito K, Takahashi J, et al. The Great East Japan Earthquake Disaster and cardiovascular diseases. *Eur Heart J* 2012; **33:** 2796–2803.
2. Watanabe H, Kodama M, Tanabe N, Nakamura Y, Nagai T, Sato M, et al. Impact of earthquakes on risk for pulmonary embolism. *Int J Cardiol* 2008; **129:** 152–154.
3. Watanabe H, Kodama M, Okura Y, Aizawa Y, Tanabe N, Chinushi M, et al. Impact of earthquakes on takotsubo cardiomyopathy. *JAMA* 2005; **294:** 305–307.
4. Suzuki S, Sakamoto S, Miki T, Matsuo T. Hanshin-Awaji Earthquake and acute myocardial infarction. *Lancet* 1995; **345:** 981.
5. Suzuki S, Sakamoto S, Koide M, Fujita H, Sakuramoto H, Kuroda T, et al. Hanshin-AwajiEearthquake as a trigger for acute myocardial infarction. *Am Heart J* 1997; **134:** 974–977.
6. Leor J, Poole WK, Kloner RA. Sudden cardiac death triggered by an earthquake. *N Engl J Med* 1996; **334:** 413–419.
7. Zhang XQ, Chen M, Yang Q, Yan SD, Huang DJ. Effect of the wenchuan earthquake in china on hemodynamically unstable ventricular tachyarrhythmia in hospitalized patients. *Am J Cardiol* 2009; **103:** 994–997.
8. Tsuchida M, Kawashiri MA, Teramoto R, Takata M, Sakata K, Omi W, et al. Impact of severe earthquake on the occurrence of acute coronary syndrome and stroke in a rural area of Japan. *Circ J* 2009; **73:** 1243–1247.
9. Esler M, Kaye D. Sympathetic nervous system activation in essential hypertension, cardiac failure and psychosomatic heart disease. *J Cardiovasc Pharmacol* 2000; **35:** S1–S7.
10. Segerstrom SC, Miller GE. Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychol Bull* 2004; **130:** 601–630.
11. Kario K. Disaster hypertension: Its characteristics, mechanism, and management. *Circ J* 2012; **76:** 553–562.
12. Satoh M, Kikuya M, Ohkubo T, Imai Y. Acute and subacute effects of the Great East Japan Earthquake on home blood pressure values. *Hypertension* 2011; **58:** e193–e194.
13. Nakano M, Kondo M, Wakayama Y, Kawana A, Hasebe Y, Shafee MA, et al. Increased incidence of tachyarrhythmias and heart failure hospitalization in patients with implanted cardiac devices after the Great East Japan Earthquake Disaster. *Circ J* 2012; **76:** 1283–1285.
14. Gerin W, Chaplin W, Schwartz JE, Holland J, Alter R, Wheeler R, et al. Sustained blood pressure increase after an acute stressor: The effects of the 11 September 2001 attack on the New York City World Trade Center. *J Hypertens* 2005; **23:** 279–284.
15. Shiba N, Nochioka K, Miura M, Kohno H, Shimokawa H, CHART-2 Investigators. Trend of westernization of etiology and clinical characteristics of heart failure patients in Japan: First report from the Chart-2 Study. *Circ J* 2011; **75:** 823–833.

European Heart Journal (2012) **33**, 2796–2803
doi:10.1093/eurheartj/ehs288

FASTTRACK
ESC HOT LINE

The Great East Japan Earthquake Disaster and cardiovascular diseases

Tatsuo Aoki[1], Yoshihiro Fukumoto[1], Satoshi Yasuda[1], Yasuhiko Sakata[1], Kenta Ito[1], Jun Takahashi[1], Satoshi Miyata[1], Ichiro Tsuji[2], and Hiroaki Shimokawa[1]*

[1]Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan; and [2]Department of Public Health, Tohoku University Graduate School of Medicine, Sendai, Japan

Received 1 July 2012; revised 3 August 2012; accepted 8 August 2012; online publish-ahead-of-print 28 August 2012

See page 2759 for the editorial comment on this article (doi:10.1093/eurheartj/ehs297)

Aims While previous studies reported a short-term increase in individual cardiovascular disease (CVD) after great earthquakes, mid-term occurrences of all types of CVDs after great earthquakes are unknown. We addressed this important issue in our experience with the Great East Japan Earthquake (11 March 2011).

Methods and results We retrospectively examined the impact of the Earthquake on the occurrences of CVDs and pneumonia by comparing the ambulance records made by doctors in our Miyagi Prefecture, the centre of the disaster area, during the periods of 2008–11 ($n = 124\,152$). The weekly occurrences of CVDs, including heart failure (HF), acute coronary syndrome (ACS), stroke, cardiopulmonary arrest (CPA), and pneumonia were all significantly increased after the Earthquake compared with the previous 3 years. The occurrences of ACS and CPA showed the rapid increase followed by a sharp decline, whereas those of HF and pneumonia showed a prolonged increase for more than 6 weeks and those of stroke and CPA showed a second peak after the largest aftershock (7 April 2011). Furthermore, the occurrence of CPA was increased in the first 24 h after the Earthquake, followed by other diseases later on. These increases were independent of age, sex, or residence area (seacoast vs. inland).

Conclusion These results indicate that the occurrences of all types of CVDs and pneumonia were increased in somewhat different time courses after the Earthquake, including the first observation of the marked and prolonged increase in HF, emphasizing the importance of intensive medical management of all types of CVDs after great earthquakes.

Keywords Earthquake • Cardiovascular disease • Heart failure • Tsunami

Introduction

On 11 March 2011, the Great East Japan Earthquake hit the northeast part of Japan with a magnitude of 9.0 on the Richter scale, which was one of the largest ocean-trench earthquakes ever recorded in Japan (*Table 1*).[1] The Earthquake caused huge damage, including 15 861 dead, 3018 missing persons, and 388 783 destroyed houses as of 6 June 2012.[2] It forced many people (~400 000) to be evacuated to temporary accommodation, such as public halls, gymnastic halls, and scholastic institutions in Northeast Japan. Since the Earthquake occurred with its epicentre located at 38° latitude, 19 min North, and 142° longitude, 22 min East, our Miyagi Prefecture with a population of 2 348 165 was the closest area to the epicentre (*Figure 1A*), where there was the largest amount of damage and number of victims, including 9512 dead, 1581 missing persons, and 232 553 destroyed houses as of 8 May 2012,[2,3] and most of the damage was observed in the seacoast area, including 9506 dead (95.8%), 1578 missing persons (99.8%) and 222 880 destroyed houses (95.8%).

It has been previously reported that the occurrences of acute coronary syndrome (ACS), stroke, pulmonary embolism, and takotsubo cardiomyopathy were increased after the large earthquakes in Japan (*Table 1*).[4–9] Furthermore, it has been reported that the occurrences of sudden cardiac death and haemodynamically unstable ventricular tachyarrhythmias were increased after the Northridge Earthquake in California, USA, and the Wenchuan Earthquake in China, respectively (*Table 1*).[10] Thus, the previous reports have revealed that the occurrences of

* Corresponding author. Tel: +81 22 717 7151, Fax: +81 22 717 7156, Email: shimo@cardio.med.tohoku.ac.jp

Table 1 Past major earthquakes and cardiovascular diseases

Place of earthquake (country)	Year	Month	Magnitude	Temperature on onset day (°C) (high/low)	No. of deaths	No. of injured	Diseases increased	Periods of increased occurrences after each earthquake
Northridge (USA)[11]	1994	January	6.7	19/9	57	5400	Sudden deaths	On the day of the earthquake
Hanshin-Awaji (Japan)[8,9,13]	1995	January	7.3	8/1.4	6434	43 792	AMI, pneumonia	AMI: from 1st to 4th week Pneumonia: first month
Indian Ocean (Indonesia)	2004	December	9.1	32/25	Over 220 000	130 000	No data available	No data available
Mid-Niigata (Japan)[6,7]	2004	Octorber	6.8	26.4/22	68	4805	Takotsubo cardiomyopathy, PE, sudden deaths	Takotsubo cardiomyopathy: from 1st to 3rd week, PE and sudden deaths: first week
Wenchuan (China)[17]	2008	May	7.9	25.0/17	69 197	18 222	VT/VF	From 1st to 3rd day
East Japan (Japan)	2011	March	9.0	6.2/-2.5	15 845	5894	HF, ACS, stroke, CPA, pneumonia	See text

AMI, acute myocardial infarction; PE, pulmonary artery embolism; ACS, acute coronary syndrome; VT/VF, ventricular tachycardia/ventricular fibrillation; HF, heart failure; CPA, cardiopulmonary arrest.

various cardiovascular diseases (CVDs) were increased after large earthquakes. However, these studies reported only the short-term occurrence of individual CVD and the longer-term occurrences of all types of CVDs after great earthquakes remain to be elucidated.

In the present study, we thus addressed this important issue by comparing the ambulance records made by medical doctors in our Miyagi Prefecture, the centre of the disaster area, during the periods of 2008–11. The present study demonstrates for the first time the marked and prolonged increase in the occurrence of heart failure (HF), in addition to other CVDs, which has not been reported previously.

Methods

This study was a collaboration study with the Miyagi Medical Association and the Fire Departments of the Miyagi Prefecture. The Ethics Committees of Tohoku University Hospital approved this study protocol.

Study population

We enrolled all ambulance transport records in the Miyagi Prefecture from 11 February to 30 June in each year of 2008–11 ($n = 124\,152$), from 4 weeks before to 16 weeks after 11 March, in order to reveal the effects of the Earthquake on the occurrence of CVDs. In Japan, medical doctors in the emergency rooms routinely make the diagnoses of transported patients at the initial visit. These reports were collected and stored in the fire departments that operate the emergency medical system. We were able to obtain all the medical records from the 12 fire departments in the Miyagi Prefecture. In our prefecture, the 12 fire departments routinely transfer patients to the 57 hospitals with emergency rooms that are registered by the prefecture. Among these 57 hospitals, 56 (98%) have an echocardiography machine, 57 (100%) have full-time physicians, and 38 (67%) have full-time cardiologists. It has been reported that the diagnostic accuracy of ACS in the emergency room is 83.4% in Japan.[10] Based on the records, we examined the weekly occurrences of HF, ACS, stroke, cardiac pulmonary arrest (CPA), and pneumonia and compared them with those in the previous 3 years (2008–10). Furthermore, we examined the daily occurrences of the diseases for a week before and after the Earthquake.

To access the impact of the Earthquake and the aftershocks on the occurrence of the diseases, we counted the number of earthquakes with a seismic intensity of 1 or greater on the Japanese scale, which were observed in the Miyagi Prefecture during the study period (Japan Meteorological Agency: http://www.jma.go.jp/jma/index.html). We defined the municipalities facing the Pacific Ocean as the seacoast area where the Tsunami directly attacked and the remaining inner area as the inland area (*Figure 1B*).

Definition of the diseases

We obtained all diagnoses from the ambulance records, which were made by attending doctors in emergency rooms based on physical examination, ECG, chest X-ray, echocardiography, and laboratory findings including the blood gas test. When definitive diagnoses are made by doctors in the emergency rooms, they write the diagnoses on the ambulance records; however, when definitive diagnoses are not confirmed in the emergency rooms, they write tentative diagnoses or only symptoms, which are defined as undiagnosed cases in the present study. We have excluded such undiagnosed cases from the analyses in the present study.

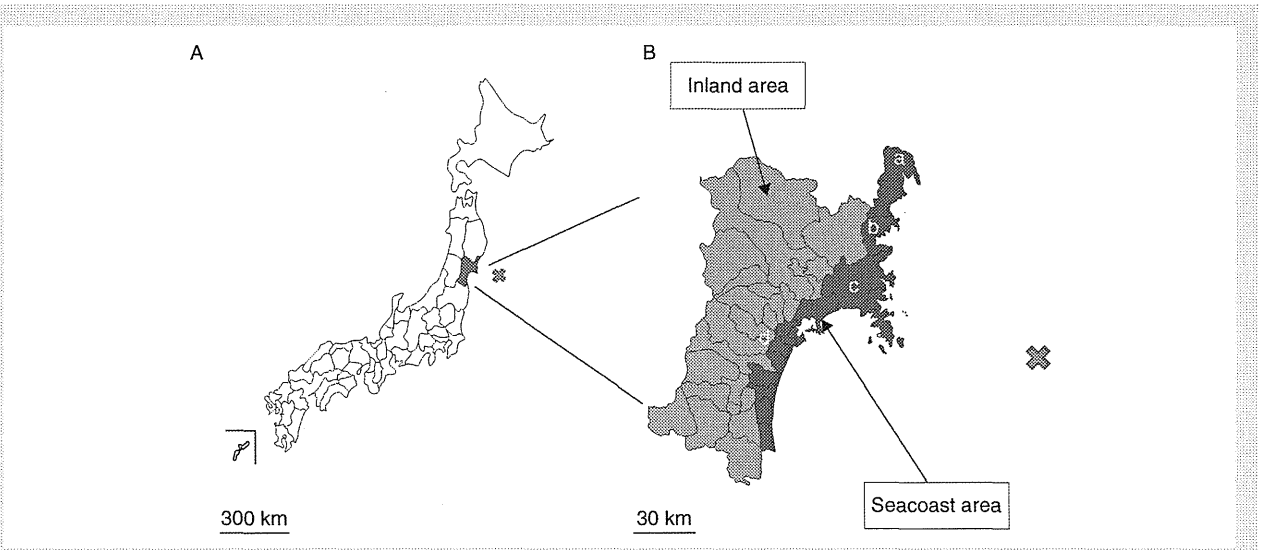

Figure 1 Locations of the epicentre of the Great East Japan Earthquake and the Miyagi Prefecture. (*A*) The epicentre of the East Japan Earthquake (cross) was under the Pacific Ocean about 150 km east of the Miyagi Prefecture. (*B*) The municipalities in the Miyagi Prefecture facing the Pacific Ocean were defined as the seacoast area (shown in red) and the other area as the inland area (shown in blue). Many cities in the coast area, including Kesennuma (a), Minami-sanriku (b), Ishinomaki (c), and Sendai (d) were seriously damaged by the Tsunami.

Acute coronary syndrome was defined as acute myocardial infarction or unstable angina, stroke as intracranial haemorrhage, cerebral infarction or subarachnoid haemorrhage, and CPA as cardiopulmonary resuscitation performance regardless of the causes. In each year, we calculated 'the rate of definitive diagnosis at admission in the emergency rooms (%)', which means the percentage of cases with definitive diagnosis made by doctors among all transported cases.

Statistical analysis

To assess the differences in the occurrences of CVDs and pneumonia before and after the Earthquake between 2011 and the previous 3 years, we applied the Poisson regression model to the daily occurrences in 2008–11 with the 'dummy' variables which indicate the individual weeks in 2011.[11] First, we defined the dummy variable of each week after 11 March 2011 that takes a value of 1 or 0, indicating whether or not the sample was observed in the corresponding week. Then, we fitted the Poisson regression model with all dummy variables to explain the daily occurrences of the CVDs. Finally, we selected effective dummies of significant weeks by the backward elimination stepwise regression method. Furthermore, we calculated odds ratio with the 4-week occurrence of the disease in 2011 before and after the Earthquake in the following subgroups; young (<75 years old) and old (≥75 years old) patients, male and female, and the inland and seacoast residence areas. We used Fisher's exact test for the subgroup analyses. Continuous variables are expressed as mean ± SD. All statistical analyses were performed using R 2.15.0 (www.r-project.org/). All *P*-values were two-sided, and *P*-values of <0.05 were considered to be statistically significant.

Results

The total number of ambulance transports in the period of 11 February to 30 June in 2008, 2009, 2010, and 2011 was 28 709, 28 069, 30 645, and 36 729, respectively. When compared with the previous 3 years (2008–10), the number of ambulance transports in 2011 peaked on Day 2 (12 March) followed by a gradual decline (see Supplementary material online, *Figure S1*). The rate of definitive diagnosis at admission in the emergency rooms made by attending doctors was 56.7% (16 265/28 709 cases), 56.6% (15 873/28 069 cases), 56.2% (17 217/30 645 cases), and 55.5% (20 400/36 729 cases), respectively. Thus, the rate of definitive diagnosis at admission in the emergency rooms was comparable among the 4 years studied. The prevalence of male sex was also comparable among the 4 years (51.9, 51.3, 51.4, and 51.8%, respectively). The age of all transported patients in 2011 (61.2 ± 25.3 years old) was significantly higher than those in the previous 3 years (57.6 ± 26.5 years old in 2008; 58.3 ± 26.2 years old in 2009; 59.3 ± 26.4 years old in 2010, all $P < 0.001$); however, the age of patients with each disease in 2011 was comparable with that in the previous 3 years (2008–10) (data not shown).

Importantly, the weekly occurrences of the five diseases examined, including HF, ACS, stroke, CPA, and pneumonia, were all significantly increased soon after the Earthquake (*Figure 2A–F*; see Supplementary material online, *Table S1*). The occurrence of CPA was significantly increased after the Earthquake even after excluding the non-cardiopulmonary cases (*Figure 2D* and *E*). Furthermore, in the time-course analyses of daily occurrences, we were able to demonstrate the significant increase in the occurrence of CPA on the day of the Earthquake even after excluding the non-cardiopulmonary cases, while the increased occurrences of other diseases were noted a few days after the Earthquake (*Figure 3A* and *C–F*). Also, the occurrence of ACS did not peak during the first 7 days (*Figure 3B*). In the subanalysis of the patients with stroke, a significant increase in the occurrence was noted only

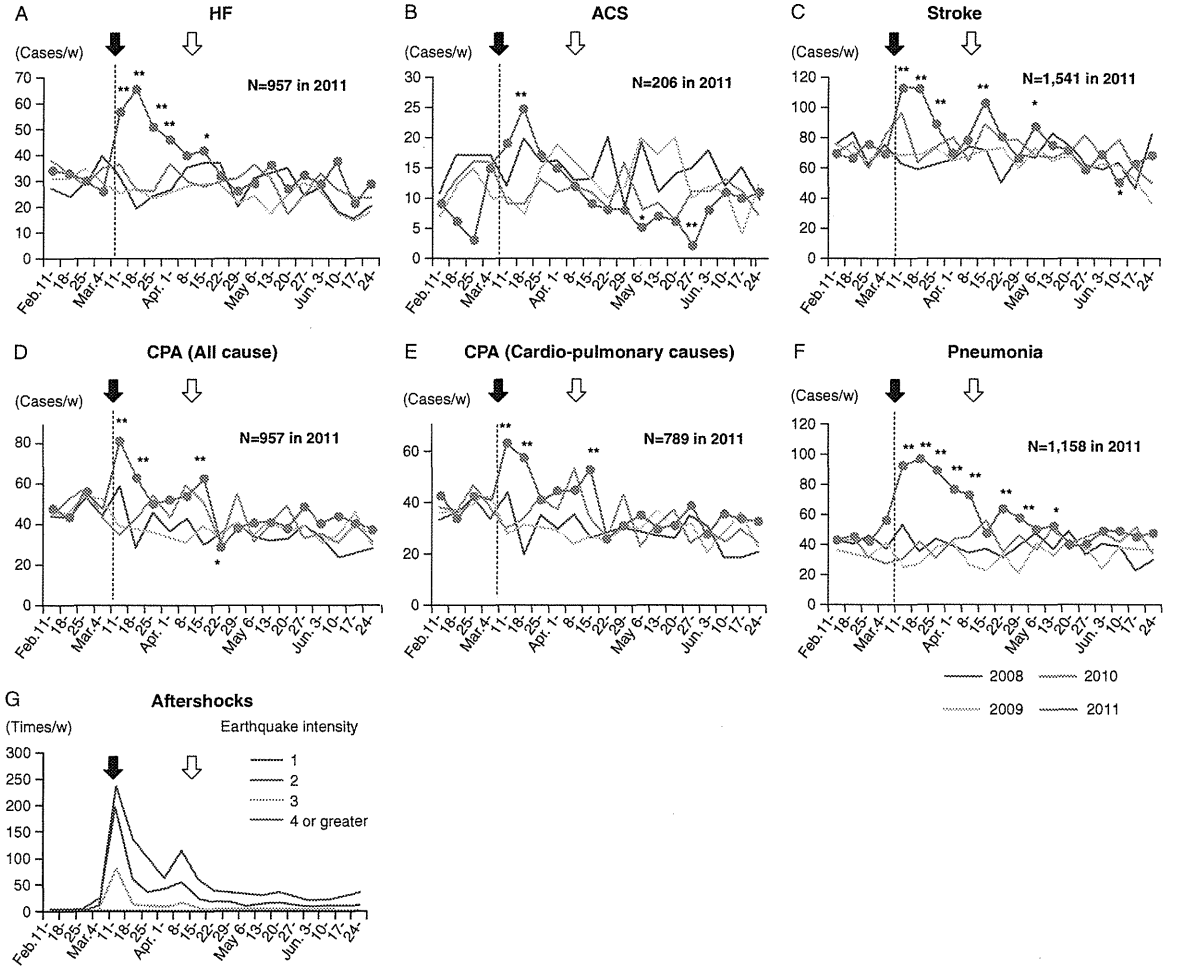

Figure 2 Time course of weekly occurrences of the diseases. (*A–F*) Weekly occurrences of heart failure (HF), stroke, cardiopulmonary arrest (CPA), and pneumonia were significantly increased after the Earthquake. $*P < 0.05$ and $**P < 0.01$. (*G*) The weekly counts of aftershocks observed in the Miyagi Prefecture with a seismic intensity of 1.0 or greater on the Japanese scale. The seismic intensity of the major Earthquake of 11 March 2011 was 7 in the Miyagi Prefecture. The number in the panels indicates the total number of the patients in 2011. Black arrows indicate the occurrence of the Great East Japan Earthquake (magnitude of 9.0, 11 March 2011) and white arrows indicate the largest aftershock (magnitude of 7.0, 11 April 2011).

for cerebral infarction but not for intracranial haemorrhage (see Supplementary material online, *Figure S2*). The number of aftershocks in the Miyagi Prefecture was frequent during the 6 weeks after the Earthquake, and the second peak was noted at the large aftershock on 7 April 2011 (magnitude of 7.0) (*Figure 2G*). When compared with the previous 3 years, the significant increases in the occurrence of HF and pneumonia were prolonged for more than 6 weeks after the Earthquake in 2011 (*Figure 2A* and *F*). On the other hand, the time course of the occurrences of stroke and CPA was shown by the second peak, corresponding to the distribution of the aftershocks (*Figure 2C–E*). We also observed that the rapid increase in the occurrence of ACS was followed by a significant decline (*Figure 2B*). Similarly, the occurrence of CPA showed a significant increase after the large aftershock followed by a rapid decline (*Figure 2D* and *E*). Those results by the Poisson regression stepwise analysis were comparable with those by the full Poisson regression analysis without stepwise methods (data not shown).

The subgroup analyses of the 2011 data showed that age, sex, or residence area did not significantly influence the occurrences of CVDs after the Earthquake (*Figure 4*). In contrast, a significant influence of residence area was noted only for pneumonia with a high occurrence in the seacoast (tsunami) area, although sex and age again had no effect (*Figure 4*).

Discussion

The novel findings of the present study are as follows: (i) the occurrences of CVDs and pneumonia were all significantly increased after the Great East Japan Earthquake in 2011 when

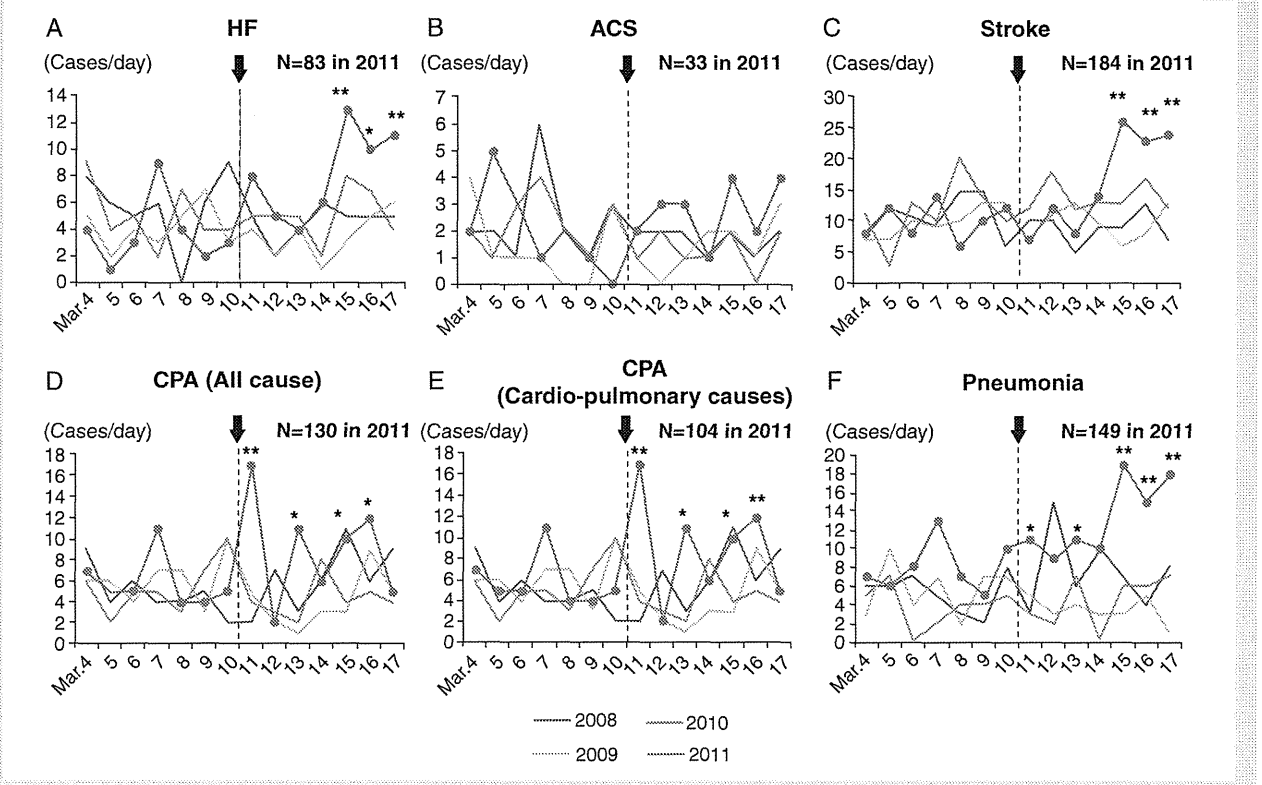

Figure 3 Daily occurrences of the diseases before and after the Earthquake. (*A–F*) Daily occurrences of heart failure (HF), stroke, cardiopulmonary arrest (CPA), and pneumonia were significantly increased after the Earthquake. $^{*}P < 0.05$ and $^{**}P < 0.01$. The number in the panels indicates that for 4 weeks before and after the Earthquake. Black arrows indicate the occurrence of the Great East Japan Earthquake (magnitude of 9.0, 11 March 2011).

compared with the previous 3 years (2008–10), (ii) the occurrences of HF and pneumonia were then gradually decreased, whereas the occurrences of ACS, stroke, and CPA were rapidly decreased when compared with those of HF and pneumonia, (iii) the occurrences of CVDs were increased independent of age, sex, or residence area, and (iv) the increase in the occurrence of pneumonia was higher in the seacoast (tsunami) area than in the inland area. To the best of our knowledge, this is the first report that demonstrates the mid-term courses of the occurrences of major CVDs and pneumonia after a great earthquake in the large-scale population. Especially, it provides the first evidence that the occurrence of HF was markedly increased for a long period after the Earthquake.

Increased occurrences of cardiovascular diseases and pneumonia

In the present study, we observed that the occurrences of HF, ACS, stroke, CPA, and pneumonia were all significantly increased after the Great East Japan Earthquake. Although previous studies demonstrated that the occurrences of acute myocardial infarction, stroke, and CPA were increased after earthquakes,[5,8,9,12–14] no study has ever demonstrated the increase in the occurrence of HF. The Earthquake forced many people in the Miyagi Prefecture to take shelter and/or to live without distribution of daily necessities, lifelines (e.g. water and electric supplies), and medicines. To make the situation worse, they were afflicted by the frequent aftershocks (the aftershocks with a seismic intensity of 1.0 or greater occurred 1025 times from 11 March to 7 April) and the freezing temperature (the average temperature in Sendai City was 3.8°C in March 2011) (*Table 1*). In these situations, where people are forced to extreme physical/mental stresses, CVDs may be caused by the activated sympathetic nervous system.[15,16] A transient increase in blood viscosity after an earthquake was observed only in those with high stress (e.g. move to shelter and loss of family member), which may increase the occurrences of ACS, stroke, and CPA.[17]

Increased occurrence of heart failure

When compared with the previous reports (*Table 1*),[5–9,12,14,18] one of the novel findings of the present study is the significant increase in the occurrence of HF, for which several factors may be involved. The activated sympathetic nervous system in the Great East Japan Earthquake should have elevated blood pressure and heart rate, as previously reported after large earthquakes.[15,19] Furthermore, the discontinued logistics distribution caused by the Earthquake resulted in insufficient delivery of regular medications,

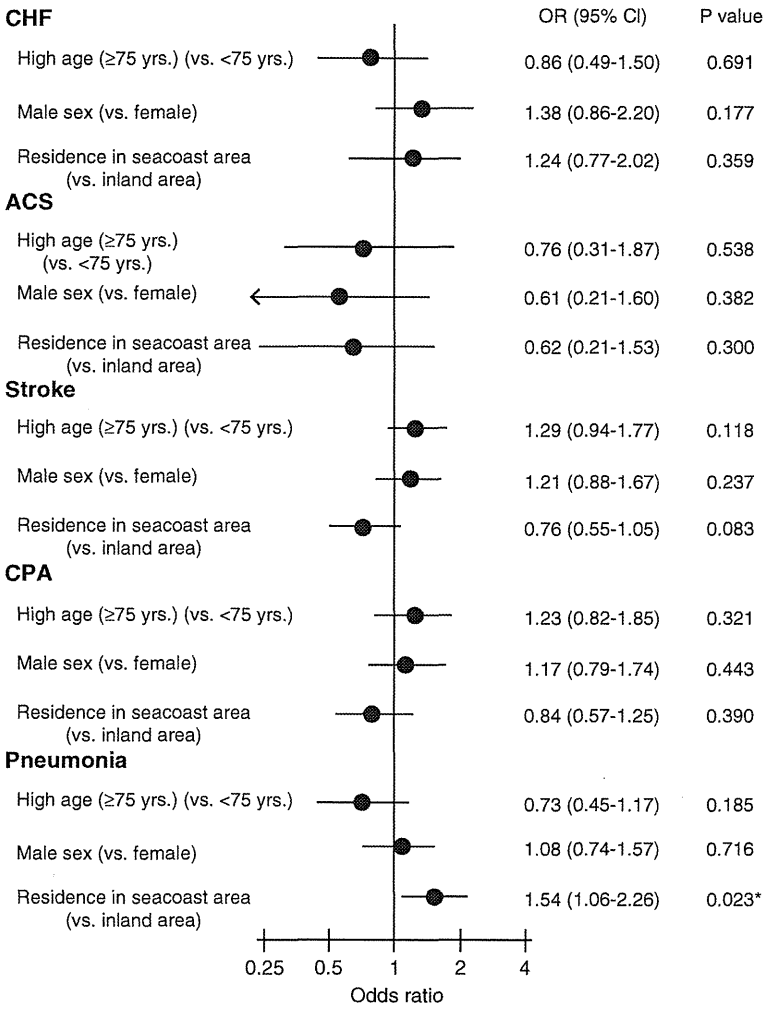

Figure 4 Subgroup analyses regarding age, sex, and residence area. We first counted the occurrence of each variable in the 4 weeks before and after the Earthquake and subsequently calculated the odds ratio. No significant influences of age, sex, or residence area were noted for the occurrences of cardiovascular diseases and pneumonia, except for the influence of the seacoast residence on the occurrence of pneumonia. HF, heart failure; ACS, acute coronary syndrome; CPA, cardiopulmonary arrest; OR, odds ratio; 95%CI, 95% confidential interval.

such as antihypertensive drugs and antithrombotic drugs, which can increase cardiovascular events as reported previously.[20] Moreover, these situations forced people to use preserved foods with high salt, and not fresh food, which also can elevate blood pressure and worsen HF.[21–23] It has been reported that high-salt intake under mental stress elevates blood pressure to a greater extent than normal conditions, thus easily worsening HF.[24,25] Additionally, the recent study has demonstrated that antecedent hypertension is associated with the increased occurrence of HF.[26] Furthermore, the recent report from our institute demonstrated that self-monitoring blood pressure was significantly elevated after the Earthquake.[27] Recently, we also have reported that the Earthquake increases the occurrence of ventricular tachyarrhythmia and hospitalization from worsening of HF among the patients with implantable cardiac defibrillators.[28] One of the well-known factors that worsen HF is infection including pneumonia, which was significantly increased after the Earthquake as shown in the present study. Taken together, we consider that discontinuation of drugs, increased salt intake, activated sympathetic nervous system, blood pressure elevation, and increased occurrences of tachyarrhythmia and infections were likely involved in the increased occurrence of HF after the Great East Japan Earthquake.

Time course of occurrences of the diseases

Unlike HF and pneumonia that showed a gradual decline for more than 6 weeks after the Earthquake, the weekly occurrence of ACS and CPA showed significant increases followed by decreases within 2–3 weeks after the Earthquake. Furthermore, the immediate

increase in the occurrence of the disease on the day of the Earthquake was noted only for CPA. The similar tendency was reported for sudden cardiac deaths related to atherosclerotic CVD after the Northridge Earthquake, although the observational period was very short (7 days)[12] when compared with the present study (16 weeks). These results suggest that the physical and/or mental stress induced by the Earthquake first facilitated CPA events, while other CVDs were due to the catastrophe occurring later on (tsunami, break down of lifelines, low temperatures, etc.). However, in the present catastrophic situation, the emergency care system itself was severely damaged for both ambulance transport and ambulance personnel availability, where the patients with CPA had a priority for ambulance transport. Thus, such a logistic factor may also have been involved in the present results. Furthermore, the onset patterns of CPA and stroke showed the second peak after the largest aftershock, suggesting that unstabilization of atherosclerotic plaques[29] and an increase in blood pressure were accelerated by the Earthquake[27] with a resultant increase followed by a decrease in the occurrence, an interesting and important difference when compared with other diseases.

Predictors for increased occurrences of cardiovascular diseases and pneumonia

Little information is available about the impacts of age and sex on the occurrences of CVDs and pneumonia after an earthquake. Although the age of all transported patients in 2011 was significantly higher than that in the previous 3 years, the age of the patients with CVDs and pneumonia was comparable with the previous 3 years, suggesting less impact of age and sex on the increased occurrences of CVDs and pneumonia (*Figure 3*).

Importantly, although the Earthquake-induced tsunami directly and seriously affected the people in the seacoast area, but not those in the inland area, the increased occurrences of CVDs after the Earthquake were comparable between the two areas. Similar indirect effects of a disaster on CVDs in a remote area have been reported in the World Trade Center Disaster in 2001, where the blood pressure of people living in Mississippi was equally elevated as that of those living in New York City.[30] These results indicate that the impact of life-threatening events, such as the Great Earthquake, could trigger CVDs even in areas distant from the disaster area. However, a certain number of people who suffered damage from the tsunami migrated from the seacoast area to the inland area after the Earthquake, which might have attenuated the influence of the tsunami on the occurrence of the diseases examined. In contrast, the increased occurrence of pneumonia was higher in the seacoast area than in the inland area, which can be explained by aspiration pneumonia in drowned people and/or the large amount of sludge carried by the tsunami.

Study limitations

Several limitations should be mentioned for the present study. First, in the present study, we analysed the occurrences of the diseases based on the initial diagnoses on the ambulance transport records that were made by attending doctors. Although the diagnoses were made based on physical examination, ECG, chest X-ray, echocardiography, and laboratory test, the process of the diagnoses were not standardized in the present study. Although this method might reduce the accuracy of diagnoses, the rate of definitive diagnosis at admission in the emergency rooms was comparable among the 4 years studied, and the process of diagnosis was the same throughout the study period. However, in our emergency medical system, we were unable to examine the accuracy of diagnoses in emergency rooms, especially in the catastrophic situations after the Earthquake. Secondly, some people were forced to move from the seacoast area to the inland area after the Earthquake. However, we have no data on how many people moved from the seacoast area to the inland area. This could have affected the increased occurrences of CVDs in the inland area. Thirdly, we do not have background data on the patients who were diagnosed as having HF, including clinical characteristics and underlying heart disease.[31,32] We are now prospectively following the patients with HF in our cohort study in the Tohoku area[33] and we will report the clinical outcomes of those patients in the future. Fourthly, we have no data regarding the number of patients who visited hospitals by themselves without the use of ambulance. We also were unable to exclude the effects of traffic disruption by the Earthquake that might have affected the use of ambulance. Fifthly, the Miyagi Prefecture is located next to the Fukushima Prefecture where the nuclear power plant accident occurred; however, the influence of the nuclear accident was minimal in our Miyagi Prefecture. Sixthly, although ACS and stroke are similarly and strongly associated with atherosclerosis, we were unable to elucidate the mechanism for the different time courses between them. This issue remains to be examined in future studies. Seventhly, we have no data regarding prior medications in each patient, which might have affected the occurrence of CVDs. Eighthly, because the diagnosis of ACS was not based on coronary angiograms, but on ECG, echocardiography, and blood test, which made it difficult to diagnose Takotsubo cardiomyopathy. Finally, we have no data that can differentiate CPA of cardiac causes from CPA of pulmonary causes.

Clinical implications

We consider that the increased occurrences of CVDs in the Great East Japan Earthquake may have been caused by the following multiple factors: (i) the activated sympathetic nervous system by physical and mental stresses, (ii) insufficient medications, (iii) increased salt intake from preserved foods, and (iv) elevated blood pressure and viscosity; however, further studies are required to elucidate the mechanisms of disaster-related CVDs.

Conclusions

The present study demonstrates that the East Japan Earthquake Disaster has significantly increased the occurrences of CVDs, including the first observation of the increased occurrence of HF, independent of age, sex, area of residence.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

Acknowledgements

We appreciate the Miyagi Medical Association (president: Dr Junzo Ito) and the Fire Departments of the Miyagi Prefecture (chiefs of the 12 Fire Departments: Fumio Takahashi, Kosaburo Hoshi, Makoto Suzuki, Masaichi Tsunoda, Mutsuo Takahashi, Shinichi Konno, Shiro Otomo, Syoichi Chiba, Takao Sakurai, Teruo Sugahara, Toshiji Omatsu, and Yasushi Shiga) for collaboration in this study. We thank E. Ishida, M. Takahashi, A. Tsunoda, and Y. Hamada for their valuable contributions to this study.

Funding

This work was supported by a grant from the Miyagi Medical Association and a contribution by the Japanese Circulation Society.

Conflict of interest: none declared.

References

1. Monthly Report on Earthquake and Volcanoes in Japan. Meteorological Agency, 2011.
2. The Report on Damage from the East Japan Earthquake. National Police Agency, 2012.
3. 2010's National Census. Ministry of Internal Affairs and Communications, 2012.
4. Ogawa K, Tsuji I, Shiono K, Hisamichi S. Increased acute myocardial infarction mortality following the 1995 Great Hanshin-Awaji earthquake in Japan. *Int J Epidemiol* 2000;**29**:449–455.
5. Tsuchida M, Kawashiri MA, Teramoto R, Takata M, Sakata K, Omi W, Okajima M, Takamura M, Ino H, Kita Y, Takegoshi T, Inaba H, Yamagishi M. Impact of severe earthquake on the occurrence of acute coronary syndrome and stroke in a rural area of Japan. *Circ J* 2009;**73**:1243–7.
6. Watanabe H, Kodama M, Okura Y, Aizawa Y, Tanabe N, Chinushi M, Nakamura Y, Nagai T, Sato M, Okabe M. Impact of earthquakes on Takotsubo cardiomyopathy. *J Am Med Assoc* 2005;**294**:305–7.
7. Watanabe H, Kodama M, Tanabe N, Nakamura Y, Nagai T, Sato M, Okabe M, Aizawa Y. Impact of earthquakes on risk for pulmonary embolism. *Int J Cardiol* 2008;**129**:152–4.
8. Suzuki S, Sakamoto S, Miki T, Matsuo T. Hanshin-Awaji earthquake and acute myocardial infarction. *Lancet* 1995;**345**:981.
9. Suzuki S, Sakamoto S, Koide M, Fujita H, Sakuramoto H, Kuroda T, Kintaka T, Matsuo T. Hanshin-Awaji earthquake as a trigger for acute myocardial infarction. *Am Heart J* 1997;**134**:974–7.
10. Inoue K, Suwa S, Ohta H, Itoh S, Maruyama S, Masuda N, Sugita M, Daida H. Heart fatty acid-binding protein offers similar diagnostic performance to high-sensitivity troponin T in emergency room patients presenting with chest pain. *Circ J* 2011;**75**:2813–20.
11. McCullagh P, Nelder JA. *Generalized Linear Models*. London, New York: Chapman & Hall Ltd, 1999.
12. Leor J, Poole WK, Kloner RA. Sudden cardiac death triggered by an earthquake. *N Engl J Med* 1996;**334**:413–9.
13. Meisel SR, Kutz I, Dayan KI, Pauzner H, Chetboun I, Arbel Y, David D. Effect of Iraqi missile war on incidence of acute myocardial infarction and sudden death in Israeli civilians. *Lancet* 1991;**338**:660–1.
14. Takakura R, Himeno S, Kanayama Y, Sonoda T, Kiriyama K, Furubayashi T, Yabu M, Yoshida S, Nagasawa Y, Inoue S, Iwao N. Follow-up after the Hanshin-Awaji earthquake: diverse influences on pneumonia, bronchial asthma, peptic ulcer and diabetes mellitus. *Intern Med* 1997;**36**:87–91.
15. Esler M, Kaye D. Sympathetic nervous system activation in essential hypertension, cardiac failure and psychosomatic heart disease. *J Cardiovasc Pharmacol* 2000; **35**:S1–S7.
16. Grippo AJ, Johnson AK. Stress, depression and cardiovascular dysregulation: a review of neurobiological mechanisms and the integration of research from pre-clinical disease models. *Stress* 2009;**12**:1–21.
17. Kario K, Matsuo T, Kobayashi H, Yamamoto K, Shimada K. Earthquake-induced potentiation of acute risk factors in hypertensive elderly patients: possible triggering of cardiovascular events after a major earthquake. *J Am Coll Cardiol* 1997; **29**:926–33.
18. Zhang XQ, Chen M, Yang Q, Yan SD, Huang dJ. Effect of the Wenchuan earthquake in China on hemodynamically unstable ventricular tachyarrhythmia in hospitalized patients. *Am J Cardiol* 2009;**103**:994–7.
19. Azuma T, Seki N, Tanabe N, Saito R, Honda A, Ogawa Y, Suzuki H. Prolonged effects of participation in disaster relief operations after the Mid-Niigata earthquake on increased cardiovascular risk among local governmental staff. *J Hypertens* 2010;**28**:695–702.
20. Corrao G, Parodi A, Nicotra F, Zambon A, Merlino L, Cesana G, Mancia G. Better compliance to antihypertensive medications reduces cardiovascular risk. *J Hypertens* 2011;**29**:610–8.
21. Fukui S, Fukumoto Y, Suzuki J, Saji K, Nawata J, Tawara S, Shinozaki T, Kagaya Y, Shimokawa H. Long-term inhibition of Rho-kinase ameliorates diastolic heart failure in hypertensive rats. *J Cardiovasc Pharmacol* 2008;**51**:317–26.
22. Fukui S, Fukumoto Y, Suzuki J, Saji K, Nawata J, Shinozaki T, Kagaya Y, Watanabe J, Shimokawa H. Diabetes mellitus accelerates left ventricular diastolic dysfunction through activation of the renin-angiotensin system in hypertensive rats. *Hypertens Res* 2009;**32**:472–80.
23. Miura Y, Fukumoto Y, Sugimura K, Oikawa M, Nakano M, Tatebe S, Miyamichi S, Satoh K, Shimokawa H. Identification of new prognostic factors of pulmonary hypertension. *Circ J* 2010;**74**:1965–71.
24. Damgaard M, Goetze JP, Norsk P, Gadsbøll N. Altered sodium intake affects plasma concentrations of BNP but not proBNP in healthy individuals and patients with compensated heart failure. *Eur Heart J* 2007;**28**:2726–31.
25. Sawai A, Ohshige K, Yamasue K, Hayashi T, Tochikubo O. Influence of mental stress on cardiovascular function as evaluated by changes in energy expenditure. *Hypertens Res* 2007;**30**:1019–27.
26. Felšöci M, Pařenica J, Spinar J, Vítovec J, Widimský P, Linhart A, Fedorco M, Málek F, Cihalík C, Miklík R, Jarkovský J. Does previous hypertension affect outcome in acute heart failure? *Eur J Intern Med* 2011;**22**:591–6.
27. Satoh M, Kikuya M, Ohkubo T, Imai Y. Acute and subacute effects of the great East Japan earthquake on home blood pressure values. *Hypertension* 2011; **58**:e193–4.
28. Nakano M, Kondo M, Wakayama Y, Kawana A, Hasebe Y, Shafee MA, Fukuda K, Shimokawa H. Increased incidence of tachyarrhythmias and heart failure hospitalization in patients with implanted cardiac devices after the Great East Japan Earthquake Disaster. *Circ J* 2012;**76**:1283–1285.
29. Libby P, Okamoto Y, Rocha VZ, Folco E. Inflammation in atherosclerosis: transition from theory to practice. *Circ J* 2010;**74**:213–20.
30. Gerin W, Chaplin W, Schwartz JE, Holland J, Alter R, Wheeler R, Duong D, Pickering TG. Sustained blood pressure increase after an acute stressor: the effects of the 11 September 2001 attack on the New York City World Trade Center. *J Hypertens* 2005;**23**:279–84.
31. Aoki T, Fukumoto Y, Sugimura K, Oikawa M, Satoh K, Nakano M, Nakayama M, Shimokawa H. Prognostic impact of myocardial interstitial fibrosis in non-ischemic heart failure. Comparison between preserved and reduced ejection fraction heart failure. *Circ J* 2011;**75**:2605–13.
32. Tatebe S, Fukumoto Y, Sugimura K, Miyamichi-Yamamoto S, Aoki T, Miura Y, Nochioka K, Satoh K, Shimokawa H. Clinical significance of reactive post-capillary pulmonary hypertension in patients with left heart disease. *Circ J* 2012; **76**:1235–1244.
33. Shiba N, Nochioka K, Miura M, Kohno H, Shimokawa H, Investigators C. Trend of westernization of etiology and clinical characteristics of heart failure patients in Japan—first report from the CHART-2 study. *Circ J* 2011; **75**:823–33.

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

RAPID COMMUNICATION

Increased Incidence of Tachyarrhythmias and Heart Failure Hospitalization in Patients With Implanted Cardiac Devices After the Great East Japan Earthquake Disaster

Makoto Nakano, MD, PhD; Masateru Kondo, MD; Yuji Wakayama, MD, PhD; Akiko Kawana, MD; Yuhi Hasebe, MD; Mohamed Abdel Shafee, MD; Koji Fukuda, MD, PhD; Hiroaki Shimokawa, MD, PhD

Background: After the East Japan Earthquake disaster there may have been a deterioration of patients with cardiovascular diseases.

Methods and Results: We examined the data from 189 consecutive patients implanted with cardiovascular devices for the 6-month period before and after the Earthquake. In 170 patients with defibrillators, the number who experienced tachyarrhythmias increased significantly after the Earthquake (28±5 vs. 34±3 patients/month, P<0.05). In 74 patients with biventricular pacemakers, the number of heart failure hospitalizations significantly increased after the Earthquake (1.2±1.0 vs. 2.7±1.2 patients/month, P<0.05).

Conclusions: The East Japan Earthquake disaster unfavorably affected patients implanted with defibrillators or biventricular pacemakers. (*Circ J* 2012; **76:** 1283–1285)

Key Words: Arrhythmias; Cardiac implantable devices; Heart failure; The Great East Japan Earthquake

The Great East Japan Earthquake on March 11, 2011 was one of the most catastrophic disasters on record, devastating the northeastern coast region of Japan and also affecting people in the surrounding area. Patients with cardiovascular disease (CVD) in this area may have been particularly adversely affected by the disaster because of both physical and psychological stress.[1–3] In this study, as one of the cardiovascular centers in the disaster area, we examined the effects of the Earthquake on CVD in patients implanted with a defibrillator (ICD) or a biventricular pacemaker (cardiac resynchronization therapy [CRT]), with a special reference to the occurrence of tachyarrhythmias and hospitalization because of worsening of heart failure (HF).

Methods

We examined 189 consecutive patients implanted before the Earthquake with ICD (n=114) or CRT with (CRT-D, n=62) or without (CRT-P, n=13) a defibrillator function and who had survived the disaster (**Data S1**). Their clinical characteristics are shown in **Table S1**. First, we analyzed the device records of tachyarrhythmias for the 6-month period before and after the Earthquake in 170 patients implanted with defibrillators. We defined tachyarrhythmia as sustained or non-sustained ventricular tachycardia (VT), ventricular fibrillation (VF) or supraventricular tachycardia. Second, we examined the effect of the disaster on HF status in 74 HF patients with CRT devices. In order to examine HF worsening in this population, we calculated the monthly number of HF hospitalizations normalized by that of the patients on follow-up in the corresponding period from 5 years before to 6 months after the Earthquake. The monthly number of HF hospitalization per follow-up patients was averaged for every 6-month period before and after the Earthquake. CRT responders were defined as patients who showed left ventricular reverse remodeling at 6 months after CRT based on recent reports.[4,5]

Statistical analysis was performed using 1-factorial ANOVA and post-hoc comparisons or unpaired t-test to compare the changes in the occurrence of tachyarrhythmias and HF hospitalization for the 6 months before and after the disaster. All results are expressed as mean±standard deviation (SD).

Results

The incidence of tachyarrhythmias significantly increased after the Earthquake followed by a gradual decrease to the pre-earthquake level (**Figure 1A**). The monthly average of the number of patients who experienced tachyarrhythmias significantly

Received February 27, 2012; revised manuscript received March 29, 2012; accepted April 2, 2012; released online April 11, 2012
Time for primary review: 13 days

Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

The Guest Editor for this article was Kazutaka Aonuma, MD.

Mailing address: Makoto Nakano, MD, PhD, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan. E-mail: vdm@cardio.med.tohoku.ac.jp

ISSN-1346-9843 doi:10.1253/circj.CJ-12-0261

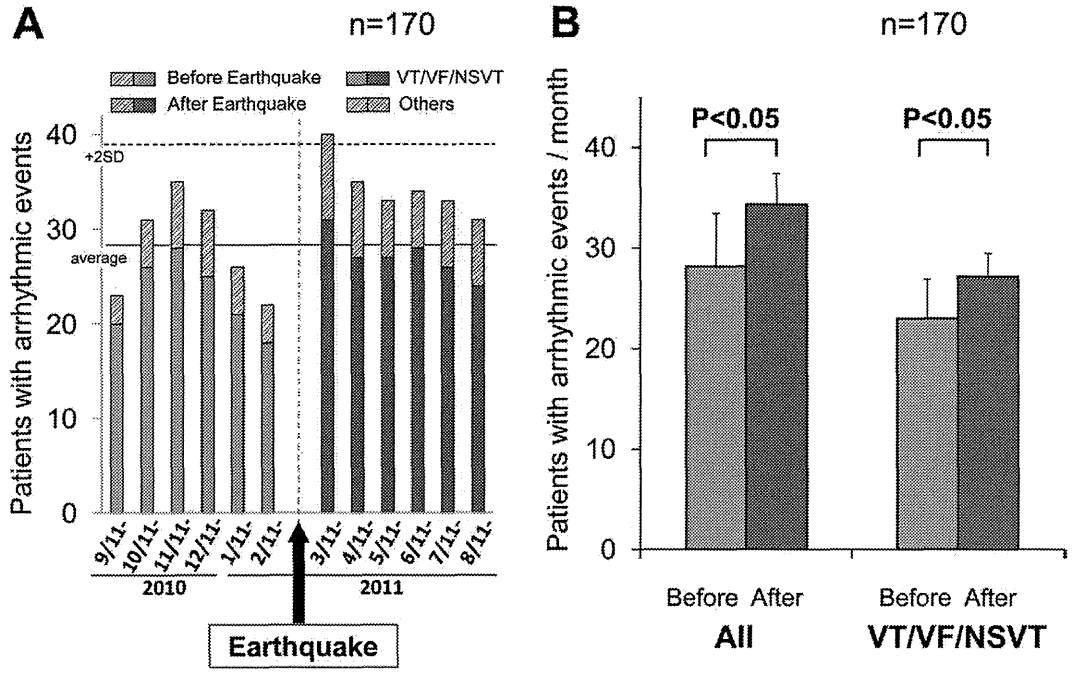

Figure 1. Tachyarrhythmias in patients with an ICD. (**A**) Time course of the number of patients with tachyarrhythmias before (blue bar) and after (red bar) the Earthquake. Horizontal lines show the monthly average (solid line) and +2SD (dotted) of the number of patients with any tachyarrhythmia for the 6-month period before the Earthquake. VT and VF, sustained ventricular tachycardia and fibrillation; NSVT, non-sustained VT. Others includes any tachyarrhythmic event except VT, VF and NSVT. (**B**) Number of patients with any tachyarrhythmia (**Left**) and ventricular arrhythmias (**Right**) detected by the device recording. ICD, implantable cardiac defibrillator.

increased after the Earthquake compared with before for any tachyarrhythmia (21±3 vs. 26±3, P<0.05) and for ventricular tachyarrhythmias (23±4 vs. 27±2, P<0.05) (**Figure 1B**). Most of the tachyarrhythmias recorded were ventricular arrhythmias, probably because undistinguishable tachyarrhythmias were recognized by the single-chamber device as ventricular in origin. In contrast, the incidence of appropriate and/or inappropriate defibrillator shocks, including anti-tachycardia pacing, was comparable before and after the Earthquake (appropriate shock: 9.2±2.5 vs. 9.0±1.4 patients/month). The storm of defibrillator shocks did not increase after the Earthquake.

In 74 CRT patients, we noted that 11 patients had 16 HF hospitalizations after the Earthquake, whereas 7 had 7 hospitalizations before the Earthquake. The incidence of HF hospitalization significantly increased after the Earthquake, followed by a gradual decrease to the pre-earthquake level (**Figure 2A**). The number of HF hospitalizations normalized by that of the patients on follow-up in the corresponding period significantly increased for the 6-month period after the Earthquake as compared with the preceding 6-month or 5-year average (both P<0.05) (**Figure 2B**). The hospitalized patients, as compared with the patients who were not hospitalized after the Earthquake, were characterized by several factors, including higher plasma B-type natriuretic peptide (BNP) levels (780±765 vs. 255±419 pg/ml; P<0.01), fewer CRT responders (45 vs. 80%; P<0.05) and a past history of more HF hospitalizations (1.9±2.0 vs. 0.27±0.75 HF hospitalizations for the previous 5 years, P=0.02). Data for intrathoracic impedance monitoring (OptiVol) were available only in 17 CRT patients, in whom the Optivol fluid index significantly increased after the Earthquake (cut-off ≥100 ohm; 2/17 vs. 8/17; P<0.05); however, no correlation was noted between the increase in the fluid index and clinical HF worsening. In this CRT population, 6 patients died during the 6 months after the Earthquake, including HF worsening in 4, cerebral hemorrhage in 1, and tsunami death in 1.

Discussion

This is the first study to demonstrate the clinical impact of the East Japan Earthquake on patients implanted with cardiac devices such as ICD and CRT. It has been reported that the incidence of CVD, such as hypertension, coronary artery disease, pulmonary embolism, ventricular arrhythmias and sudden cardiac death, increases after an earthquake.[1–3] Because almost all the study patients with ICD or CRT lived in the City of Sendai or the surrounding area, where the disaster affected ordinary life for more than 1 month, we were able to closely follow them even after the Earthquake. Importantly, in the present study, the recordings of the ICD/CRT device for most of the patients were available to examine the changes in cardiac rhythm abnormalities.

It has been previously reported that arrhythmic events deteriorate after an earthquake[2,3] or similar large-scale disaster.[6] In the present study, although defibrillator shocks were not increased, the device recordings clearly showed a significant increase in tachyarrhythmias after the Earthquake. Importantly, this phenomenon was sustained for a few months after the Earthquake, when the effect of aftershocks, deteriorated quality of life and physical/mental stress might have been involved.

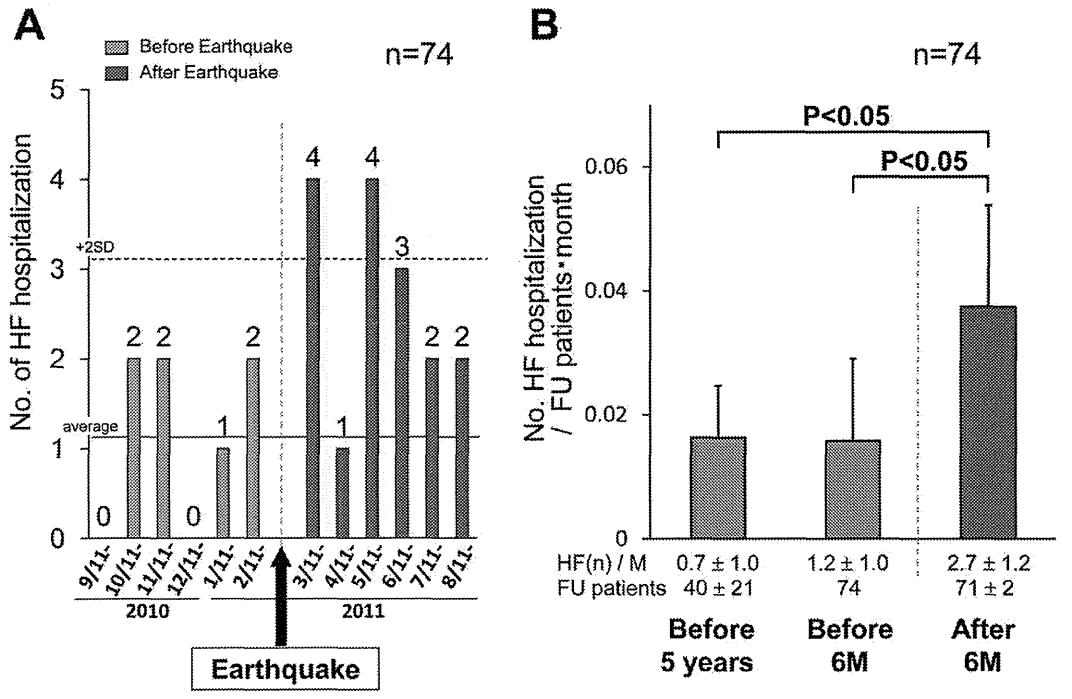

Figure 2. Heart failure (HF) hospitalization in patients with biventricular pacemakers (cardiac resynchronization therapy [CRT]). (A) Time course of the number of HF hospitalizations before (blue bar) and after (red bar) the Earthquake. Horizontal lines show the monthly average (solid line) and +2SD (dotted) of the number of patients with HF hospitalization for the 6-month period before the Earthquake. (B) Normalized monthly number of HF hospitalizations. The mean numbers of monthly HF hospitalization and follow-up patients are shown under the panel (mean±SD).

There has been no report on HF development and/or worsening after an earthquake. However, several causes related to a great earthquake could worsen clinical scenarios in patient with heart diseases, leading to the development and/or worsening of HF, including high-salt diet with preserved food and elevated blood pressure because of physical/mental stress, although drug withdrawal was less noted in the present study.

We observed an unfavorable effect of the Earthquake on HF worsening because we selected CRT patients who were prone to develop HF worsening. The present results suggest that CRT non-responders[4,5] and HF hospitalization repeaters are a high-risk population for cardiovascular events after an earthquake or other disaster.

Several limitations of the present study should be mentioned. First, it is retrospective and observational in design, which is inevitable for this type of study of a rare disaster. Second, the number of ICD or CRT patients examined was relatively small. Third, the diagnosis of tachyarrhythmias was based on the device report and depended on the device's settings.

In conclusion, we were able to demonstrate that the East Japan Earthquake disaster unfavorably affected patients with an ICD or CRT. We believe that the present results will contribute to the improvement of disaster medicine in the future.

Acknowledgement

This work was supported in part by the grant from the Miyagi Medical Association and the contribution by the Japanese Circulation Society.

Disclosure

There is no financial support to disclose in this study.

References

1. Kario K, Ohashi T, on behalf of the Tsuna Medical Association. Increased coronary heart disease mortality after the Hanshin-Awaji earthquake among the older community on Awaji Island. *J Am Geriatr Soc* 1997; **45:** 610–613.
2. Zhang XQ, Chen M, Yang Q, Yan SD, Huang de J. Effect of the Wenchuan earthquake in China on hemodynamically unstable ventricular tachyarrhythmia in hospitalized patients. *Am J Cardiol* 2009; **103:** 994–997.
3. Leor J, Poole WK, Kloner RA. Sudden cardiac death triggered by an earthquake. *N Engl J Med* 1996; **334:** 413–419.
4. Seo Y, Ito H, Nakatani S, Takami M, Naito S, Shiga T, et al; on behalf of J-CRT investigators. The role of echocardiography in predicting responders to cardiac resynchronization therapy. *Circ J* 2011; **75:** 1156–1163.
5. Auricchio A, Prinzen FW. Non-responders to cardiac resynchronization therapy: The magnitude of the problem and the issues. *Circ J* 2011; **75:** 521–527.
6. Steinberg JS, Arshad A, Kowalski M, Kukar A, Suma V, Vloka M, et al. Increased incidence of life-threatening ventricular arrhythmias in implantable defibrillator patients after the World Trade Center attack. *J Am Coll Cardiol* 2004; **44:** 1261–1264.

Supplemental Files

Supplemental File 1

Data S1. Methods

Table S1. Patients' Characteristics

Please find supplemental file(s);
http://dx.doi.org/10.1253/circj.CJ-12-0261

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

RAPID COMMUNICATION

Enhanced Rho-Kinase Activity in Patients With Vasospastic Angina After the Great East Japan Earthquake

Taro Nihei, MD; Jun Takahashi, MD, PhD; Yoku Kikuchi, MD, PhD; Yusuke Takagi, MD, PhD; Kiyotaka Hao, MD, PhD; Ryuji Tsuburaya, MD, PhD; Takashi Shiroto, MD, PhD; Yoshitaka Ito, MD, PhD; Yasuharu Matsumoto, MD, PhD; Masaharu Nakayama, MD, PhD; Kenta Ito, MD, PhD; Satoshi Yasuda, MD, PhD; Hiroaki Shimokawa, MD, PhD

Background: It remains unclear whether disease activity of vasospastic angina (VSA) is altered during a disaster.

Methods and Results: Before and after the Great East Japan Earthquake, we examined Rho-kinase activity in circulating neutrophils of 11 VSA patients and their mental stress with the post-traumatic stress disorder (PTSD) questionnaire. Rho-kinase activity was significantly increased at 6 months after the Earthquake, and was returned to baseline level at 12 months. Importantly, percent change in Rho-kinase activity was significantly correlated with the PTSD score.

Conclusions: These results indicate that the Rho-kinase activity of VSA patients was transiently enhanced associated with disaster-related mental stress. (*Circ J* 2012; **76:** 2892–2894)

Key Words: Angina; Stress; Vasospasm

On March 11, 2011, we experienced the Great East Japan Earthquake in our Tohoku area. The Earthquake-related physical and psychological stress persisted for several months. Coronary vasomotor reactivity is known to be enhanced by stress[1] and we have previously demonstrated that Rho-kinase plays a key role in the molecular mechanisms of vasospastic angina (VSA).[2] We have also recently demonstrated that Rho-kinase activity in circulating neutrophils is a useful biomarker for the diagnosis and disease activity assessment of VSA.[3] We thus examined whether Rho-kinase activity was increased in VSA patients after the Earthquake.

Methods

The protocol of the present study was approved by the Ethical Committees of Tohoku University and all patients provided written informed consent. In 11 patients with VSA, all of whom had been previously diagnosed based on spasm provocation test with acetylcholine in accordance with the Guidelines for Diagnosis and Treatment of Patients with Vasospastic Angina of the Japanese Circulation Society,[4] we were able to measure Rho-kinase activity in circulating neutrophils at 3 time points: before and 6 and 12 months after the Earthquake. Rho-kinase activity was defined by the ratio of the phosphorylated form/total form of myosin-binding subunit, a substrate of Rho-kinase.[3] We also quantified the extent of mental stress at 6 and 12 months after the Earthquake with the post-traumatic stress disorder (PTSD) questionnaire that is widely used for screening of PTSD.[5] The PTSD questionnaire consists of 22 questions for major PTSD symptoms in order to categorize symptom severity into 5 different levels (0–4), where the cut-off value for PTSD is 25 points.[5] All results are expressed as mean±standard deviation (SD) and P values <0.05 were considered to be statistically significant.

Results

The mean age of the 11 patients (8 males, 3 females) was 62±11 years. The prevalence of hypertension, diabetes mellitus and dyslipidemia was 55%, 27% and 91%, respectively. Their left ventricular ejection fraction was well-preserved (71±9%) and 2 of them continued to smoke after the Earthquake. All patients continued their medical treatment with calcium-channel blockers (CCBs) and although there was no change in the levels of serological markers after the Earthquake, including high-sensitivity C reactive protein and lipid profiles (Table), Rho-kinase activity in circulating neutrophils was significantly increased at 6 months after the Earthquake and was returned

Received October 2, 2012; revised manuscript received October 15, 2012; accepted October 24, 2012; released online November 3, 2012 Time for primary review: 7 days
Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai (T.N., J.T., Y.K., Y.T., K.H., R.T., T.S., Y.I., Y.M., M.N., K.I., H.S.); National Cerebral and Cardiovascular Center, Suita (S.Y.), Japan
The Guest Editor for this article was Ken-ichi Hirata, MD.
Mailing address: Hiroaki Shimokawa, MD, PhD, Professor and Chairman, Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, 1-1 Seiryo-machi, Aoba-ku, Sendai 980-8574, Japan. E-mail: shimo@cardio.med.tohoku.ac.jp
ISSN-1346-9843 doi:10.1253/circj.CJ-12-1238

Table. Changes in Serological Markers After the Great East Japan Earthquake

	Baseline (n=11)	6 months (n=11)	12 months (n=11)	P value
WBC (/μl)	4,900 (4,600, 6,100)	5,200 (4,600, 5,900)	4,500 (4,200, 7,100)	0.78
Hb (g/dl)	13.4±1.1	13.5±1.2	13.7±1.4	0.87
Ht (%)	39.2±3.2	39.5±3.5	39.4±4.1	0.98
hs-CRP (mg/dl)	0.084 (0.031/0.173)	0.046 (0.022/0.254)	0.052 (0.036/0.166)	0.86
LDL (mg/dl)	108±23	106±32	113±26	0.59
HDL (mg/dl)	46±13	50±16	48±10	0.45
TG (mg/dl)	169±81	171±92	123±54	0.23
Fasting serum glucose (mg/dl)	113±18	117±35	110±37	0.54
HbA_{1c} (%)	5.7±0.6	5.8±0.6	5.8±0.8	0.83

Values are mean±SD or median (25^{th} percentile/75^{th} percentile).
WBC, white blood cells; Hb, hemoglobin; Ht, hematocrit; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides.

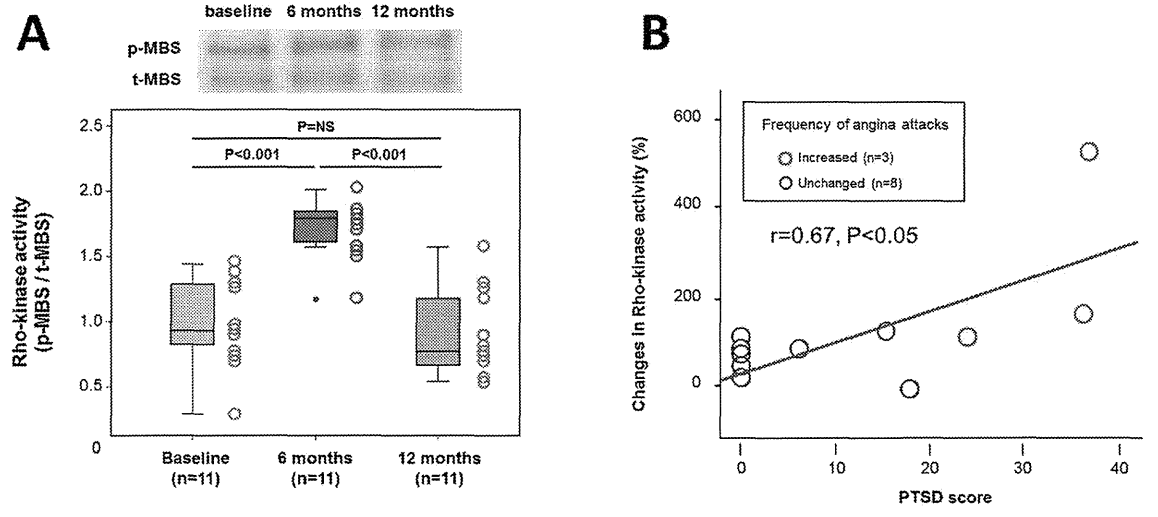

Figure. Changes in Rho-kinase activity in circulating neutrophils of patients with vasospastic angina (VSA). (**A**) Representative Western blotting of phosphorylated myosin-binding subunit (MBS) and total MBS in circulating neutrophils. Comparisons of Rho-kinase activity at 3 time points were performed with one-way ANOVA followed by Tukey's test. (**B**) Positive correlation between the PTSD score and the percent change in Rho-kinase activity from the baseline at 6 months after the Great East Japan Earthquake. Red circles represent VSA patients with increased symptoms after the Earthquake, and blue circles those with unchanged symptoms after the Earthquake, respectively. The relationship between the 2 values was examined with linear regression analysis. PTSD, post-traumatic stress disorder.

to the baseline level at 12 months (0.99±0.34 at baseline, 1.71±0.23 at 6 months, 0.90±0.34 at 12 months) (Figure A). Among the 11 patients, 3 were directly hit by the tsunami and complained of increased frequency of angina attacks after the Earthquake. In these 3 patients, as compared with the remaining 8 patients without direct tsunami-hit or worsening symptoms, both PTSD score (32±7 vs. 5±8, P=0.01) and the percent change in Rho-kinase activity from the baseline (268±232% vs. 55±40%, P<0.05) were significantly higher at 6 months after the Earthquake. Importantly, there was a significant positive correlation between the PTSD score and the percent change in Rho-kinase activity from the baseline at 6 months after the Earthquake (r=0.67, P<0.05) (Figure B). We also confirmed that elevated levels of PTSD score at 6 months after the Earthquake declined at 12 months, as in the case of Rho-kinase, although there was no significant correlation between the changes in the PTSD score and those in Rho-kinase activity from 6 to 12 months after the Earthquake (Table S1).

Discussion

The novel findings of the present study were that Rho-kinase activity in circulating neutrophils of VSA patients was changed dynamically in one year after the Earthquake and that the percent change in Rho-kinase activity from the baseline was positively correlated with the PTSD score in those patients. We have recently demonstrated that a ratio of 1.18 is the best cut-off level of Rho-kinase activity for the diagnosis of VSA and that medical treatment with CCBs ameliorated the level to below the cut-off value in VSA patients.[3] In the present study, although all the patients continued to take CCBs and no significant changes were noted for coronary risk factors or sys-