(Table S4) and in 410 (26%) of those in stage C/D (Table S5); younger patients in the early stages of CHF tended to maintain higher levels of physical activity (Tables S4,S5).

### Yearly Change in Physical Activity Level and Cardiovascular Events During Follow-up

We subdivided the patients into 4 groups according to their baseline and follow-up physical activity levels as "low to low (n=988)", "low to high (n=321)", "high to low (n=638)" and "high to high (n=809)" (Table S4). Among the 4 groups, survival free from CHF hospitalization was best in the "high to high" group and was worst in the "low to low" group in both stage A/B and C/D (Figures 4A–D). In stage A/B patients, survival free from CHF hospitalization in the "high to low" and "low to high" groups was between that in the "high to high" and "low to low" groups, suggesting that physical activity level was well associated with CHF hospitalization (Figure 4B).

Furthermore, other cardiovascular events (except AMI, stroke, and HF hospitalization) were well associated with yearly change in physical activity level in both stage A/B and C/D (Figures 5A–D). Survival free from other cardiovascular events was best in the "high to high" group and worst in the "low to low" group in both stage A/B and C/D (Figures 5A–D). In female patients especially, high physical activity was associated with other cardiovascular events (Figure 5D).

In contrast, although a yearly change in physical activity was significantly associated with the occurence of AMI, its impact was small (Figures S2A–D). In stages A–D, the occurrence of AMI was comparable between the "high to high" and "high to low" groups, as in the case of "low to high" and "low to low" groups (Figure S2A). In stage C/D, only "low to low" tended to be worst for AMI (Figure S2C).

The impact of a yearly change in physical activity on stroke was also small (Figures S4A–C). Multivariate analyses indicated that "high to high" was the only significant predictor of the occurrence of stroke in stages A–D (Figure S4D).

## Discussion

The novel findings of the present study were that (a) the baseline physical activity level was significantly associated with all-cause death, HF hospitalization and other cardiovascular events (except AMI, stroke and HF hospitalization) and (b) a yearly change in physical activity level was also significantly associated with HF hospitalization and cardiovascular events during the 3-year follow-up in both stage A/B and C/D patients. To the best of our knowledge, this is the first study to demonstrate that physical activity is associated with cardiovascular events in CHF patients.

### Influence of Baseline Physical Activity Level on Cardiovascular Events and Mortality

In the present study, the high-exercise group was characterized by younger age and less advanced CHF stage compared with the low-exercise group in both stage A/B and C/D, whereas no significant difference in BNP level was noted between the 2 groups. Because physical activity level and CHF stage are closely linked, it is difficult to simply dissect the effects of physical activity on CHF stage. However, the present study suggests that physical activity is an important therapeutic target for CHF patients.

It has been demonstrated that exercise training is associated with significant reductions in mortality, HF hospitalization, health status and depressive symptoms, as well as improvement of endothelial function in CHF patients.[12–16] Furthermore, regular physical activity and aerobic exercise training are associated with reduced risk of fatal and nonfatal coronary events as primary and secondary prevention in a wide range of ages.[17,18] Consistently, the present study demonstrated that a higher level of physical exercise was associated with reductions in all-cause mortality, HF hospitalization, acute coronary syndrome and other cardiovascular events in HF patients in both stage A/B and C/D.

### Yearly Change in Physical Activity Level

Only a few studies have previously examined yearly change in physical activity. In children, physical activity is known to decrease with age, depending on the length of morning school breaks and the issue of road safety in the maintenance of moderate and vigorous activities.[19] Also in adults, the CPS II Nutrition Cohort, a prospective study of cancer incidence and mortality in the USA, reported that in half of the participants the level of physical activity declined over 10 years.[20] WHAS II, another prospective cohort study with 436 women aged 70–79 years, who were representative of the two-thirds highest functioning women living in the community, also demonstrated that the prevalence of maintaining a high-exercise level accounted for only 16.6%,[21] a consistent finding with the present study ("high to high" group accounted for 28.0%). Furthermore, the present study demonstrated that most of the patients with CHF (both stage A/B and C/D) decreased their level of physical activity over 3 years, which was associated with various cardiovascular events. To prevent this decline, it is important in future studies to clarify the factors that prevent physical activity in CHF patients.

It has been reported that LV systolic dyssynchrony predicts impaired physical activity level, independently of history of previous MI or regional wall motion abnormality in patients with IHD.[22] In both stage A/B and C/D, the "high to high" group was characterized by younger age and high baseline level of physical activity. Additionally, the prevalence of valvular heart disease in stage A/B and the use of statins in stage C/D were significantly associated with the yearly change in physical activity level, although the clinical significance of these findings remains to be examined in future studies.

### Change in Physical Activity Level and Cardiovascular Events

Few studies have examined the influence of changes in physical activity on cardiovascular events in adults. In the WHAS II study, there was a stepwise association between decreased level of physical activity and increased risk of mortality in old women.[21] The present study also demonstrated that decreased physical activity was associated with increased risk of mortality, HF hospitalization and other cardiovascular events (except AMI, stroke, and HF hospitalization) in male and female patients with CHF in both stage A/B and C/D, supporting the notion that exercise training is associated with significant reductions in mortality, HF hospitalization and atherosclerosis development.[12,17]

### Study Limitations

First, in the present study, physical activity level was evaluated only by subjective questionnaire not by objective method, which might have caused overestimation of the level. Evaluation of physical activity by objective methods is needed in future studies. Second, in order to evaluate the yearly change in physical activity, we simply divided the patients by the median value of physical activity. Again, evaluation of the yearly change in physical activity by objective methods is needed in future studies. Third, although we were able to obtain data for a relatively large number of CHF patients, some were lacking.

Fourth, we were unable to clarify the factors that prevented physical activity by CHF patients or to clarify whether a decrease in physical activity was a cause or a result of cardiovascular diseases. Fifth, in some groups, the use of drugs, such as ACEI/ARB or $\beta$-blocker, which are usually recognized as protective agents for HF, was rather associated with worsening of HF, probably because these agents were administered to patients with severe HF. We are currently performing a clinical study to address this issue.

## Conclusions

The present study demonstrates that the baseline and yearly change in physical activity level are associated with all-cause death and HF hospitalization, suggesting that physical activity could be an important therapeutic target to improve the prognosis of CHF patients.

## Acknowledgments

This work was supported by the grants-in-aid from the Japanese Ministry of Health, Labor, and Welfare, Tokyo, Japan (18190401, 21170901, 24120301). We thank the members of the Tohoku Heart Failure Association for their contribution and E. Ishida for excellent technical assistance.

## Disclosures

None.

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## Supplementary Files

**Supplementary File 1**

**Figure S1.** Baseline physical activity level and the occurrence of acute myocardial infarction.

**Figure S2.** Yearly change in physical activity level and the occurrence of acute myocardial infarction.

**Figure S3.** Baseline physical activity level and the occurrence of stroke.

**Figure S4.** Yearly change in physical activity level and the occurrence of stroke.

**Table S1.** Physical activity questionnaire

**Table S2.** Baseline characteristics of CHF patients with low and high physical activity levels (stages A/B/C/D)

**Table S3.** Baseline characteristics of CHF patients with yearly changes in physical activity level during 3-year follow-up (stages A/B/C/D)

**Table S4.** Baseline characteristics of stage A/B CHF patients categorized by yearly change in physical activity level during 3-year follow-up

**Table S5.** Baseline characteristics of stage C/D CHF patients categorized by yearly change in physical activity level during 3-year follow-up

Please find supplementary file(s);
http://dx.doi.org/10.1253/circj.CJ-13-0746

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

**ORIGINAL ARTICLE**
**Critical Care**

# Emergency Care of Acute Myocardial Infarction and the Great East Japan Earthquake Disaster

## – Report From the Miyagi AMI Registry Study –

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***Background:*** Although emergency care of acute myocardial infarction (AMI) could theoretically be improved through improved patient delay, this notion remains to be confirmed. Additionally, the influence of large earthquakes on the emergency care of AMI cases remains to be elucidated. The Great East Japan Earthquake (March 11, 2011) has enabled us to address these issues.

***Methods and Results:*** We analyzed the data from 2008 to 2011 (n=3,937) in the Miyagi AMI Registry Study. In-hospital mortality was significantly lower in 2011 as compared with the previous 3 years (7.3% vs. 10.5%, P<0.05). This improvement was noted especially during the first 2 months after the Earthquake, associated with shorter elapsing time from onset to admission (120 vs. 240 min, P<0.001) and higher performance rate of primary percutaneous coronary intervention (PCI) (86.8% vs. 76.2%, P<0.01). Importantly, after the Earthquake, patients with early admission (≤3 h from onset) was significantly increased (59.1% vs. 47.0%, P<0.05) and their prognosis became better (7.9% vs. 11.4%, P=0.02), associated with a lower prevalence of heart failure on admission (6.9% vs. 16.2%, P=0.02) and higher performance rate of primary PCI (89.1% vs. 76.4%, P<0.01).

***Conclusions:*** Emergency care of AMI improved soon after the Great East Japan Earthquake compared with ordinary times by the contribution of earlier admission from onset and higher performance rate of primary PCI. (*Circ J* 2014; **78:** 634–643)

**Key Words:** Disaster management; Earthquakes; Emergency care; Myocardial infarction

Mortality from acute myocardial infarction (AMI) has decreased during the past decades associated with the widespread use of primary percutaneous coronary intervention (PCI).[1–3] In addition, it has been shown that a shorter elapsing time from onset of AMI to reperfusion (treatment delay) improves the clinical outcome of AMI patients.[4–6] Thus, it has been repeatedly pointed out that emergency care of AMI could theoretically be further improved through improved chain of survival, especially the patient delay.[4,7,8] However, this notion remains to be confirmed in a large community.[7,8] In addition, the influence of large earthquakes on the emergency care of AMI remains to be elucidated.

**Editorial p 586**

On March 11, 2011, the Great East Japan Earthquake followed by a tsunami hit the northeastern coast region of Japan, one of the largest ocean-trench earthquakes ever recorded.[9–11] The Earthquake caused huge damage to Miyagi prefecture, the area closest to the epicenter, where 9,537 people have died, 1,297 are still missing and 266,871 houses were destroyed as of 10 October, 2013, 2.5 years after the Earthquake.[12] Many people have been severely inconvenienced and have suffered from physical and mental stress, increased salt intake from preserved foods and elevated blood pressure.[9,10,13] We recently

Received October 17, 2013; revised manuscript received November 24, 2013; accepted November 26, 2013; released online January 21, 2014 Time for primary review: 11 days
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ISSN-1346-9843 doi:10.1253/circj.CJ-13-1286

**Table 1. Clinical Characteristics and Outcomes of Patients With AMI in 2008–2010 and 2011**

| | 2008–2010 (n=2,995) | 2011 (n=942) | P value |
|---|---|---|---|
| Age [median (IQR)], years | 71 (60–79) | 70 (59–80) | 0.69 |
| Female (%) | 28.6 | 25.2 | 0.04 |
| Hypertension (%) | 65.1 | 70.0 | 0.06 |
| Diabetes (%) | 34.0 | 36.1 | 0.24 |
| Dyslipidemia (%) | 49.2 | 39.5 | 0.42 |
| Smoking (%) | 33.4 | 35.9 | 0.15 |
| Anterior infarction (%) | 46.3 | 47.1 | 0.67 |
| Prior infarction (%) | 8.8 | 8.1 | 0.46 |
| Ambulance use (%), (n) | 66.1 (1979) | 66.8 (629) | 0.69 |
| Time elapsing from onset to admission [median (IQR)], min* | 228 (90–647) | 150 (72–450) | <0.001 |
| Killip ≥2 on admission (%) | 12.7 | 10.9 | 0.15 |
| Primary PCI (%) | 80.2 | 84.8 | 0.001 |
| Peak CPK [median (IQR)], IU/L | 1,373 (632–2,713) | 1,565 (740–2,963) | 0.01 |
| Door-to-balloon time [median (IQR)], min† | 75 (46–120) | 70 (46–115) | 0.21 |
| In-hospital mortality (%), (n) | 10.5 (315) | 8.3 (78) | <0.05 |

*Only patients with data available on onset time (n=2,771 in 2008–2010 and n=887 in 2011). †Only patients who underwent primary PCI with data available on door-to-balloon time (n=1,605 in 2008–2010 and n=745 in 2011).
CPK, creatinine phosphokinase; PCI, percutaneous coronary intervention.

demonstrated that the Earthquake significantly increased the occurrence of various cardiovascular diseases, including heart failure, ventricular arrhythmias and coronary vasospasm.[11,14–16]

AMI has been a leading cause of morbidity and mortality worldwide, including Japan.[2,17] In order to establish the system of emergency care of AMI in Miyagi prefecture, we have been conducting the Miyagi AMI Registry Study for 34 years since 1979, whereby all AMI patients in Miyagi prefecture are prospectively registered.[2,18–20] The Great East Japan Earthquake has enabled us to examine how the emergency care system for AMI operated during the disaster.

The aim of the present study was to elucidate how the Great East Japan Earthquake affected the emergency care of AMI in Miyagi prefecture using the data from the Miyagi AMI Registry Study.

## Methods

This study was approved by the Institutional Review Broad of Tohoku University Graduate School of Medicine under the condition that personal data are protected at all times.

### The Miyagi AMI Registry Study and Study Population

The Miyagi AMI Registry Study is a prospective, multicenter and observational study. As previously reported, the registry was established in 1979 and all 44 hospitals with a coronary care unit and/or cardiac catheterization facility in Miyagi prefecture have been participating (**Appendix**).[2,18–20] Miyagi prefecture has a population of approximately 2.35 million people, and almost all AMI patients are transferred to one of the participating hospitals via the emergency medical service. The diagnosis of AMI was based on the WHO-MONICA criteria, including typical severe chest pain accompanied by abnormal ECG changes and increased serum levels of cardiac enzymes.[21] Treatment, including reperfusion therapies, was left to the discretion of the individual cardiologists in charge. In the present study, we analyzed a total of 3,937 AMI patients registered in the Miyagi AMI Registry from 11 January (8 weeks before March 11) to November 15 (40 weeks after 11 March) in 2008–2011.

### Statistical Analysis

To examine the effects of the Earthquake on both the clinical characteristics of AMI patients and the emergency care system, we divided the study period of 12 months into six 2-month periods and compared in-hospital mortality between 2011 and 2008–2010 for the following subgroups; age (≥70 and <70 years), sex, elapsing time from onset to admission (≤3 and >3 h) and ambulance use or not. We also compared the clinical characteristics, including elapsing time from onset to admission, door-to-balloon time defined as the time from admission to first balloon dilatation (only in the patients who received primary PCI), treatment delay defined as the time from onset to first balloon dilation (only in the patients who received primary PCI) (**Figure S1**), ambulance use, performance rate of primary PCI, peak creatine phosphokinase (CPK) level, prevalence of symptomatic heart failure with Killip class ≥2 on admission, sex, and age between 2011 and 2008–2010. As a subgroup analysis, we divided the patients into 2 groups according to time from onset to admission as ≤3 h (early admission) and >3 h (late admission), and compared in-hospital mortality and the clinical characteristics of the patients between 2011 and 2008–2010 during the 2 months just before and after the Earthquake.

Furthermore, the tsunami following the Earthquake directly and severely damaged the seacoast area.[9–11] Therefore, to examine the influence of the tsunami on the emergency care of AMI, we divided the patients in 2011 into 2 groups according to transfer hospitals located within 5 km of the sea (seacoast area) or not (inland area) (**Appendix**). We used the Mann-Whitney test for continuous values and chi-square test for categorical variables. Continuous variables are expressed as median and interquartile range (IQR).

In addition, to assess the effect of the Earthquake on in-hospital mortality, we performed multivariate logistic regression analysis by the period before and after the Earthquake and calculated the odds ratios and 95% confidence intervals. The following variables were included in the logistic regression model: age, sex, infarction site, prior MI, transport by ambulance, admission within 3 h of onset, coexisting heart failure with Killip class ≥2 and performance rate of primary

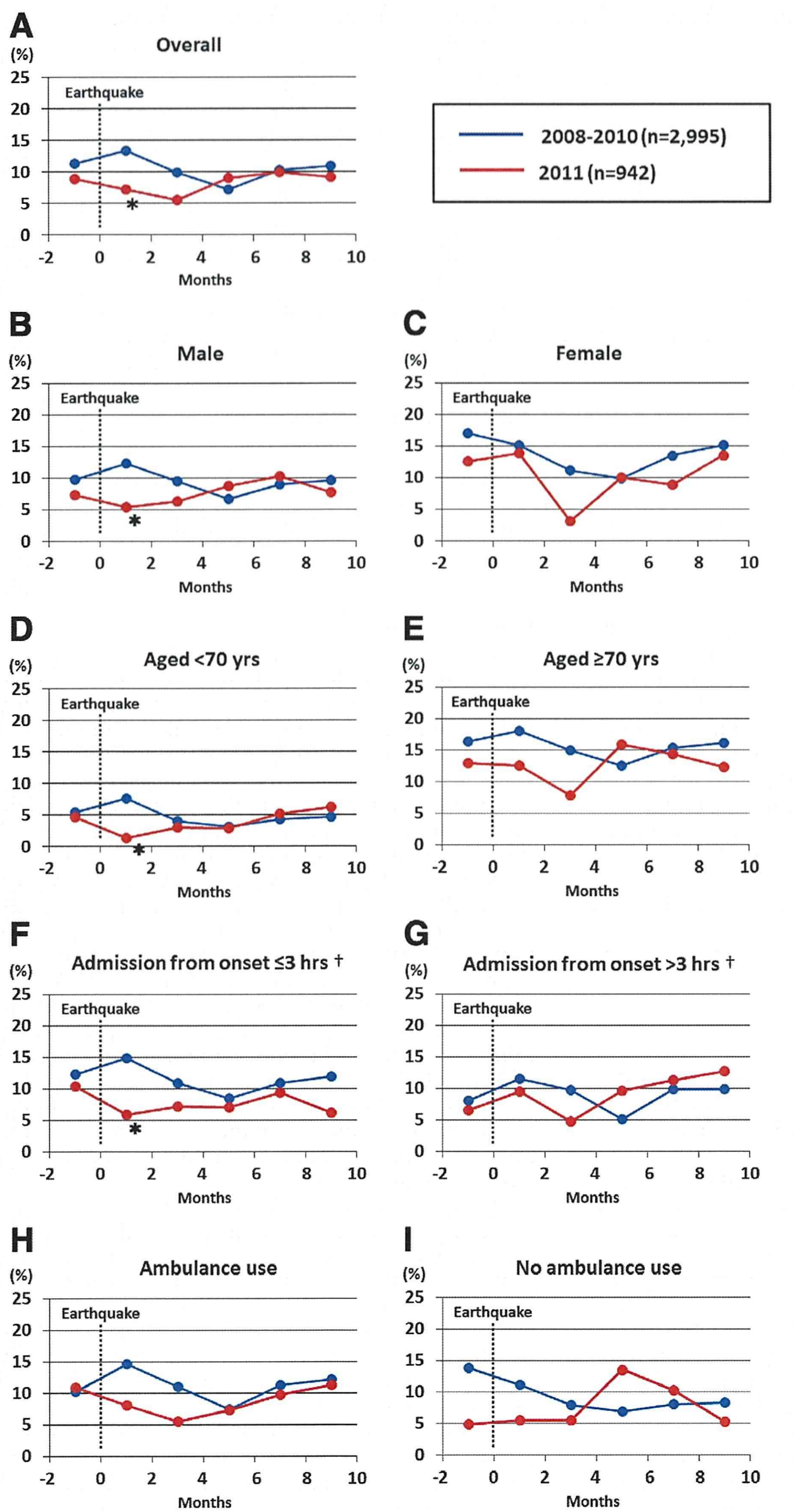


**Figure 1.** Time course of in-hospital mortality from acute myocardial infarction in 2011 and 2008–2010 in overall population (**A**) and subgroups divided by sex (**B**,**C**), age (**D**,**E**), elapsing time from onset to admission (**F**,**G**) and use of ambulance (**H**,**I**). *P<0.05 vs. 2008–2010. †Only patients with data available on time of onset were enrolled (n=2,944 in 2008–2010 and n=907 in 2011).

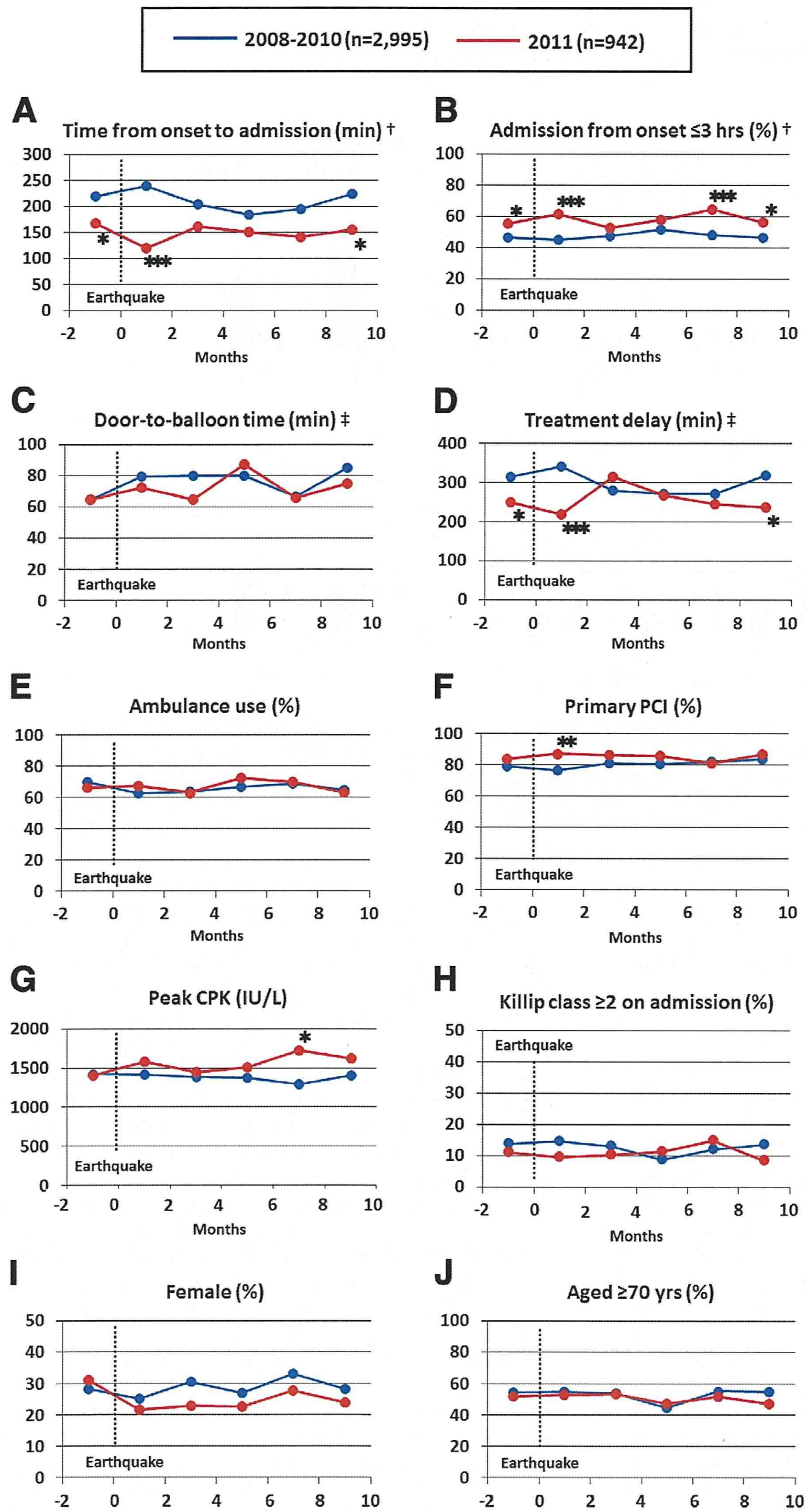


**Figure 2.** Time course of the clinical characteristics of acute myocardial infarction patients in 2011 and 2008–2010, in terms of elapsing time from onset to admission (**A**), prevalence of early admission (≤3 h from onset) (**B**), door-to-balloon time (**C**), treatment delay (**D**), ambulance use (**E**), performance of primary PCI (**F**), peak CPK level (**G**), prevalence of HF with Killip class ≥2 (**H**), sex (**I**) and age (**J**). Continuous values (eg, time elapsing from onset to admission, treatment delay, door-to-balloon time, and peak CPK level) are expressed as median. *P<0.05, **P<0.01, ***P<0.001 vs. 2008–2010. †Only patients with data available on time of onset (n=2,944 in 2008–2010 and n=907 in 2011). ‡Only patients who underwent primary PCI with data available on door-to-balloon time (n=1,678 in 2008–2010 and n=750 in 2011). §Only patients who underwent primary PCI with data available on onset time and door-to-balloon time (n=1,649 in 2008–2010 and n=738 in 2011). CPK, creatine phosphokinase; HF, heart failure; PCI, percutaneous coronary intervention.

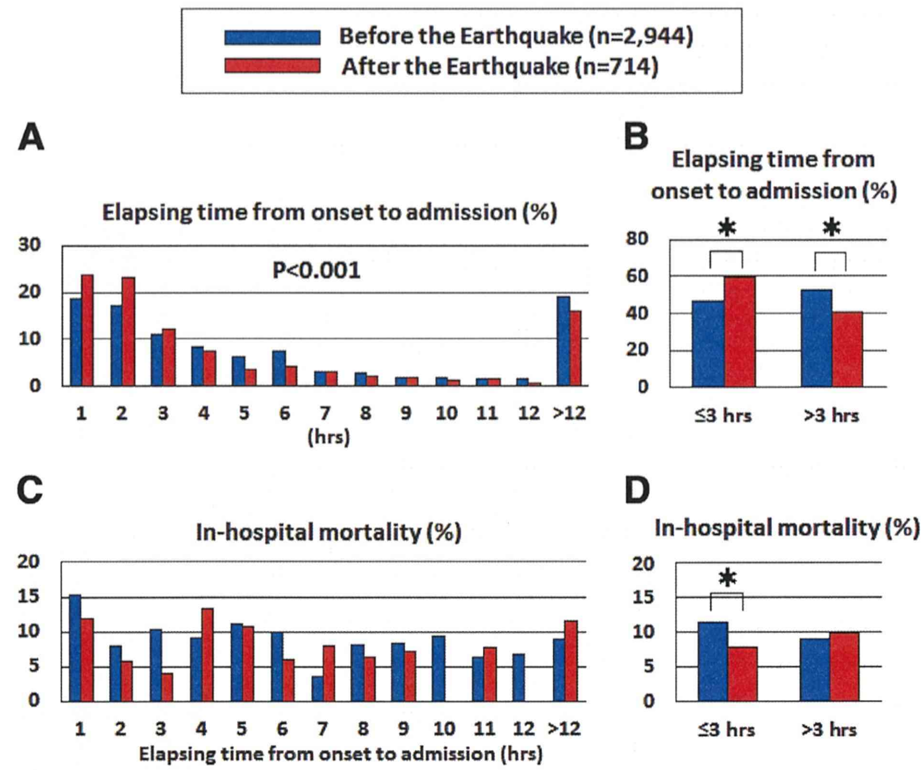


**Figure 3.** Distribution of the elapsing time from onset to admission before and after the Great East Japan Earthquake (March 11, 2011) (**A**,**B**), and the in-hospital mortality by the elapsing time from onset to admission before and after the Earthquake (**C**,**D**). *P<0.05 between before and after the Earthquake.

PCI. P<0.05 was considered statistically significant. All statistical analyses were performed using the statistical software R. 2.15.2 (http://www.r-project.org/) (See **Supplementary File 1**: **Methods** for details).

## Results

The total number of AMI patients in the study period (from January 11 to November 15) in 2008, 2009, 2010 and 2011 was 985, 972, 1038 and 942, respectively. The weekly occurrence of AMI in Miyagi prefecture did not differ significantly after the Great East Japan Earthquake of March 11, 2011 compared with the previous 3 years (**Figure S2**). The clinical characteristics and outcomes of AMI patients in 2008–2010 and 2011 are summarized in **Table 1**. Importantly, the emergency care of AMI was significantly improved in 2011 compared with the previous 3 years, as evidenced by shorter elapsing time from onset to admission, higher performance rate of primary PCI and lower in-hospital mortality despite higher CPK levels. The time-courses of in-hospital mortality according to sex, age, early (≤3 h) and late (>3 h) admission and ambulance use are shown in **Figure 1**. As compared with 2008–2010, significant improvement of in-hospital mortality was noted during the first 2 months after the Earthquake in 2011 (**Figure 1A**), particularly in male patients (**Figures 1B**,**C**), younger patients (<70 years) (**Figures 1D**,**E**) and those with early admission (≤3 h) (**Figures 1F**,**G**), whereas the using an ambulance had no significant effects (**Figures 1H**,**I**).

To explore the factors involved in the improved in-hospital mortality of AMI patients soon after the Earthquake, we performed time-course analyses of the clinical characteristics of AMI patients in 2011 compared with the previous 3 years. In accordance with the imprived in-hospital mortality, the time from onset to admission shortened significantly in 2011 compared with the previous 3 years (**Figures 2A**,**B**), whereas, the door-to-balloon time was comparable (**Figure 2C**). Accordingly, treatment delay, defined as the time from onset to reperfusion, was significantly improved during the first 2 months after the Earthquake (**Figure 2D**) despite no significant change in the ambulance use rate (**Figure 2E**). Performance rate of primary PCI was correspondingly also significantly increased (**Figure 2F**). In contrast, peak CPK levels (**Figure 2G**) and the prevalences of symptomatic heart failure (Killip class ≥2 on admission) (**Figure 2H**), females (**Figure 2I**) and elderly patients (≥70 years) (**Figure 2J**) were almost comparable between 2011 and the previous 3 years.

Furthermore, distribution of the elapsing time from AMI onset to admission showed that the proportion of patients with early admission (≤3 h from onset) was significantly increased after the Earthquake (**Figures 3A**,**B**). We also found a significant reduction in the in-hospital mortality of these patients after the Earthquake (**Figures 3C**,**D**). Multivariate logistic regression analysis demonstrated that before the Earthquake, early admission was significantly associated with a higher incidence of in-hospital mortality but became insignificant after the Earthquake (**Figure 4**). As shown in **Table 2**, the patients with early admission during the first 2 months after the Earthquake were characterized by lower in-hospital mortality as-

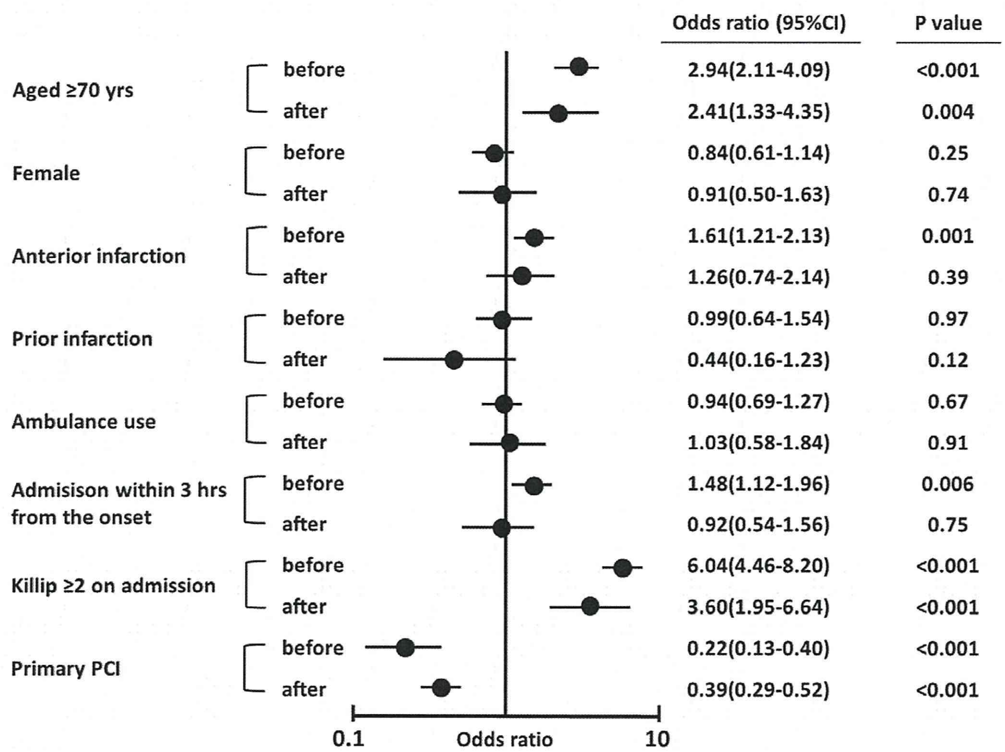


**Figure 4.** Multivariate adjusted odds ratio and 95% confidence intervals (CI) for in-hospital mortality of patients with acute myocardial infarction patients before and after the Earthquake. PCI, percutaneous coronary intervention.

**Table 2. Clinical Characteristics and Outcome of Patients With Early Admission (≤3h From Onset) in 2008–2010 and 2011***

| | 2 months before March 11 | | | 2 months after March 11 | | |
|---|---|---|---|---|---|---|
| | 2008–2010 (n=243) | 2011 (n=96) | P value | 2008–2010 (n=216) | 2011 (n=101) | P value |
| Age [median (IQR)], years | 68 (57–78) | 69 (55–79) | 0.62 | 70 (60–79) | 72 (61–82) | 0.44 |
| Female (%) | 26.1 | 29.2 | 0.56 | 24.0 | 19.8 | 0.41 |
| Anterior infarction (%) | 50.8 | 41.7 | 0.13 | 42.7 | 54.5 | 0.05 |
| Prior infarction (%) | 10.7 | 8.3 | 0.51 | 11.6 | 8.9 | 0.48 |
| Ambulance use (%), (n) | 72.8 (177) | 79.2 (76) | 0.23 | 69.9 (151) | 66.3 (67) | 0.52 |
| Killip ≥2 on admission (%) | 13.2 | 14.6 | 0.73 | 16.2 | 6.9 | 0.02 |
| Primary PCI (%) | 83.1 | 81.3 | 0.68 | 76.4 | 89.1 | 0.008 |
| Peak CPK [median (IQR)], IU/L | 1,622 (618–3,003) | 1,653 (615–2,886) | 0.80 | 1,386 (590–3,058) | 1,634 (712–3,389) | 0.28 |
| Door-to-balloon time [median (IQR)], min† | 62 (45–109) | 58 (40–92) | 0.61 | 67 (43–113) | 68 (45–110) | 0.90 |
| In-hospital mortality (%), (n) | 12.3 (30) | 10.4 (10) | 0.62 | 14.8 (32) | 5.9 (6) | 0.02 |

*Only patients with data available on onset time (n=459 in 2008–2010 and n=197 in 2011). †Only patients who received primary PCI with data available on door-to-balloon time (n=276 in 2008–2010 and n=165 in 2011).
Abbreviations as in Table 1.

sociated with lower prevalence of heart failure with Killip class ≥2 on admission and higher performance rate of primary PCI, compared with those in 2008–2010. In contrast, the clinical characteristics of the patients with late admission (>3h) did not significantly change after the Earthquake (**Table 3**).

Although the tsunami directly and severely damaged the seacoast area, there was no regional difference between the seacoast area and inland areas in the factors relevant to the emergency care of AMI (**Table 4**), suggesting that the emergency medical system of AMI was fairly maintained throughout Miyagi prefecture soon after the Earthquake.

## Discussion

The novel findings of the present study are that emergency care of AMI improved soon after the Great East Japan Earthquake as compared with ordinary times, for which a shorter elapsing time from onset to admission and a higher perfor-

**Table 3.** Clinical Characteristics and Outcome of Patients With Late Admission (>3 Hours From the Onset) in 2008–2010 and 2011*

| | 2 months before March 11 | | | 2 months after March 11 | | |
|---|---|---|---|---|---|---|
| | 2008–2010 (n=296) | 2011 (n=77) | P value | 2008–2010 (n=261) | 2011 (n=63) | P value |
| Age [median (IQR)], years | 73 (63–81) | 75 (64–84) | 0.02 | 72 (61–80) | 70 (63–78) | 0.44 |
| Female (%) | 29.4 | 35.1 | 0.34 | 25.0 | 23.8 | 0.85 |
| Anterior infarction (%) | 45.6 | 48.1 | 0.70 | 48.5 | 36.5 | 0.09 |
| Prior infarction (%) | 6.1 | 7.8 | 0.59 | 12.3 | 7.9 | 0.33 |
| Ambulance use (%), (n) | 69.6 (206) | 53.2 (41) | 0.007 | 57.9 (151) | 68.3 (43) | 0.13 |
| Killip ≥2 on admission (%) | 12.2 | 6.5 | 0.16 | 14.2 | 12.7 | 0.76 |
| Primary PCI (%) | 77.7 | 85.7 | 0.12 | 77.4 | 82.5 | 0.37 |
| Peak CPK [median (IQR)], IU/L | 1,396 (616–2,691) | 1,267 (600–2,624) | 0.62 | 1,451 (702–2,812) | 1,481 (876–3,228) | 0.84 |
| Door-to-balloon time [median (IQR)], min† | 65 (45–102) | 73 (50–108) | 0.91 | 84 (55–123) | 80 (50–120) | 0.51 |
| In-hospital mortality (%), (n) | 8.1 (24) | 6.5 (5) | 0.64 | 11.5 (30) | 9.5 (6) | 0.66 |

*Only patients with data available on onset time (n=557 in 2008–2010 and n=140 in 2011). †Only patients who received primary PCI (n=294 in 2008–2010 and n=106 in 2011).
Abbreviations as in Table 1.

**Table 4.** Differences in the Clinical Characteristics and Outcomes of AMI Patients in the Inland and Seacoast Areas*

| | 2 months before 11 March | | | 2 months after 11 March | | |
|---|---|---|---|---|---|---|
| | Inland (n=146) | Seacoast (n=33) | P value | Inland (n=136) | Seacoast (n=31) | P value |
| Age [median (IQR)], years | 70 (58–81) | 70 (61–81) | 0.91 | 69 (60–79) | 76 (65–85) | 0.009 |
| Female (%) | 31.5 | 27.3 | 0.63 | 20.6 | 25.8 | 0.52 |
| Anterior infarction (%) | 44.5 | 45.5 | 0.92 | 46.3 | 58.1 | 0.24 |
| Prior infarction (%) | 6.8 | 12.1 | 0.31 | 9.6 | 3.2 | 0.25 |
| Ambulance use (%), (n) | 67.8 (99) | 57.6 (19) | 0.26 | 69.1 (94) | 58.1 (18) | 0.24 |
| Time elapsing from onset to admission [median (IQR)], min† | 156 (60–516) | 189 (74–458) | 0.68 | 150 (66–402) | 90 (60–312) | 0.23 |
| Killip ≥2 on admission (%) | 12.3 | 6.1 | 0.30 | 8.8 | 12.9 | 0.72 |
| Primary PCI (%) | 82.2 | 87.9 | 0.43 | 87.5 | 83.9 | 0.59 |
| Peak CPK [median (IQR)], IU/L | 1,325 (740–2,470) | 1,618 (413–3,336) | 0.84 | 1,597 (755–3,521) | 1,316 (670–2,689) | 0.60 |
| Door-to-balloon time [median (IQR)], min‡ | 65 (45–94) | 80 (38–128) | 0.78 | 71 (50–120) | 78 (45–106) | 0.65 |
| In-hospital mortality (%), (n) | 9.6 (14) | 6.1 (2) | 0.64 | 7.4 (10) | 6.5 (2) | 0.86 |

*Patients were divided into 2 groups according to transferred hospital located within 5 km of the sea (seacoast area, n=64) or not (inland area, n=282). †Only patients with data available on onset time (n=278 in the inland area and n=63 in the seacoast area). ‡Only patients who received primary PCI with data available on door-to-balloon time (n=220 in the inland area and n=55 in the seacoast area).
Abbreviations as in Table 1.

mance rate of primary PCI may be involved. To the best of our knowledge, this is the first report demonstrating that the emergency care of AMI can be improved through improved chain of survival, especially earlier admission from onset, following a natural disaster in a large community.

## Occurrence of AMI After the Great East Japan Earthquake

The present study demonstrated that the occurrence of AMI per se did not significantly increase after the Earthquake, a finding consistent with our recent report.[14] In contrast, it has been reported that the occurrence of AMI increased after previous earthquakes that occurred in the early morning, such as the Northridge earthquake in 1994 (Los Angeles, CA, USA), and the Hanshin-Awaji earthquake in 1995 (Kobe, Japan).[22,23] This discrepancy might be attributable, at least in part, to the type of earthquake (ocean-trench earthquake in the present study vs. inland ones in the previous studies) and when the earthquake occurred (afternoon in the present study vs. early morning in the previous studies). AMI would be more likely to occur if an extreme emotional stress following abrupt awakening by an earthquake is superimposed, as in the previous studies, whereas it was reported that the incidence of AMI did not significantly increase after earthquakes in the afternoon such as the Loma Prieta earthquake in 1989 (San Francisco, CA, USA) and the Niigata-Chuetsu earthquake in 2004 (Niigata, Japan).[24,25] In addition, the discrepancy could also be explained by differences in subject numbers and study period, as the present study had a large study population and a longer study period compared with previous studies.[22,23] We also had the advantage of being able to compare the data after the Earthquake with historical data from the previous 3 years.

## Increased Rate of Performing Primary PCI After the Great East Japan Earthquake

During the first 2 months after the Earthquake, in-hospital mortality of AMI patients was significantly improved in Miyagi prefecture, associated with a shorter elapsing time from onset to admission and higher performance rate of primary PCI, as compared with the previous 3 years. Previous clinical studies have demonstrated that coronary reperfusion therapies, including primary PCI, effectively reduce infarct size and improve the clinical outcomes of AMI patients.[1,3] In the Miyagi AMI Registry Study, the use of primary PCI has dramatically increased since the 1990s and more than 80% of AMI patients underwent the therapy in recent years.[2] In the present study, the performance rate of primary PCI was approximately 85% in 2011 and during the first 2 months after the Earthquake, it was significantly higher compared with the previous 3 years.

Such a higher performance rate of primary PCI may have substantially contributed to the better prognosis of AMI patients in 2011.

### Improved Chain of Survival of AMI After the Great East Japan Earthquake

In addition to the increased performance rate of primary PCI, the elapsing time from symptom onset of AMI to reperfusion therapy (ie, the chain of survival) is another important factor in the clinical outcome of AMI patients.[4–6] This treatment delay is divided into 2 major components: (1) the time from onset to the first contact by a patient with emergency care (patient delay) and (2) from the first contact with emergency care to first balloon dilatation (system delay)[4] (**Figure S2A**). Although previous trials have succeeded in improving the system delay,[26,27] no attempt has been made regarding the patient delay.[7,8] In the present study, we found that the time from onset to admission was significantly shortened after the Earthquake and that the trend continued throughout the year of 2011. Before the Earthquake, patients with early admission had a significantly higher mortality despite their younger age compared with those with late admission (**Table S1**). These paradoxical findings were consistent with a recent report from Japan[28] that indicated patients with signs of left ventricular failure have a significantly shorter patient delay.[29] Indeed, a multivariate analysis also showed that early admission correlated with worse in-hospital mortality before the Earthquake, suggesting that the severity of AMI in those patients were high (eg, complicated with cardiac arrest or cardiogenic shock). In contrast, after the Earthquake, the patients with early admission had a better in-hospital outcome, associated with a lower prevalence of symptomatic heart failure, despite peak CPK levels comparable to those before the Earthquake. These findings indicate that after the Earthquake, AMI patients were transferred to hospitals earlier regardless of the severity of the disorder. As demonstrated in previous studies,[1,30] it is probably the earlier admission and less severe condition on admission that were associated with the higher performance rate of primary PCI after the Earthquake than in ordinary times (**Figure S2B**). In contrast, the ambulance use rate was unchanged before and after the Earthquake. Thus, it is highly possible that the patient delay was reduced with a resultant favorable prognosis soon after the Earthquake. Indeed, a recent study also emphasized that efforts to minimize patient delay are recommended to improve clinical outcomes in AMI patients because the benefit of a short door-to-balloon time was limited only to patients with early admission.[31] The present study also demonstrates that in-hospital mortality in the acute phase of AMI was improved after the Earthquake, together with the increased rate of early admission and unchanged door-to-balloon time as compared with ordinary times (**Figure S2B**). Additionally, based on the fact that the Niigata-Chuetsu earthquake significantly increased long-term mortality from AMI,[32] we have to recognize the need for long-term prevention of AMI in the future.

It remains to be elucidated why patients with AMI presented earlier after the Earthquake. Disaster-related mental and physical stresses are known to activate the sympathetic nervous system and enhance the activity of key molecules associated with coronary artery vasomotion such as Rho/Rho-kinase.[13,16] It is possible that those activated pathways reduce the threshold level of ischemia-related symptoms. Furthermore, disasters can cause various manifestations of psychological distress in survivors, including feelings of tension and anxiety, concentration difficulty, hostility and rage, sleep problems and intrusion/avoidance of disaster-related memories.[33,34] It has been reported that exposure to extreme stressors may enhance an individual's reactivity to subsequent stressors. That process is termed "stress sensitization", in which an organism responds more strongly to a variety of stimuli after exposure to a potentially threatening or noxious stimulus.[35–37] In the present critical situation caused by the Earthquake, tsunami and subsequent aftershocks, many residents in Miyagi prefecture would have experienced stress sensitization. Generally, the human instinct to survive is the most powerful drive and the fight-or-flight reaction, which is the best-known expression of our survival instinct, is triggered when we perceive a situation as a threat to our existence.[38–40] Thus, it is highly possible that in the present disaster, stress sensitization and enhanced survival instincts made the AMI patients more sensitive to their health or physical disorder with resultant earlier admission than in ordinary times.

However, it is important to note that a previous study of a community intervention targeting mass media and patient education failed to improve appropriate action for AMI symptoms.[7] In the present study, we also found no difference in door-to-balloon time that would reflect the system delay before and after the Earthquake, suggesting that the medical system itself functioned as well as in ordinary times, despite the fact that the Earthquake damaged infrastructure and caused shortages of medicines. We also found no difference in the ambulance use rate, elapsing time from onset to admission, performance rate of primary PCI or in-hospital mortality between the inland and seacoast areas, which suggests that the emergency medical system was well maintained throughout the prefecture during the disaster period.

### Study Limitations

First, although almost all AMI patients were transferred to participating hospitals in Miyagi prefecture, not all patients may have been registered in the registry, especially during the disaster period. Second, as shown by several previous studies, including our own recent reports, the occurrence of cardiopulmonary arrest significantly increases after large earthquakes.[11,41] Thus, it is conceivable that patients who died from AMI-related cardiopulmonary arrest were not included in the present study and the incidence of AMI after the Earthquake could be underestimated. However, we found that the emergency care of AMI worked better soon after the Great East Japan Earthquake than in ordinary times. Third, there was no detailed angiographic data in our database. Thus, we were unable to determine the subtypes of MI based on the universal definition[42] or the incidence of takotsubo cardiomyopathy misdiagnosed as AMI. In addition, because we have no data available on the prevalence of pre-infarction angina and glucose levels on admission, both of which have been shown to be associated with the prognosis of AMI patients,[43,44] we were unable to examine how those prognostic factors had been affected by the Earthquake. Fourth, since the present study was observational in nature, the precise mechanisms of the improvement in the emergency care of AMI, especially that of the improved time from onset to admission, remain to be fully elucidated.