Background: Worldwide, the rate of aging is highest in Japan, especially the female population. To explore the trends for acute myocardial infarction (AMI) in Japan, the MIYAGI-AMI Registry Study has been conducted for 30 years since 1979, whereby all AMI patients in the Miyagi prefecture are prospectively registered.

Methods and Results: In 1979–2008, 22,551 AMI patients (male/female 16,238/6,313) were registered from 43 hospitals. The age-adjusted incidence of AMI (/100,000 persons/year) increased from 7.4 in 1979 to 27.0 in 2008 (P<0.001). Although control of coronary risk factors remained insufficient, the rates of ambulance use and primary percutaneous coronary intervention (PCI) have increased, and the overall in-hospital mortality (age-adjusted) has decreased from 20.0% in 1979 to 7.8% in 2008 (P<0.0001). However, the in-hospital mortality remains relatively higher in female than in male patients (12.2% vs 6.3% in 2008). Female patients were characterized by higher age and lower PCI rate.

Conclusions: The MIYAGI-AMI Registry Study demonstrates the steady trend of an increasing incidence, but decreasing mortality, for AMI in Japan over the past 30 years, although the female population still remains at higher risk for in-hospital death, despite improvements in the use of ambulances and primary PCI. (Circ J 2010; 74: 93–100)

Key Words: Acute myocardial infarction; Aging; Gender; Risk factors

Trends in Acute Myocardial Infarction Incidence and Mortality Over 30 Years in Japan: Report From the MIYAGI-AMI Registry Study

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Acute myocardial infarction (AMI) is a major cause of morbidity and mortality worldwide. In the United States, nearly 1 million patients suffer from AMI each year.1 In the past decades, industrialization, urbanization, and associated life-style changes have taken place worldwide as the population grows older in association with the epidemics of obesity and metabolic syndrome. Especially in Japan, these changes have become more evident because the rate of aging is the highest in the world and the westernization of lifestyle has progressed rapidly.2 In order to estimate the trends in the burden of disease, particularly that of AMI, it is important to monitor and track the incidence and mortality of AMI in the same community for a long time. Indeed, the World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease (WHO-MONICA) project reported the prevalence and case-fatality rate in 21 countries,3 but Japan was not included. Moreover, in Japan, there have been few studies specifically for AMI and most of them have included a small number of annual events with a relatively short monitoring period.4–7

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To explore the actual trend for AMI reflecting “real-world” practice in Japan, we have been conducting the MIYAGI-AMI Registry Study for 30 years since 1979, whereby all AMI patients in the Miyagi prefecture have been prospectively registered and there has been a relatively stable population over those years.8,9

Methods

The MIYAGI-AMI Registry Study

The Miyagi prefecture is located in northeastern Japan and has had a relatively stable population of approximately 2 million over the last 30 years (2,054,000 in 1979 and...
The MIYAGI-AMI Registry Study is a prospective, multicenter, observational study. Details of data collection have been published previously. 

Briefly, this registry was established in 1978 and the 43 major hospitals with a coronary care unit and/or cardiac catheterization facilities in the Miyagi prefecture have been participating (Appendix 1). In our study, almost all the patients with AMI were finally admitted to 1 of the 43 participating hospitals in the Miyagi prefecture, enabling us to precisely examine the practice for AMI. This study was approved by the Institutional Review Board of Tohoku University Graduate School of Medicine, under the condition that personal data are protected at all times.

Diagnosis of AMI was made by the individual cardiologists in charge, based on the WHO-MONICA criteria. Generally, it was based on the findings of typical chest pain symptoms, ECG changes and increased serum levels of cardiac enzymes (i.e., creatine phosphokinase, aspartate aminotransferase and lactate dehydrogenase).

The registration form included the date and time of symptom onset, age, sex, pre-hospital management (e.g., use of ambulance, time interval from the onset of symptoms to admission), infarction site, coronary risk factors (hypertension, diabetes mellitus, dyslipidemia, and smoking), reperfusion therapies (e.g., thrombolysis or percutaneous coronary intervention (PCI)), duration of hospitalization and in-hospital outcome (e.g., in-hospital mortality). In the Miyagi-AMI Registry Study, we have revised the registration form step by step over the past 30 years. Thus, although the incidence of AMI and related data (time of onset, age and sex) are available for those 30 years, the date of pre-hospital management, infarction site, coronary risk factors, reperfusion therapies, duration of hospitalization, and in-hospital outcome are available for the past 10–20 years.

In the Miyagi-AMI Registry Study, the decision of reperfusion was made by the individual cardiologists in charge. Primary PCI has been commonly performed since 1992, according to the protocol of each hospital. Thrombolysis was performed with intravenous administration of urokinase (480–960×10^3 IU for 30 min) or alteplase (290–435×10^3 IU/kg for 60 min) or with intracoronary administration of alteplase (maximum 6.4×10^6 IU) or urokinase (maximum 960×10^3 IU).

Rescue PCI was performed when thrombolysis was unsuccessful in terms of symptoms, ECG changes and/or coronary blood flow.

Data Analysis

In the present study, we registered a total of 22,551 patients with AMI (males/females 16,238/6,313) who were hospitalized between 1979 and 2008. Sex- and age-adjusted incidence rates of AMI per 100,000 person-years were calculated. To adjust the age distribution differences among the periods, we applied the direct method using the Japanese population from the 2000 census, as the standard population.

Results

The overall age-adjusted incidence of AMI (/100,000 persons/year) markedly increased by 3.6-fold, from 7.4 in 1979 to 27.0 in 2008 (P<0.001) (Figure 1). The average age of the male and female AMI patients in the whole period was 65±13 and 75±11 years, respectively. In males, the age-adjusted incidence of AMI (/100,000 persons/year) significantly increased by 2.5-fold, from 18.7 in 1979 to 46.4 in 2008 (P<0.0001), whereas in females, it tended to be increased by
The distribution of age significantly changed with the increased population of elderly patients, especially that of ≥80-year-old patients, in both sexes (both P<0.001) (Figure 2). Moreover, the prevalence of hypertension, diabetes mellitus, and dyslipidemia also significantly increased over time in both sexes (all P<0.01) (Figure 3). Smoking habit also remained at ~40% in male and ~10% in female patients (Figure 3). The peak time of onset of AMI remained in the early morning (Figure 4), and the distribution of the infarct site was the anterior wall in 45%, inferior/posterior wall in 43%, and other in 12%.

Over the past 30 years, the use of ambulances significantly increased from 47% in 1980 to 64% in 2008 (P<0.0001) (Figure 5). Along with this increased use, the overall in-hospital mortality has markedly decreased from 20% in 1979 to 8% in 2008 (P<0.0001) (Figure 5). However, the in-hospital mortality of female patients remained relatively higher than for male patients over the past 30 years (6.3% in males and 12.2% in females in 2008) (Figure 5).

Use of primary PCI has dramatically increased from 20% in
Figure 4. Peak time of onset of acute myocardial infarction has remained in the early morning.

Figure 5. Age-adjusted in-hospital mortality (/100,000 persons/year) and ambulance use. Together, with the increased use of ambulances, in-hospital mortality has dramatically decreased; however, female patients still are at higher risk than male patients.
Figure 6. Prevalence of reperfusion therapy (Tx) for acute myocardial infarction. The prevalence of primary percutaneous coronary intervention (PCI) has increased, especially in the past 10 years.

Figure 7. Time interval from the onset of symptoms to admission shows no change.
1992 to 80% in 2008 (P<0.0001) (Figure 6). In contrast, the prevalence of patients without reperfusion therapy significantly decreased from 38% in 1992 to 18% in 2008 (P<0.0001). In-hospital mortality was significantly lower for patients with primary PCI (5%, n=8,693) than for those without it (17%, n=254) (P<0.01). Importantly, the prevalence of primary PCI was significantly lower for female patients (71%, n=2,412) than for male patients (80%, n=6,061) (P<0.01).

In 1979, approximately 30% of patients had more than 12 h from the onset of AMI to hospitalization, while 60% of patients were hospitalized within 6 h after the onset (Figure 7). This tendency for the majority of AMI patients to be hospitalized within 6 h was fairly consistent throughout the study period (Figure 7).

Finally, the duration of hospital stay has significantly shortened over the past 30 years; the prevalence of discharge within 20 days after the onset of AMI significantly increased from 20% in 1979 to 66% in 2008 (P<0.0001) (Figure 8).

Discussion
The data from the 30-year MIYAGI-AMI Registry Study demonstrates that there is the steady trend of increasing incidence, but decreasing mortality, for AMI in Japan and that the female population still remains at higher risk for in-hospital mortality, despite progress in both patient transfer and reperfusion therapy.

Increasing Incidence of AMI
There have been few studies regarding the incidence of AMI in Japan and most were performed between the 1960s and 1980s.\textsuperscript{4,13,14} Their results were conflicting as they reported either a declining or flattened\textsuperscript{4,13,14} trend in the incidence of AMI. After the 1990s, the rate of aging has been the highest in Japan and westernization of the lifestyle has rapidly accelerated; however, no detailed data are yet available regarding the actual incidence and outcome of AMI.

The Miyagi prefecture is located on the Pacific Ocean side of Japan and has a typical balance of urban and rural districts. Our MIYAGI-AMI Registry Study provides important insights into the 30-year trend for AMI in Japan from 1979 to 2008. As shown in Figure 1, the overall age-adjusted incidence of AMI (/100,000 persons/year) increased from 7.4 in 1979 to 27.0 in 2008, indicating a steady trend of increasing incidence of AMI. The incidence of AMI was male-predominant (males 46.4 vs females 9.6 in 2008), a consistent finding with the Takashima AMI registry (males 100.7 vs females 35.7 in 1999–2001)\textsuperscript{5} and the Niigata and Nagaoka study (males 41.9 vs females 5.3 in 1994–1996).\textsuperscript{6} However, the current incidence of AMI in Japan is still lower than that in North America and Europe; the incidence of AMI for males (/100,000 persons/year) is 824 in Finland, 823 in United Kingdom, 605 in Canada, 508 in the United States, 314 in France, and 270 in Italy.\textsuperscript{15}

Age is a most important risk factor for the development of cardiovascular diseases and accompanying clinical events. In the present study, the aging of the population is evident; the number of aged patients, especially that of ≥80-year-old patients, increased significantly in the past 30 years (Figure 2).

Even a relatively short-term survey (1992–2001) of Medicare in 4 US states demonstrated that the age of AMI patients is older and that the proportion of the population >85 years old has increased.\textsuperscript{16} These findings indicate the urgent need for evidence-based management strategies applicable to increas-
Insufficient Control of Coronary Risk Factors
The WHO-MONICA studies, as well as the Japanese epidemiological studies, have previously shown that the risk of cardiovascular diseases increases with clustering of risk factors, such as hypertension, hyperlipidemia and diabetes mellitus. The present study demonstrates that the control of major coronary risk factors is still insufficient in Japan, which could largely account for the increasing incidence of AMI. The westernization of lifestyle and the high rate of aging in Japan are apparent causative factors for the trend. Furthermore, the prevalence of smoking still remains high at ~40% in male patients with AMI, although it has been reported that the smoking rate has declined by 20% in the general Japanese population.

Higher Risk for Females for In-Hospital Mortality of AMI
One of the important findings in the present study is that the in-hospital mortality still remains relatively higher for female patients than for male patients. A similar trend has been reported from the American Heart Association Heart Disease and Stroke Statistics. Several factors could be involved in the sex difference in in-hospital mortality, including higher age, longer time elapsed from onset to hospitalization, and low prevalence of PCI in female AMI patients. Indeed, in the present study, the average age of the female patients was 10 years older than that of the male patients. The older age of female patients at the time of admission may further limit the use of several therapies, which could have been the case in the present study. In addition, the incidence of death from procedural complications, such as vascular and hemorrhagic complications, is greater in females. Thus, more attention should be paid to these factors when treating female AMI patients.

Unchanged Time of Onset and Infarct Site
It has been repeatedly demonstrated that the onset of AMI peaks early in the morning in both Japan and Western countries. The present study not only confirmed this point but also demonstrated that such a tendency has remained unchanged for the past 30 years in Japan. These results suggest that the triggering mechanism(s) for AMI has remained unchanged despite the increasing incidence of the disease.

The present study also demonstrated that the AMI site has unchanged in the last 30 years. Although anterior AMI is associated with worse outcome, as compared with inferior AMI, the present result indicates that the improvement of morality is likely to be related to factors other than the AMI site.

Improvement of Critical Care and In-Hospital Care for AMI
The present study demonstrated the overall in-hospital mortality (age-adjusted) has significantly reduced from ~20% in 1979 to 12.2% in 2008. The duration of hospital stay was also significantly shortened over the past 30 years, during which the paradigm of AMI management has shifted from a conservative strategy to an interventional strategy. In fact, in the present study, use of primary PCI has been increasing from 20% in 1992 to ~80% in 2008, and in-hospital mortality was lower in patients who underwent primary PCI than in those who did not. The progress in reperfusion therapy, especially that of primary PCI, appears to have contributed to the reduction in in-hospital mortality and hospital stay, as previously reported from this registry.

Currently, approximately half of AMI patients in the Western countries are transported to hospital by ambulance. The present study demonstrated the ambulance use in Japan has increased to ~70% in the past 10 years. Because the majority of AMI patients in the past 30 years were hospitalized within 6 h, the increased use of ambulances may not have directly contributed to the shortened interval from onset of symptoms to hospitalization. However, the increased use of ambulances should have resulted in increased use of primary PCI with a resultant improvement in the in-hospital mortality.

The increasing incidence of, but decreasing in-hospital mortality from, AMI in Japan may have resulted from the recent increase in the number of patients with ischemic heart failure, as reported in the Chronic Heart Failure Analysis and Registry in the Tohoku District (CHART) registry study. For surviving AMI patients, it is important to understand the underlying risk factors that lead to secondary cardiac events. Indeed, a more effective strategy to improve the management of post-infarction heart failure needs to be developed.

Conclusions
Our MIYAGI-AMI Registry Study demonstrates that over the past 30 years in Japan, there has been a steady trend of increasing incidence, but decreasing mortality, for AMI in the Japanese population, although female patients are still at higher risk for in-hospital mortality than male patients, a result in which both positive (eg, increased use of ambulance and primary PCI) and negative factors (eg, insufficient control of coronary risk factors and aging of the whole society) may be involved.

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Appendix 1
List of Participating Hospitals

1. Fukaya Hospital, Hiroshi Akiho, MD; Hikarigaoka Spettman Hospital, Tomofumi Mimata, MD; Ishinomaki Municipal Hospital, Kenjiro Akai, MD; Ishinomaki Red-Cross Hospital, Hironosuke Sugekawa, MD; JR Sendai Hospital, Masao Kuroha, MD; Katta General Hospital, Hirokuni Kanno, MD; Kesen-numa Hospital, Kazunori Ogata, MD; Kurihara Central Hospital, Seiji Komori, MD; Tokohu Rosai Hospital, Tatsuya Komarum, MD; Marumori National Health Insurance Hospital, Masatuka Otomo, MD; Miyagi Eastern Cardiovascular Institute, Toru Naganuma, MD; Miyagi Cancer Center, Nobuo Tomisawa, MD; Miyagi Cardiovascular and Respiratory Center, Noboru Osawa, MD; Mori Hospital, Akio Mori, MD; Nagamachi Hospital, Hidetsoshi Mitobe, MD; Nishitagai National Hospital, Shigenori Kitaoa, MD; NTT EAST Tohoku Hospital, Aki Yamada, MD; Otsu Memorial Hospital, Yoshirou Koiwa, MD; Osaka City Hospital, Tetsuya Hiramoto, MD; Saito Hospital, Keiji Otsuka, MD; Saka General Hospital, Atsushi Obata, MD; Sanuma Municipal General Hospital, Hiroshi Ishii, MD; Sendai Cardiovascular Center, Shin-yu Fujii, MD; Sendai City Hospital, Tetsuo Yagi, MD; Sendai Kosei Hospital, Taichiro Meguro, MD; Sendai Medical Center, Tsuyoshi Shinozaki, MD; Sendai Open Hospital, Masaharu Kanazawa, MD; Sendai Public Health Insurance Hospital, Yoshichika Oikawa, MD; Sendai Red-Cross Hospital, Yuji Kono, MD; Sendai Tokukai Hospital, Kimihiko Ogata, MD; Sen-En General Hospital, Ryuichi Hashiguchi, MD; Shichigashuku National Health Insurance Clinic, Takahiro Nagashima, MD; Shigahama City Hospital, Jun Goto, MD; South Miyagi Medical Center, Kan-ichi Inoue, MD; Tokohu Kosai Hospital, Mitsumasa Fukuchi, MD; Tokohu University Hospital, Department of Cardiovascular Medicine, Hiroaki Shimokawa, MD; Department of Cardiovascular Surgery, Kouichi Tabayashi, MD; Department of Gastroenterology, Toru Shimosegawa, MD; Tohoku Welfare and Pension Hospital, Yoshihito Katahira, MD; Tome Public Hospital, Munehiko Ishii, MD.