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Trends in Acute Myocardial Infarction Incidence and Mortality Over 30 Years in Japan:

Report From the MIYAGI-AMI Registry Study

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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

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

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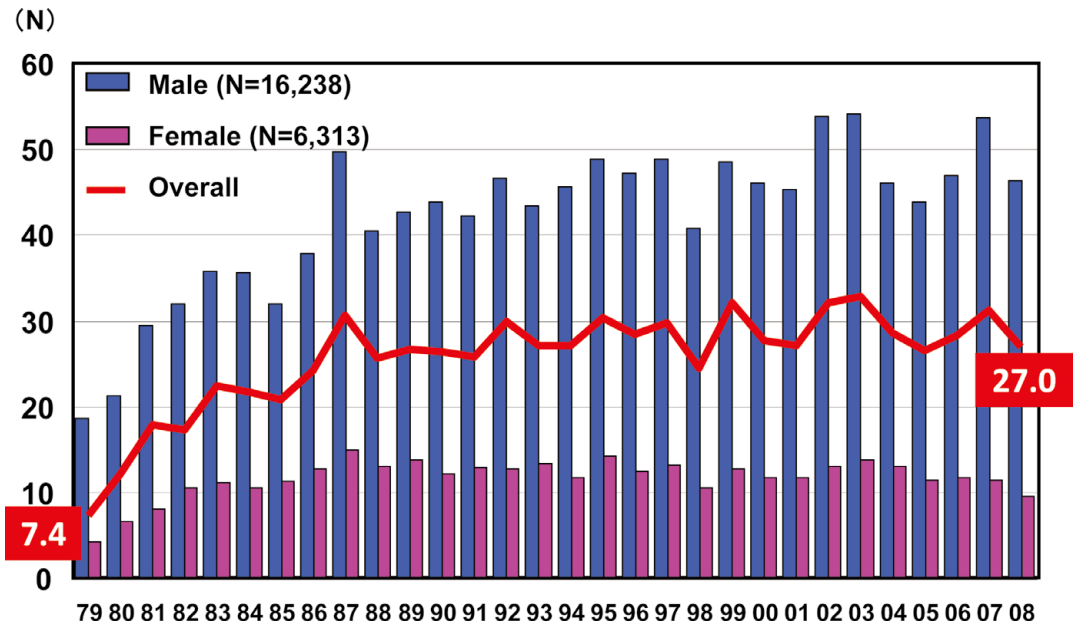

Figure 1. Age-adjusted incidence (/100,000 persons/year) of acute myocardial infarction has increased over the last 30 years, especially evident in the male population.

2,340,000 in 2008). The MIYAGI-AMI Registry Study is a prospective, multicenter, observational study. Details of data collection have been published previously.[8,9] 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.[3] Generally, it was based on the findings of typical chest pain symptoms, ECG changes and increased serum levels of cardiac enzymes (ie, creatine phosphokinase, aspartate aminotransferase and lactate dehydrogenase).

The registration form included the date and time of symptom onset, age, sex, pre-hospital management (eg, 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 (eg, thrombolysis or percutaneous coronary intervention (PCI)), duration of hospitalization and in-hospital outcome (eg, 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).[2,3] Rescue PCI was performed when thromolysis 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,[10] as the standard population.

Results are expressed as mean±SD. Trend in age-adjusted incidence, age-adjusted in-hospital mortality, and use of ambulance were assessed using the Cochran-Armitage trend test.[11,12] Age and therapy differences were estimated by the χ^2-test. These analyses were carried out with SAS software version 9.1 (SAS Institute, Inc, Cary, NC, USA). P-values <0.05 were considered to be statistically significant.

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

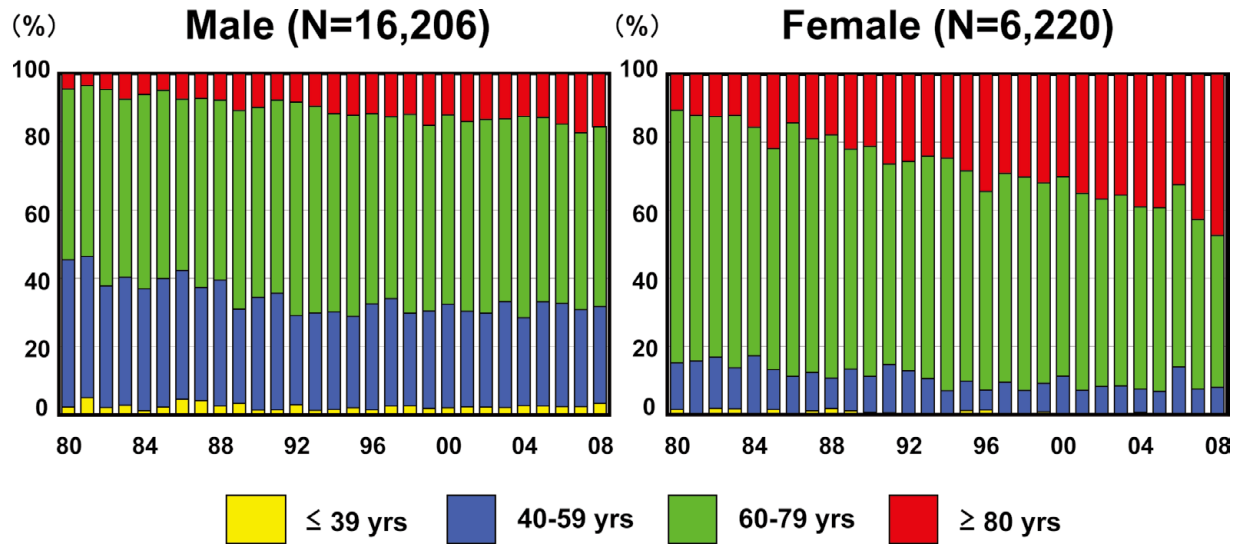

Figure 2. Serial changes in the age distribution of patients with acute myocardial infarction. The increasing prevalence of elderly patients is evident, especially females.

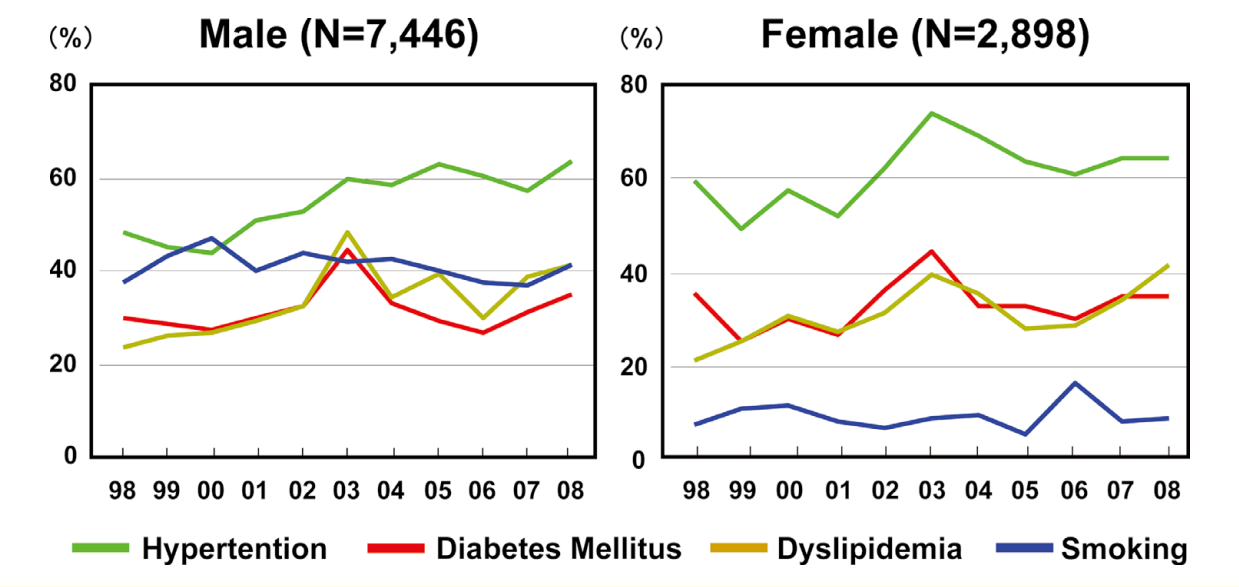

Figure 3. Prevalence of coronary risk factors in patients with acute myocardial infarction. It is evident that the control of all 4 major coronary risk factors is insufficient.

2.3-fold, from 4.2 in 1979 to 9.6 in 2008, but did not reach a statistically significant level (P=0.15).

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

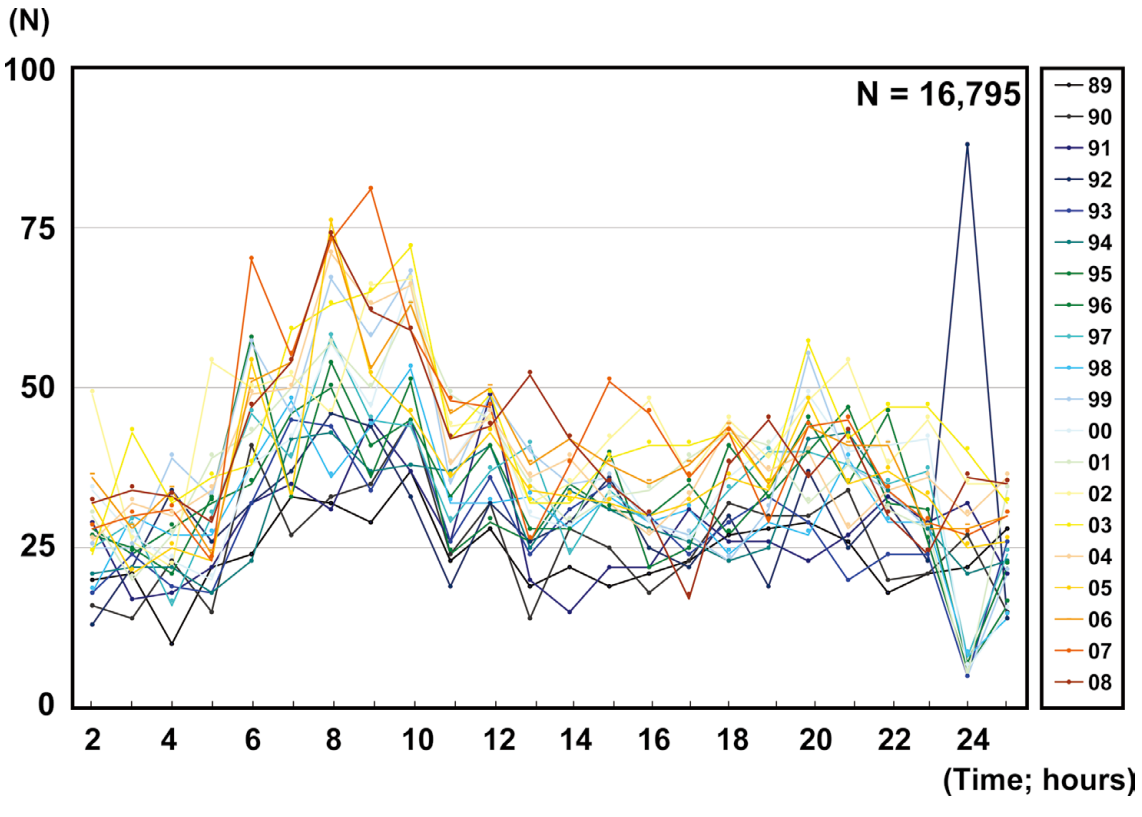

Figure 4. Peak time of onset of acute myocardial infarction has remained in the early morning.

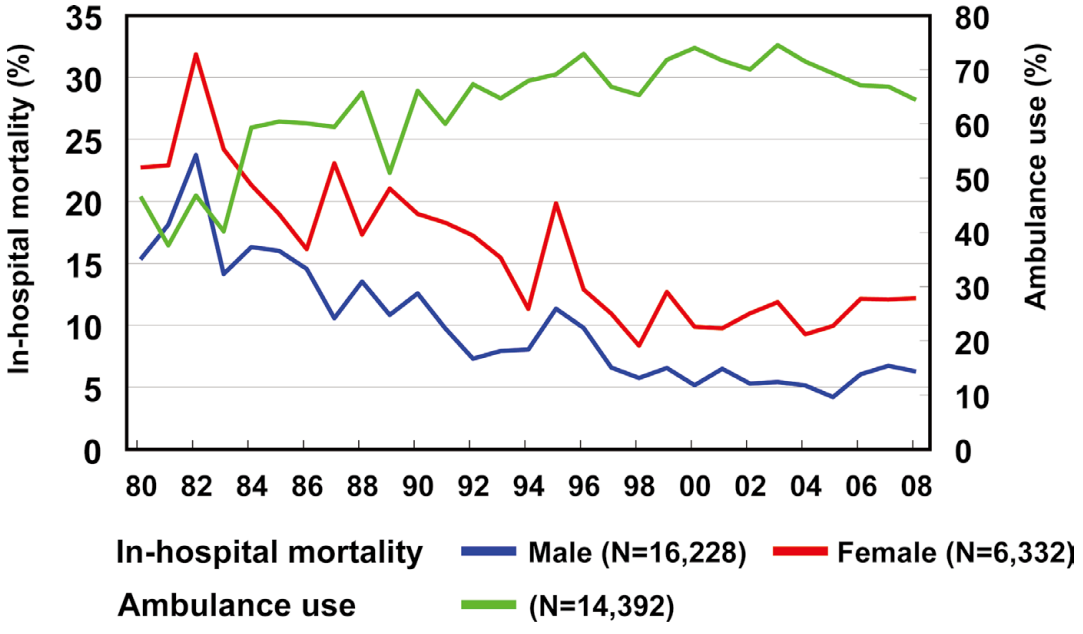

Figure 5. Age-adjusted in-hospital mortality (/100,000 persons/year) and ambulance use. Together, with the increased use of ambulances, in-hospital mortality has dramatically decreased; however, female patients still are at higher risk than male patients.

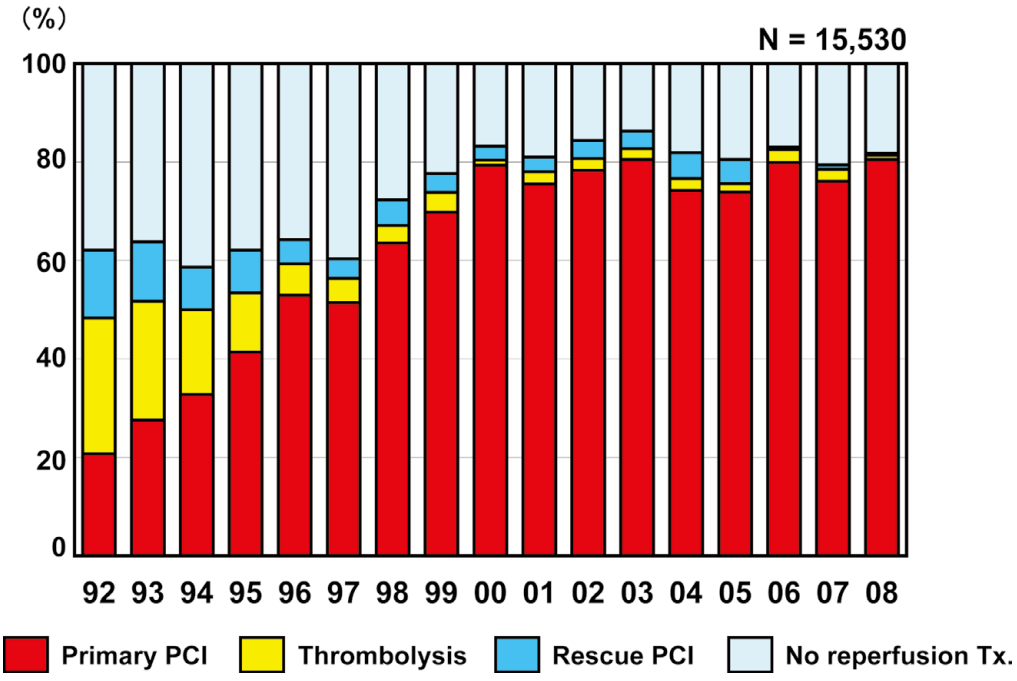

Figure 6. Prevalence of reperfusion therapy (Tx) for acute myocardial infarction. The prevalence of primary percutaneous coronary intervention (PCI) has increased, especially in the past 10 years.

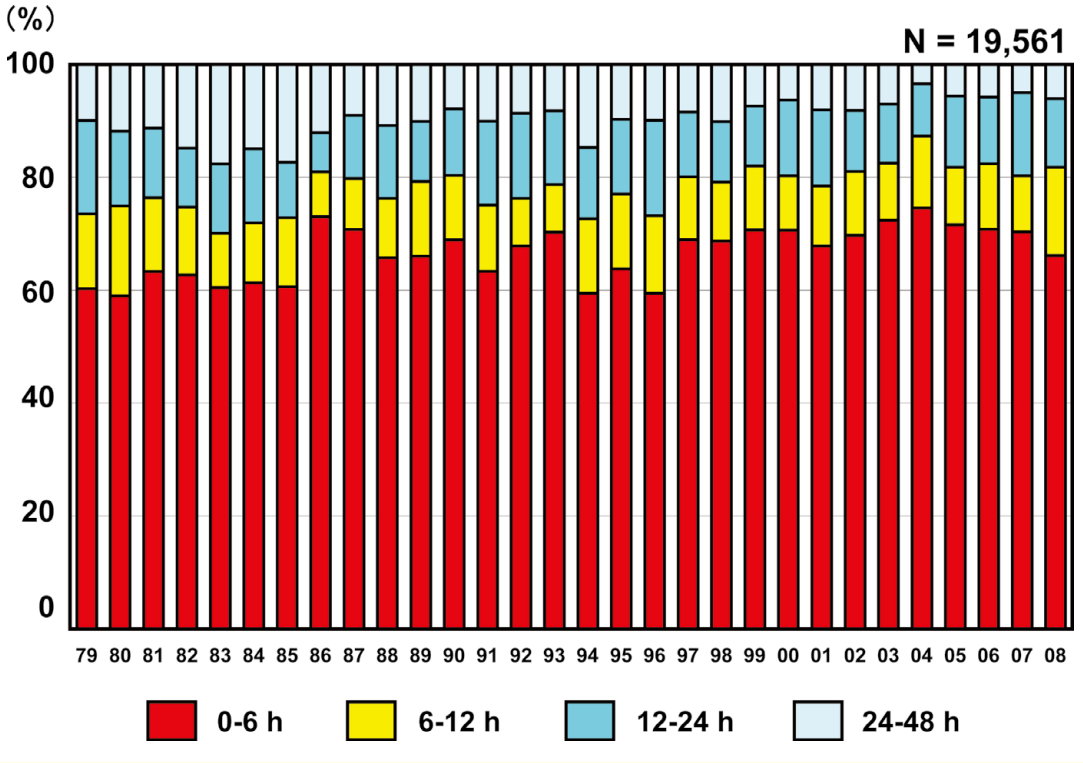

Figure 7. Time interval from the onset of symptoms to admission shows no change.

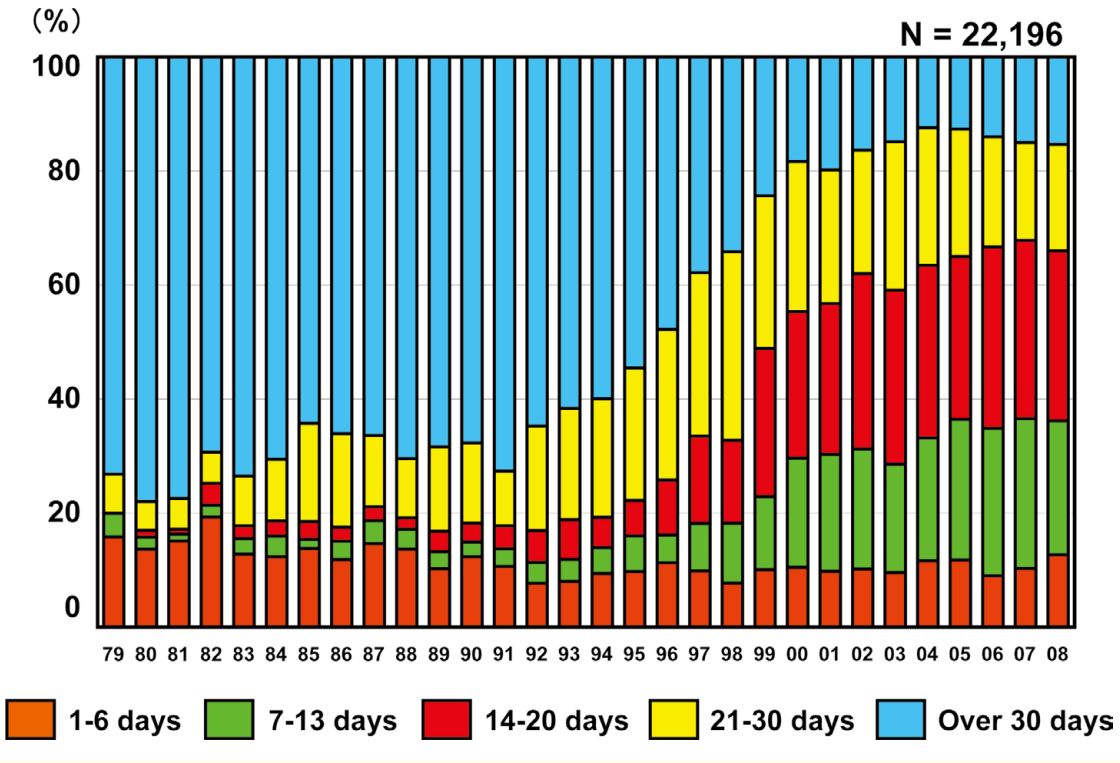

Figure 8. Hospitalization for acute myocardial infarction has been dramatically shortened.

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.[4,13,14] Their results were conflicting as they reported either a declining or flattened[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)[5] and the Niigata and Nagaoka study (males 41.9 vs females 5.3 in 1994–1996).[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.[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.[16] These findings indicate the urgent need for evidence-based management strategies applicable to increas-

ingly elderly AMI patients.[17]

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.[18–20] The present study demonstrates that the control of major coronary risk factors is still insufficient in Japan (**Figure 3**), 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.[21,22]

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 (**Figure 5**). A similar trend has been reported from the American Heart Association Heart Disease and Stroke Statistics.[23] 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,[24] 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.[25] 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[26] and Western countries.[27,28] 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 (**Figure 4**). 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,[29] 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 (**Figure 8**), during which the paradigm of AMI management has shifted from a conservative strategy to an interventional strategy.[30] In fact, in the present study, use of primary PCI has been increasing from 20% in 1992 to ~80% in 2008 (**Figure 6**), 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.[8,9]

Currently, approximately half of AMI patients in the Western countries are transported to hospital by ambulance.[31,32] The present study demonstrated the ambulance use in Japan has increased to ~70% in the past 10 years (**Figure 5**). Because the majority of AMI patients in the past 30 years were hospitalized within 6 h (**Figure 7**), 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.[33] For surviving AMI patients, it is important to understand the underlying risk factors that lead to secondary cardiac events.[34] Indeed, a more effective strategy to improve the management of post-infarction heart failure needs to be developed.[33,34]

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.

Acknowledgments

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References

1. The American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statics 2009 Update: A Report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 2009; **119:** e21–e181.
2. Yamada M, Wong FL, Kodama K, Sasaki H, Shimaoka K, Yamakido M. Longitudinal trends in total serum cholesterol levels in a Japanese cohort, 1958–1986. *J Clin Epidemiol* 1997; **50:** 425–434.
3. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project: Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation* 1994; **90:** 583–612.
4. Kinjo K, Kimura Y, Shinzato Y, Tomori M, Komine Y, Kawazoe N, et al. Incidence of stroke and acute myocardial infarction in subtropical islands, Okinawa, Japan. *Am J Hypertens* 1991; **4:** 793.
5. Rumana N, Kita Y, Turin TC, Murakami Y, Sugihara H, Morita Y, et al. Trend of increase in the incidence of acute myocardial infarction in a Japanese population: Takashima AMI Registry, 1990–2001. *Am J Epidemiol* 2008; **167:** 1358–1364.
6. Tanabe N, Saito R, Sato T, Hayashi S, Toyoshima H, Seki N, et al. Event rates of acute myocardial infarction and coronary deaths in Niigata and Nagaoka cities in Japan. *Circ J* 2003; **67:** 40–45.
7. Tanizaki Y, Kiyohara Y, Kato I, Iwamoto H, Nakayama K, Shinohara N, et al. Incidence and risk factors for subtypes of cerebral infarction in a general population: The Hisayama Study. *Stroke* 2000; **31:** 2616–2622.
8. Watanabe J, Iwabuchi K, Koseki Y, Fukuchi M, Shinozaki T,

Miura M, et al. Declining trend in the in-hospital case-fatality rate from acute myocardial infarction in Miyagi Prefecture from 1980 to 1999. *Jpn Circ J* 2001; **65:** 941–946.
9. Sakurai K, Watanabe J, Iwabuchi K, Koseki Y, Kon-no Y, Fukuchi M, et al. Comparison of the efficacy of reperfusion therapies for early mortality from acute myocardial infarction in Japan: Registry of Miyagi Study Group for AMI (MsAMI). *Circ J* 2003; **67:** 209–214.
10. Ministry of Public Management, Home Affairs, Posts, and Telecommunications of Japan. 2000 population census of Japan. Tokyo, Japan: Statistical Bureau, Ministry of Public Management, Home Affairs, Posts, and Telecommunications, Government of Japan, 2001 (in Japanese).
11. Fonarow GC, Heywood JT, Heidenreich PA, Lopatin M, Yancy CW; ADHERE Scientific Advisory Committee and Investigators. Temporal trends in clinical characteristics, treatments, and outcomes for heart failure hospitalizations, 2002 to 2004: Findings from Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J* 2007; **153:** 1021–1028.
12. Fox KA, Steg PG, Eagle KA, Goodman SG, Anderson FA Jr, Granger CB, et al; GRACE Investigators. Decline in rates of death and heart failure in acute coronary syndromes, 1999–2006. *JAMA* 2007; **297:** 1892–1900.
13. Kodama K, Sasaki H, Shimizu Y. Trend of coronary heart disease and its relationship to risk factors in a Japanese population: A 26-year follow-up, Hiroshima/Nagasaki study. *Jpn Circ J* 1990; **54:** 414–421.
14. Shimamoto T, Komachi Y, Inada H, Doi M, Iso H, Sato S, et al. Trends for coronary heart disease and stroke and their risk factors in Japan. *Circulation* 1989; **79:** 503–515.
15. Sekikawa A, Ueshima H, Kadowaki T, El-Saed A, Okamura T, Takamiya T, et al. Less subclinical atherosclerosis in Japanese men in Japan than in White men in the United States in the post-World War II birth cohort. *Am J Epidemiol* 2007; **165:** 617–624.
16. Masoudi FA, Foody JM, Havranek EP, Wang Y, Radford MJ, Allman RM, et al. Trends in acute myocardial infarction in 4 US states between 1992 and 2001: Clinical characteristics, quality of care, and outcomes. *Circulation* 2006; **114:** 2806–2814.
17. Peterson PN, Masoudi FA. Cardiovascular disease and the elderly: Can the evidence base avoid irrelevance? *Eur Heart J* 2007; **28:** 1277–1278.
18. Kuulasmaa K, Tunstall-Pedoe H, Dobson A, Fortmann S, Sans S, Tolonen H, et al. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. *Lancet* 2000; **355:** 675–687.
19. Nakamura T, Tsubono Y, Kameda-Takemura K, Funahashi T, Yamashita S, Hisamichi S, et al. Group of the Research for the Association between Host Origin and Atherosclerotic Diseases under the Preventive Measure for Work-related Diseases of the Japanese Labor Ministry: Magnitude of sustained multiple risk factors for ischemic heart disease in Japanese employees: A case–control study. *Jpn Circ J* 2001; **65:** 11–17.
20. Nakamura Y, Yamamoto T, Okamura T, Kadowaki T, Hayakawa T, Kita Y, et al; The NIPPON DATA 80 Research Group. Combined cardiovascular risk factors and outcome: NIPPON DATA80, 1980–1994. *Circ J* 2006; **70:** 960–964.
21. Ueshima H. Explanation for the Japanese paradox: Prevention of increase in coronary heart disease and reduction in stroke. *J Atheroscler Thromb* 2007; **14:** 278–286.
22. Japan health promotion and fitness foundation. http://www.health-net.or.jp/tobacco/product/pd100000.html (accessed 21 August, 2009).
23. American Heart Association. 2004 Statistical Fact Sheet. http://www.americanheart.org/downloadable/heart/1136818052118Females06.pdf (accessed 21 August, 2009).
24. Gan SC, Beaver SK, Houck PM, MacLehose RF, Lawson HW, Chan L. Treatment of acute myocardial infarction and 30-day mortality among women and men. *N Engl J Med* 2000; **343:** 8–15.
25. Malenka DJ, O'Rourke D, Miller MA, Hearne MJ, Shubrooks S, Kellett MA Jr, et al. Cause of in-hospital death in 12,232 consecutive patients undergoing percutaneous transluminal coronary angioplasty: The Northern New England Cardiovascular Disease Study Group. *Am Heart J* 1999; **137:** 632–638.
26. Kinjo K, Sato H, Sato H, Shiotani I, Kurotobi T, Ohnishi Y, et al; Osaka Acute Coronary Insufficiency Study (OACIS) Group. Circadian variation of the onset of acute myocardial infarction in the Osaka area, 1998–1999: Characterization of morning and nighttime peaks. *Jpn Circ J* 2001; **65:** 617–620.
27. Ridker PM, Manson JE, Buring JE, Muller JE, Hennekens CH. Circadian variation of acute myocardial infarction and the effect of low-dose aspirin in a randomized trial of physicians. *Circulation* 1990; **82:** 897–902.
28. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Morning peak in the incidence of myocardial infarction: Experience in the ISIS-2 trial. *Eur Heart J* 1992; **13:** 594–598.
29. Stone PH, Raabe DS, Jaffe AS, Gustafson N, Muller JE, Turi ZG, et al. Prognosis significance of location and type of myocardial infarction: Independent adverse outcome associated with anterior location. *J Am Coll Cardiol* 1988; **11:** 453–463.
30. Kohro T, Hayashi D, Okada Y, Yamazaki T, Nagai R, JCAD Investigators. Demographics and changes in medical/interventional treatment of coronary artery disease patients over a 3.5-year period in Japan: The Japanese Coronary Artery Disease Study: Trend examination. *Circ J* 2008; **72:** 1397–1402.
31. Canto JG, Zalenski RJ, Ornato JP, Rogers WJ, Kiefe CI, Magid D, et al, National Registry of Myocardial Infarction 2 Investigators. Use of emergency medical services in acute myocardial infarction and subsequent quality of care: Observations from the National Registry of Myocardial Infarction 2. *Circulation* 2002; **106:** 3018–3023.
32. So DY, Ha AC, Turek MA, Maloney JP, Higginson LA, Davies RF, et al. Comparison of mortality patterns in patients with ST-elevation myocardial infarction arriving by emergency medical services versus self-transport (from the prospective Ottawa Hospital STEMI Registry). *Am J Cardiol* 2006; **97:** 458–461.
33. Shiba N, Shimokawa H. Chronic heart failure in Japan: Implications of the CHART studies. *Vasc Health Risk Manag* 2008; **4:** 103–113.
34. Takeno M, Yasuda S, Otsuka Y, Morii I, Kawamura A, Yano K, et al. Impact of metabolic syndrome on the long-term survival of patients with acute myocardial infarction: Potential association with C-reactive protein. *Circ J* 2008; **72:** 415–419.

Appendix 1

List of Participating Hospitals

Fukaya Hospital, Hiroshi Akiho, MD; Hikarigaoka Spellman Hospital, Tomofumi Mimata, MD; Ishinomaki Municipal Hospital, Kenjirou Akai, MD; Ishinomaki Red-Cross Hospital, Hiroyasu Sukegawa, MD; JR Sendai Hospital, Masao Kuroha, MD; Katta General Hospital, Hiroyuki Kanno, MD; Kesen-numa Hospital, Kazunori Ogata, MD; Kurihara Central Hospital, Seiji Komatsu, MD; Tohoku Rosai Hospital, Tatsuya Komaru, MD; Marumori National Health Insurance Hospital, Masataka 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, Hidetoshi Mitobe, MD; Nishitaga National Hospital, Shigenori Kitaoka, MD; NTT EAST Tohoku Hospital, Aki Yamada, MD; Oizumi Memorial Hospital, Yoshirou Koiwa, MD; Osaki Citizen 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-ya Fujii, MD; Sendai City Hospital, Tetsuo Yagi, MD; Sendai Kosei Hospital, Taiichirou 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 Konno, MD; Sendai Tokushukai Hospital, Kimihiko Ogata, MD; Sen-en General Hospital, Ryouichi Hashiguchi, MD; Shichigashuku National Health Insurance Clinic, Takahiro Nagashima, MD; Shiogama City Hospital, Jun Goto, MD; South Miyagi Medical Center, Kan-ichi Inoue, MD; Tohoku Kosai Hospital, Mitsumasa Fukuchi, MD; Tohoku 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, Yoshiaki Katahira, MD; Tome Public Hospital, Munehiko Ishii, MD.