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# Urbanization, Life Style Changes and the Incidence/In-Hospital Mortality of Acute Myocardial Infarction in Japan

## – Report From the MIYAGI-AMI Registry Study –

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***Background:*** It remains to be examined whether urbanization and lifestyle changes are associated with the incidence and mortality from acute myocardial infarction (AMI) in Japan.

***Methods and Results:*** A total of 19,921 AMI patients (male/female 14,290/5,631) registered by the MIYAGI-AMI Registry Study from 1988 to 2009 were divided into 2 groups according to their residences; inside (urban area, n=7,316) and outside (rural area, n=11,402) of Sendai City. From 1988 to 2009, the incidence of AMI (/100,000 persons/year) increased more rapidly in the rural area (24.2 to 51.4) than in the urban area (31.3 to 40.8) (P<0.001), with rapid aging in both areas. Moreover, from 1998 to 2009, the age-adjusted incidence of AMI in young (<44 years) and middle-aged (45–64 years) male patients (both P<0.05) in the rural area increased significantly, along with a markedly increased prevalence of dyslipidemia (P<0.001). Although in-hospital mortality from AMI decreased in both areas over the last 20 years (both P<0.001), it remained relatively higher in female than in male patients and was associated with higher age of the onset, longer elapsing time for admission and lower prevalence of primary coronary intervention in female patients in both areas.

***Conclusions:*** These results demonstrate that urbanization and lifestyle changes have been associated with the incidence and mortality from AMI, although sex differences still remain to be improved. (*Circ J* 2012; **76:** 1136–1144)

**Key Words:** Acute myocardial infarction; Aging; Life-style; Risk factors; Sex

The incidence and mortality from coronary artery disease (CAD) has been declining in the United States and European countries.[1–4] These declines have been attributed to the control of risk factors (eg, hypertension, dyslipidemia and smoking) and the improvement in critical care (eg, coronary revascularization therapy).[5–7] In contrast to the Western countries, in Japan, a highly developed and racially homogeneous country that is rapidly aging, total cholesterol levels and the prevalence of obesity have been increasing as a result of lifestyle Westernization influence since the 1960 s.[8,9] However, the mortality from CAD has been declining and has remained much lower compared with other Western countries from 1960 to 2000.[9–11] Importantly, there are some differences in lifestyle between people living in rural and urban areas in Japan. Indeed, it was reported that people in urban areas had greater intakes of fat and cholesterol than those in rural areas in Japan.[8] However, only a few studies have previously addressed the difference in the incidence and mortality from CAD between the rural and urban areas in Japan.[8,12]

In order to explore the annual trend for acute myocardial infarction (AMI) in Japan, we have been conducting the MIYAGI-AMI Registry Study for more than 30 years since 1979, where almost all AMI patients in the Miyagi prefecture have been prospectively registered.[10,13,14] The Miyagi prefecture, which is located in northeastern Japan, includes Sendai City, one of the 19 government-designed cites, and has a typical balance of urban and rural areas in Japan. Sendai City merged with neighboring municipalities in 1987–1988 and the population of Sendai City increased to 1,008,130 in 2000, which accounted for approximately 40% of the population of

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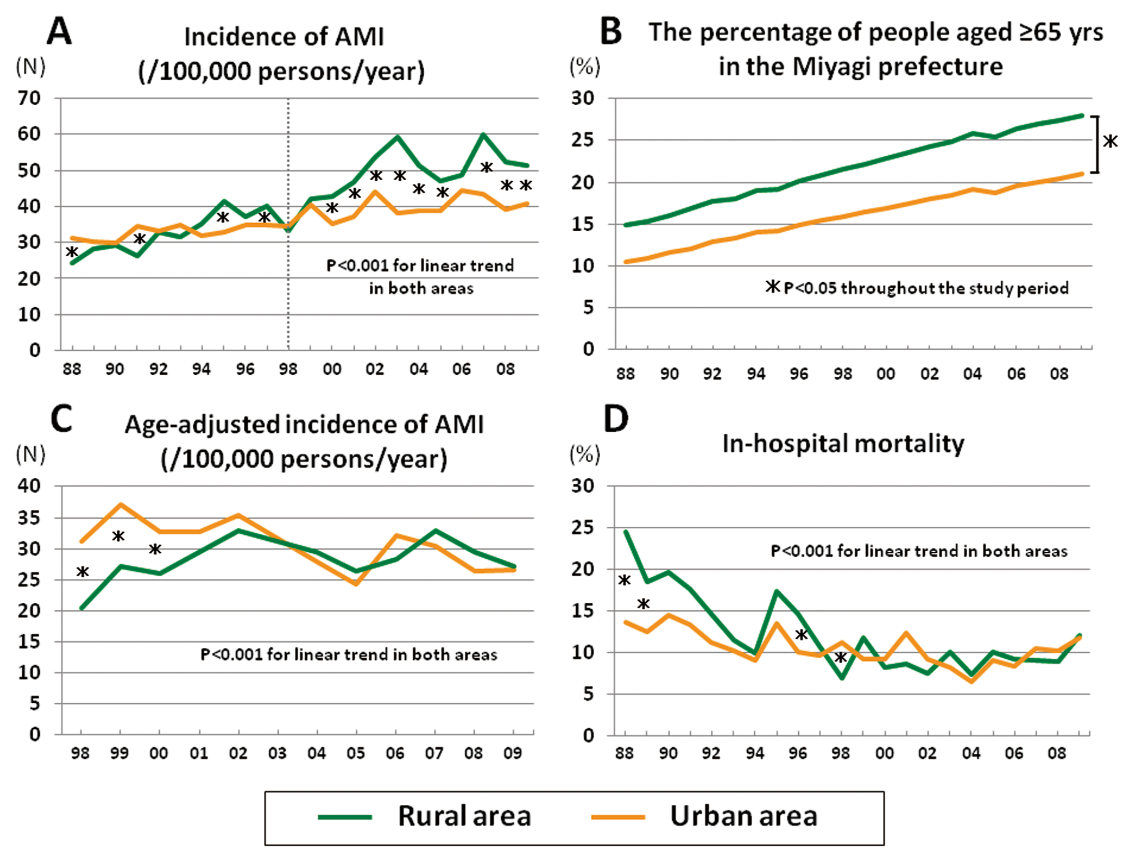


**Figure 1.** The 20-year trend of acute myocardial infarction (AMI) in the Miyagi prefecture. (**A**) The incidence of AMI (/100,000 persons/year) has significantly increased in both areas (both P<0.001) with a greater extent in the urban area over the last 20 years, accompanied with rapid aging in both areas (**B**). (**C**) The age-adjusted incidence of AMI (/100,000 persons/year) in the rural area increased significantly (P<0.001), whereas that in the urban area decreased significantly (P<0.001) in the recent 10 years (between 1998 and 2009). (**D**) In-hospital mortality (%) decreased and remained at a low level in the past 10 years in both areas. *P<0.05 for the difference between the rural and the urban areas.

the Miyagi prefecture, which was 2,365,320 in 2000. The population density of Sendai City (1,279/km$^2$ in 2000) has been much higher than that of any other parts of the Miyagi prefecture (209/km$^2$ in 2000).[15]

In the present study, we examined whether urbanization and lifestyle changes were associated with the incidence and mortality from AMI, with special reference to the difference between the urban and rural areas in our MIYAGI-AMI Registry Study.

## Methods

### The MIYAGI-AMI Registry Study

The MIYAGI-AMI Registry Study is a prospective, multicenter and observational study. As previously reported,[10,13,14] this registry was established in 1979 and all 43 hospitals with a coronary care unit and/or cardiac catheterization facility in the Miyagi prefecture have been participating (**Appendix 1**). In the Miyagi prefecture, almost all AMI patients are transferred to one of those participating hospitals via the emergency medical service. 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.

In the MIYAGI-AMI Registry Study, the diagnosis of AMI and decision to use reperfusion therapy were made by individual cardiologists in charge. Diagnosis of AMI was made based on the WHO-MONICA criteria.[16] Briefly, it was based on the finding of typical severe chest pain accompanied by abnormal ECG changes and increased serum levels of cardiac enzymes (ie, creatine phosphokinase, aspartate amino transferase and lactate dehydrogenase). Coronary 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 urokinase (maximum 960×10$^3$ IU) or alteplase (maximum 6.4×10$^6$ IU). Rescue percutaneous coronary intervention (PCI) was performed when thrombolysis was unsuccessful. Primary PCI has been widely performed in the Miyagi prefecture since 1992, as reported previously.[10,13,14]

The registration form of the MIYAGI-AMI Registry includes 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 and/or PCI), and in-hospital outcome (eg, in-hospital mortality). In our MIYAGI-AMI Registry Study, we have revised the registra-

**Table. Clinical Characteristics and Outcome of the Study Population**

| | Rural area | | | P value for trend | Urban area | | | P value for trend |
|---|---|---|---|---|---|---|---|---|
| | 1998–2001 (n=2,145) | 2002–2005 (n=2,699) | 2006–2009 (n=2,807) | | 1998–2001 (n=1,529) | 2002–2005 (n=1,508) | 2006–2009 (n=1,682) | |
| **Male** | | | | | | | | |
| Age (years) | 66.2±12.4* | 67.0±12.9* | 66.7±12.7 | 0.373 | 65.0±12.7 | 65.2±12.9 | 65.9±12.9 | 0.046 |
| Age-adjusted incidence of AMI (/$10^5$ persons/year) | | | | | | | | |
| All | 42.3±3.8* | 47.2±3.2 | 47.3±2.5 | 0.274 | 55.1±4.7 | 49.3±10.9 | 47.9±4.1 | 0.163 |
| <45 years old | 4.9±0.9 | 5.8±0.7 | 6.9±1.2 | 0.018 | 5.1±0.7 | 5.7±0.5 | 6.0±2.7 | 0.460 |
| 45–64 years old | 66.6±6.3* | 83.2±5.5 | 88.9±14.9 | 0.016 | 91.2±4.9 | 85.9±21.0 | 83.7±8.2 | 0.402 |
| 65–74 years old | 170.2±32.9 | 186.3±39.2 | 179.3±17.8 | 0.679 | 228.2±18.1 | 208.1±56.3 | 180.1±15.6 | 0.065 |
| ≥75 years old | 253.5±47.0* | 261.1±62.9 | 250.8±33.4 | 0.937 | 355.0±48.0 | 277.8±73.4 | 308.0±19.7 | 0.207 |
| Hypertension (%) | 46.1 | 59.5* | 60.9 | <0.001 | 48.2 | 54.3 | 63.0 | <0.001 |
| Diabetes mellitus (%) | 27.5 | 32.9 | 29.5* | 0.265 | 30.6 | 31.6 | 34.1 | 0.070 |
| Dyslipidemia (%) | 22.4* | 34.1* | 41.4 | <0.001 | 32.2 | 39.0 | 42.0 | <0.001 |
| Smoking (%) | 40.6 | 42.1 | 40.6 | 0.956 | 44.0 | 41.8 | 38.6 | 0.008 |
| In-hospital mortality (%) | 7.6 | 6.8 | 7.8 | 0.832 | 8.8 | 5.7 | 8.7 | 0.997 |
| **Female** | | | | | | | | |
| Age (years) | 74.1±9.7 | 76.1±11.1 | 75.3±11.4 | 0.017 | 74.4±10.4 | 74.6±12.0 | 75.3±11.4 | 0.224 |
| Age-adjusted incidence of AMI (/$10^5$ persons/year) | | | | | | | | |
| All | 11.5±2.4* | 13.6±1.1 | 13.2±1.0 | 0.202 | 15.1±1.2 | 11.9±2.0 | 12.4±2.4 | 0.077 |
| <45 years old | 0.2±0.4 | 0.4±0.2 | 0.7±0.5 | 0.114 | 0.2±0.2 | 0.5±0.3 | 0.5±0.7 | 0.297 |
| 45–64 years old | 10.5±4.2 | 13.7±3.1 | 18.1±4.1 | 0.102 | 10.1±1.6 | 11.0±2.2 | 16.1±7.1 | 0.102 |
| 65–74 years old | 54.5±1.8* | 65.0±8.4 | 56.4±4.4 | 0.602 | 84.5±5.8 | 55.3±6.5 | 48.9±9.1 | <0.001 |
| ≥75 years old | 100.8±17.4* | 135.7±14.9 | 120.8±7.9 | 0.076 | 165.9±13.9 | 131.4±19.4 | 129.8±17.2 | 0.016 |
| Hypertension (%) | 55.8 | 69.3 | 67.5 | <0.001 | 60.2 | 63.5 | 65.0 | 0.137 |
| Diabetes mellitus (%) | 29.3 | 36.1 | 35.1 | 0.032 | 32.5 | 33.2 | 34.5 | 0.510 |
| Dyslipidemia (%) | 25.8 | 30.9 | 38.6 | <0.001 | 31.0 | 37.1 | 37.7 | 0.039 |
| Smoking (%) | 8.9 | 6.6* | 10.6 | 0.163 | 12.1 | 13.4 | 14.1 | 0.383 |
| In-hospital mortality (%) | 12.3 | 11.1 | 14.5 | 0.254 | 14.4 | 15.3 | 14.1 | 0.892 |

Values are mean±SD or n (%). *P<0.05 for the difference between rural and urban areas. AMI, acute myocardial infarction.
Study population was divided into 2 groups according to the residence: inside (urban area) and outside Sendai City (rural area).

tion form gradually over the last 30 years. Thus, although the incidence of AMI and related data (time of onset, age and sex) are available for the last 30 years, the date on the pre-hospital management, infarction site, coronary risk factors, reperfusion therapies, duration of hospitalization and in-hospital outcome are only available for the last 10–20 years, which were analyzed in the present study.

## Data Analysis

In the present study, we have registered a total of 19,921 patients with AMI (male/female 14,290/5,631) over the last 20 years after the municipal merger in 1988. In particular, we have focused on the patients registered between 1998 and 2009 (total, 12,491; male/female, 8,969/3,522), who were divided into 2 groups according to their residences; inside (urban area, n=4,719) and outside Sendai City (rural area, n=7,651), after excluding the patients whose residences were unknown (n=159). We also divided the total observational period of 12 years into the 3 periods: 1998–2001, 2002–2005 and 2006–2009. To calculate the sex- and age-adjusted incidence of AMI (/100,000 person/years), we applied the direct standardization method using the age distribution of the Japanese population from the 2000 census,[5] as the standard population. In addition, in order to clarify the age-specific trend, we categorized the age at AMI onset into the 4 groups: ≤44 (young), 45–64 (middle-aged), 65–74 (old) and ≥75 years old (high-old).[15]

Results are expressed as mean±SD. Linear trends were examined for continuous variables by using analysis of variance (ANOVA) with repeated measures or the Jonckheere-Terpstra trend test as appropriate, and for categorical variables by using the chi-square test for trend. Differences in mean values were examined with a t-test, Mann-Whitney test or chi-square test as appropriate. Multiple logistic regression analysis was used to examine determinants of risk factor prevalence in AMI patients. Variables used for analysis included: sex, age at onset of AMI (per 10 years), study periods (1998–2001, 2002–2005 and 2006–2009), residence (rural vs. urban), and other risk factors. The odds ratios (ORs) and 95% confidence intervals (95%CI) were calculated. A P-value less than 0.05 were considered to be statistically significant. All statistical analyses were performed using the statistical software SPSS version 18 for Windows.

# Results

Over the last 20 years, the incidence of AMI (/100,000 persons/year) significantly increased in both the rural and the urban areas in the Miyagi prefecture (2.1- and 1.3-fold, respectively, both P<0.001) (Figure 1A). Furthermore, the extent of the increase in AMI incidence was greater in the rural area than in the urban area, finally exceeding that in the urban area after 2000. These changes were accompanied with rapid aging

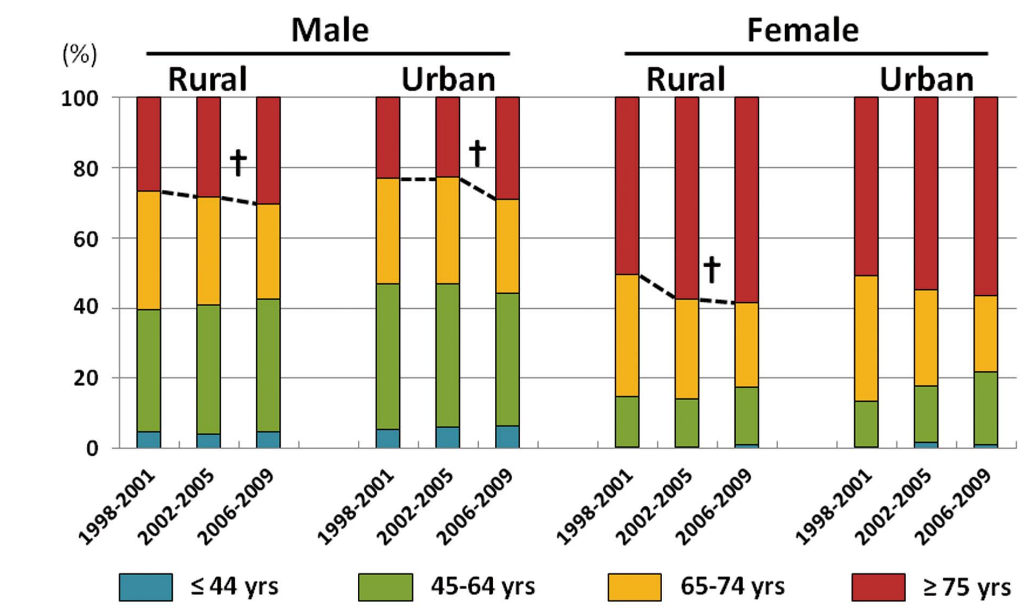


**Figure 2.** Age-distribution of acute myocardial infarction (AMI) patients. The percentage of high-old patients (≥75 years old) was markedly higher in female patients than in the patients in the rural and urban areas and has been increasing significantly in male patients in both areas and rural female patients. †P<0.05 for linear trend.

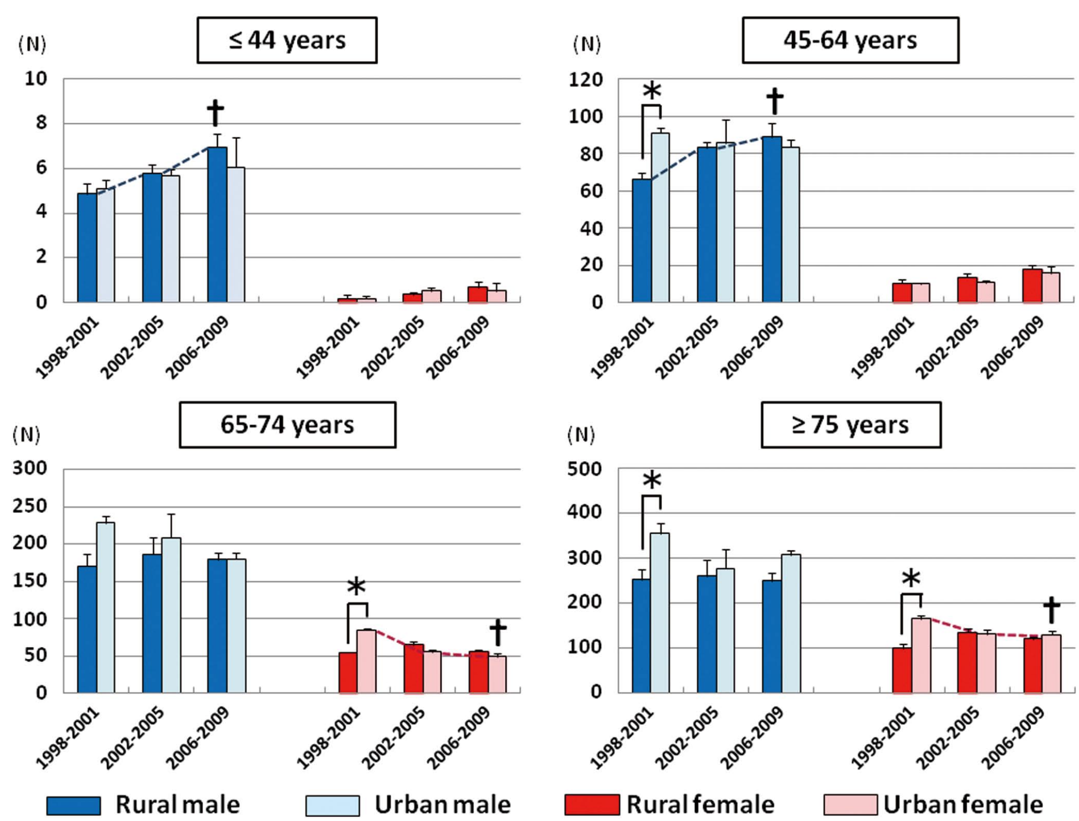


**Figure 3.** Age-specific incidence of acute myocardial infarction (AMI) (/100,000 persons/year). The significant increase in the age-adjusted incidence of AMI was noted in <44 and 45–64 year old rural male patients, and the significant decrease was noted in 65–74 and >75 year old urban female patients. Values are presented as mean±SE. *P<0.05 for the difference between rural and urban areas. †P<0.05 for linear trend.

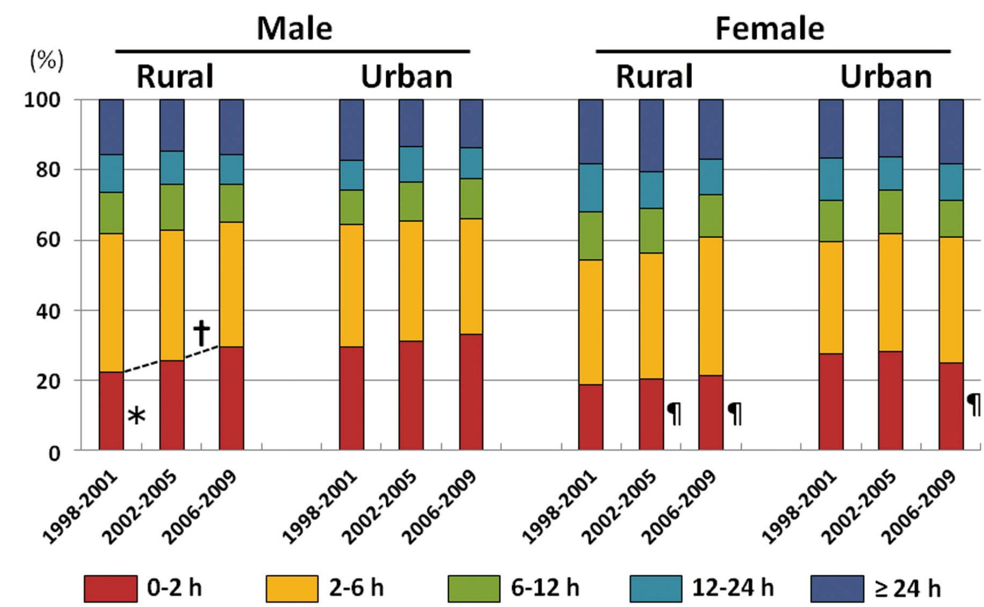


**Figure 4.** Time interval from the onset of symptoms to hospitalization. The percentage of patients with less than 2h of elapsing time for hospitalization has significantly increased in rural male patients. The percentage was significantly lower in female patients than in male patients in both areas in 2006–2009. *P<0.05 for the difference between rural and urban areas. ¶P<0.05 for the difference between the sexes in the same rural or urban areas. †P<0.05 for a linear trend.

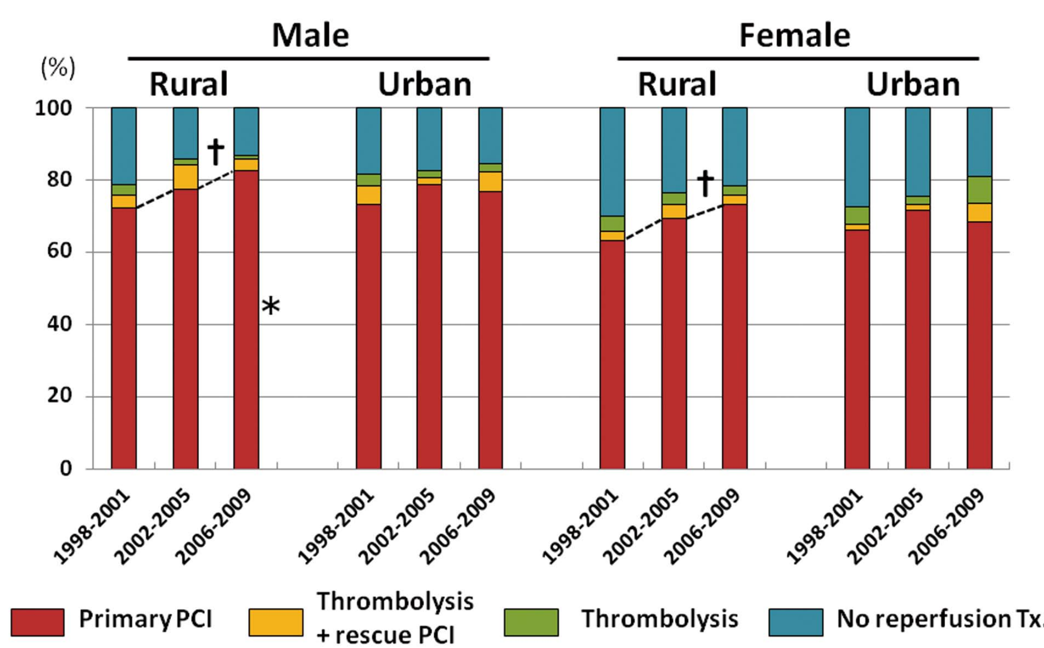


**Figure 5.** Prevalence of reperfusion therapy for acute myocardial infarction (AMI). The prevalence of primary percutaneous coronary intervention (PCI) steadily increased in the rural area in both sexes. Importantly, the prevalence of PCI was approximately 10% lower in female patients than in male patients in both rural and urban areas. *P<0.05 for the difference in male patients between rural and urban areas. †P<0.05 for linear trend.

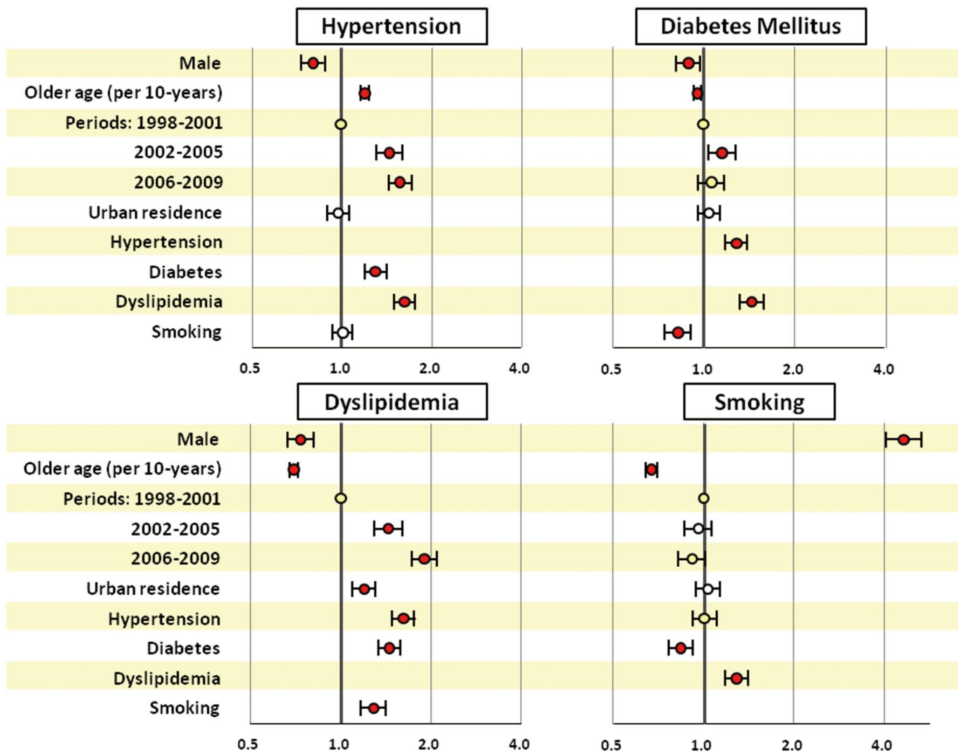


**Figure 6.** Multivariate analysis of coronary risk factors in acute myocardial infarction (AMI) patients. During the study periods, the prevalence of hypertension and dyslipidemia significantly increased in AMI patients. Hypertension was associated with older age but not with residence, whereas dyslipidemia was associated with younger age and urban residence. Smoking was associated with male sex and younger age. The odds ratios and 95% confidence intervals for factors are shown with red circles for P<0.05.

in both areas in the Miyagi prefecture (**Figure 1B**). Following age adjustment (**Figure 1C**), the incidence of AMI in the rural area increased significantly (P<0.001), whereas that in the urban area decreased significantly (P<0.001) in the recent 10-year period (between 1998 and 2009). In contrast, in-hospital mortality significantly decreased in both areas (both P<0.001), but to a greater extent in the rural area (0.5-fold in the rural area and 0.9-fold in the urban area) (**Figure 1D**). In 1998–2001, there was no significant difference in in-hospital mortality between the rural and urban male patients (P=0.263), and in-hospital mortality remained low (~8%) from 1998–2001 to 2006–2009 in both the rural and urban male patients (rural: P=0.832; urban: P=0.997) (**Table**). Importantly, in-hospital mortality of the female patients in both the rural and the urban areas remained doubled compared with the male patients during the study period (**Table**).

The clinical characteristics of the AMI patients in the present study are shown in **Table**. The female patients were approximately 10 years older than the male patients and approximately a half of them were ≥75 years-old in 1998–2001 in both areas, with a significant further increase in the rural area (male, P<0.001; female, P<0.001) and such a trend in the urban area (male, P=0.054; female, P=0.176) (**Figure 2**). In 1998–2001, the age-adjusted incidence of AMI was significantly lower in the rural area than in the urban area for both sexes (male, P=0.019; female, P=0.035) (**Table**). However, the difference between the 2 areas became insignificant in 2006–2009 for both sexes (male, P=0.824; female, P=0.530). When investigating the age-specific trend, the significant increase in the age-adjusted incidence of AMI was noted in the young (<44 years-old) and middle age (45–64 years-old) male patients only in the rural area (young, P=0.018; middle age, P=0.016), and the significant decrease was noted in the old (65–74 years-old) and high-old (>75 years-old) female patients in the urban area (old, P<0.001; high-old, P=0.016) (**Table**, **Figure 3**).

Regarding the time from the onset of AMI to admission, the percentage of the patients with less than 2h of elapsing time at admission was significantly lower in the rural area than in the urban area for the male patients in 1998–2001 (P<0.001) (**Figure 4**). However, the difference became insignificant in 2006–2009 (P=0.051), accompanied with the significant increase in the percentage in the rural area (rural, P<0.001; urban, P=0.082). Importantly, in the rural female patients, the percentage of patients with less than 2h of elapsing time at admission remained at a low level (~20%), and the difference between the sexes in the rural area became greater from 1998–2001 (P=0.086) to 2006–2009 (P<0.001). In contrast, the difference between the sexes in the urban area was significant in 2006–2009 (P=0.04). Moreover, the prevalence of primary PCI in the female patients was lower by ~10% compared with the male patients in both areas (**Figure 5**). In the male patients, the prevalence of primary PCI significantly increased only in the rural area from 1998–2001 to 2006–2009 (rural, P<0.001; urban, P=0.054), and a similar trend was also noted in the female patients (rural, P<0.001; urban, P=0.176).

Multivariate analysis of the coronary risk factors in AMI patients showed that the prevalence of hypertension and dys-

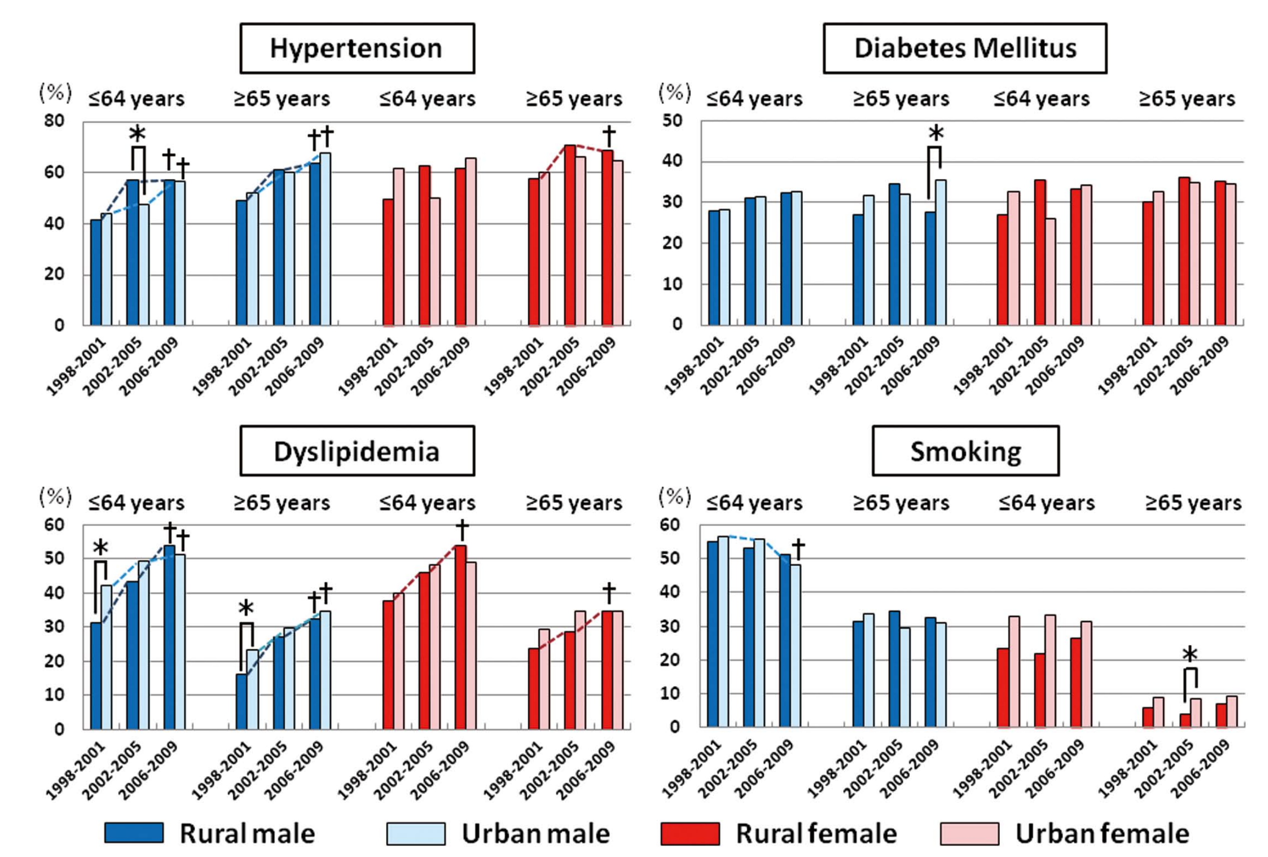


**Figure 7.** Prevalence of coronary risk factors in acute myocardial infarction (AMI) patients. The prevalence of hypertension and dyslipidemia had a trend of increase in both rural and urban areas. In particular, the prevalence of dyslipidemia in rural male patients aged ≤64 years markedly increased. *P<0.05 for the difference between rural and urban areas. †P<0.05 for linear trend.

lipidemia significantly increased and that of diabetes tended to increase (**Figure 6**). Hypertension was associated with older age but not with residence, whereas dyslipidemia was associated with younger age and urban residence. Although the prevalence of dyslipidemia in the male patients was significantly lower in the rural area than in the urban area in 1998–2001, it significantly increased in the rural area and the difference between the 2 areas became insignificant in 2006–2009 (**Table**). Moreover, the progressive increase in the prevalence of dyslipidemia was noted in both areas for both sexes with a more sharp increase in the rural area (**Figure 7**). Smoking was associated with male sex and younger age, but not with residence (**Figure 6**), and the prevalence of smoking largely remained unchanged in both areas for both sexes (**Figure 7**).

## Discussion

The novel findings of the present study were that the incidence of AMI increased more rapidly in the rural area than in the urban area, with rapid aging in both areas. Moreover, the incidence of AMI in the rural male patients ≤64 years-old was increased along with the marked increase in the prevalence of dyslipidemia in Japan. Although in-hospital mortality from AMI markedly decreased in both areas over the last 20 years, it remained relatively high in female patients than in male patients in both areas. To the best of our knowledge, this is the first study that demonstrates the association between urbanization, life-style changes and the incidence and mortality of AMI in the largest number of patients in Japan.

### Comparison of the Incidence of AMI Between Rural and Urban Areas

Although in the United States and European countries, the incidence of CAD has been declining in the last decades,[1,2,4] the present study demonstrates that the incidence of AMI has been rapidly increasing in both the rural and urban areas over the last 20 years, with a more noted increase in the former than in the latter. However, this tendency has disappeared following age adjustment in recent years only in the urban area, which implied that the increased tendency in the incidence of AMI in the rural area might be not be associated with rapid aging alone in recent years.

There were few studies that addressed the difference in the incidence of CAD between rural and urban areas in Japan. The Akita-Osaka study is the community-based survey, where the residents of the Yao City, Osaka prefecture (an urban community with a total census population of 23,552 in 2000) and those of Ikawa Town, Akita prefecture (a rural community with a total census population of 6,116 in 2000) were compared during the period of 1964–2003.[12] In this study, significant increases in the age-adjusted incidence of AMI and sudden cardiac death were noted in Yao City (in male patients from 1980 to 2003) but not in Ikawa City in both sexes.[12] The present study confirmed the results of the Akita-Osaka study in the rural and urban areas of the same Miyagi prefecture. The Yamagata AMI Registry study provided more recent data and an age-specific trend in the period of 1993–2007.[17] The population density of the Yamagata prefecture was 133/km² in 2000, which was comparable with that of the rural area in the present study.[15] In this study, the age-adjusted incidence of AMI in the male but not that in the female patients significantly increased. In particular, the male population who were younger than 65 years old showed a marked increase in AMI, a consistent finding with the present results for the rural area. These results indicate that the incidence of AMI has been increasing in the younger male population in the rural areas of Japan. Taken together, unlike the trend in Western countries, it appears that the incidence of AMI has been increasing in Japan to a greater extent in the rural area than in the urban area over the last 20 years and has been associated with rapid aging.

### Decreasing In-Hospital Mortality and Improvement in Critical Care

In the present study, the in-hospital mortality from AMI significantly decreased in both the urban and the rural areas over the last 20 years. The present study also demonstrates that primary PCI was performed more frequently in the rural area than in the urban area, along with the shortening in the elapsing time from the onset to hospitalization. The recent progress in critical care might have beneficial effects, overcoming the rapid aging in AMI patients.

In the most recent 10 year period, the in-hospital mortality remained at a low level in male patients, whereas in female patients, the mortality remained doubled compared with the male patients in both the rural and the urban areas. It was previously reported that the poorer outcome of the female AMI patients could be caused by multiple factors, including higher age, higher risk profiles, longer elapsing time from the onset to hospitalization, higher incidence of Killip class ≥2, and less frequent use of primary PCI.[18–20] Indeed, in the present study, the female patients were approximately 10 years older than the male patients and half of them were older than 75 years and needed a longer time from the onset of AMI to hospitalization in the both areas in 2006–2009. These points might have limited the use of primary PCI with a resultant poor outcome for the female AMI patients in the present study.

### Changes in the Prevalence of Coronary Risk Factors in AMI Patients

The WHO-MONICA studies, as well as several Japanese cohort studies, demonstrated that the incidence of cardiovascular diseases increased and were associated with the clustering of risk factors.[21–23] In the present study, the prevalence of hypertension and dyslipidemia in AMI patients significantly increased in both the rural and urban areas. Importantly, there was a significant difference in the prevalence of dyslipidemia between the rural and urban areas with a marked increase noted in the rural area, especially in those male patients aged ≤64 years. Indeed, previous studies demonstrated that dyslipidemia is an independent risk factor in male but not in female patients,[17,24] and in the Yamagata-AMI Registry study, the increased prevalence of dyslipidemia in the younger male patients with AMI was also associated with an increased incidence of AMI.[17] In the Miyagi prefecture, the intake of animal fat was significantly higher in the rural than in the urban area in 2000 (rural 20.7 g/day vs. urban 23.4 g/day, P<0.05).[25] Moreover, in Japan, fat intake and serum levels of total cholesterol were higher in the urban than in the rural areas in 1966; however, the difference in cholesterol levels between the 2 areas became smaller in 1966–1985 along with the influence of Westernization of food habits in the rural area.[8] Taken together, it might indicate that the increase in the incidence of AMI in younger male patients in the rural area was likely to be associated with the marked increase in the prevalence of dyslipidemia.

The present study also demonstrates the increase in the prevalence of hypertension in AMI patients. In the Tohoku district, including the Miyagi prefecture, the prevalence of hypertension was relatively higher compared with other parts of Japan,[12,26] and thus more careful and strict control of risk factors is needed.

The prevalence of smoking remained high not only in the urban areas but also in the rural areas. In particular, in the younger male patients, the prevalence of smoking (~50%) was higher compared with the general Japanese population (36.8% in males and 9.1% in females in 2008).[27] Importantly, in the younger urban female patients, it remained more than 30%; 3 times higher than in the general Japanese population.

### Study Limitations

Several limitations should be mentioned for the present study. First, although in the Miyagi prefecture, almost all AMI patients are transferred to our participating hospitals via the established emergency medical system, we cannot completely confirm that all patients have been registered in our registry. Second, while the MIYAGI-AMI Registry Study has been conducted over 20 years, the diagnosis of AMI has been changing.[28] In the present study, the diagnosis was made on the basis of the WHO-MONICA criteria with creatine kinase (CK).[16] Indeed, troponins are widely used in recent clinical practice and are more sensitive and specific biomarkers of myocyte necrosis than CK,[29] which might affect the results. Third, this study is an observational study and cannot reach the cause-effect relationship. Moreover, we did not examine the prevalence of risk factors in control subjects and did not collect the data of medical treatment for prevention, thus we were unable to precisely estimate the influence of risk factors on the incidence of AMI. Finally, in the present study, we did not examine the long-term mortality but only examined in-hospital mortality. The increasing incidence of decreasing in-hospital mortality from AMI in the Japanese population has apparently resulted in the recent increase in the number of patients with ischemic heart failure, as recently demonstrated in our heart failure cohort study, the CHART-1 and the CHART-2 studies.[30,31] Thus, 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 urbanization and life-style changes have been associated with the incidence and mortality of AMI in Japan, although sex differences still remain to be improved.

### Acknowledgments

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