Trends in Coronary Risk Factors Among Patients with Acute Myocardial Infarction Over the Last Decade: The Yamagata AMI Registry

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Aim: Recently, there has been an increase in the prevalence of coronary risk factors, such as diabetes and dyslipidemia, in Japan; however, it is unclear whether this has resulted in an increased incidence of acute myocardial infarction (AMI). We investigated the relationship between risk factors changes and AMI incidence in a Japanese population.

Methods: Trends in AMI incidence (per 100,000 person-years) were examined using data from the Yamagata AMI Registry from 1993 to 2007. We included 6,222 patients with a first-ever AMI (4175 men). The prevalence of coronary risk factors was investigated in three age groups of AMI patients (<65, 65−74, and ≥75 years) for the periods 1993−1997, 1998−2002, and 2003−2007. Coronary risk factors were further compared between recently registered AMI patients and 2,400 age-matched controls.

Results: The age-adjusted incidence of AMI increased significantly in men, but not in women. Younger men particularly showed a significant increase in the incidence of AMI. The prevalence of hypertension and diabetes increased in both genders; however, the prevalence of treatment for risk factors was significantly lower in men than women. Younger men showed significant increases in obesity and hypertriglyceridemia. Consequently, risk factors associated with the metabolic syndrome had accumulated among younger men. We revealed that hypertension, diabetes, hypercholesterolemia and current smoking were independent risk factors for AMI.

Conclusions: The incidence rate for AMI increased significantly in men, especially younger men. Preventive care for risk factors associated with metabolic syndrome, in addition to conventional risk factors, may be required in younger men.


Key words; Acute myocardial infarction, Coronary risk factor, Metabolic syndrome
changed; however, a recent AMI registry study from 1990 to 2001 reported that the age-adjusted incidence of AMI had increased by 7–8% annually.

Previous studies indicated differences in coronary risk factors between Western and Asian countries. A recent Japanese case-control study showed that hypercholesterolemia was an independent coronary risk factor in men, but not in women, and that obesity was not associated with AMI; however, there have been marked increases in the prevalence of obesity, diabetes mellitus and hypercholesterolemia, due to the westernization of dietary habits in Japan. Furthermore, metabolic syndrome has gained attention as a novel cardiovascular risk factor, and its prevalence is also reported to have increased in Japan. At present, there is little information on the relationship between recent changes in coronary risk factors and the incidence of AMI in Japan. In the present study, we investigated the trends in coronary risk factors among patients with a first-ever AMI who were registered between 1993 and 2007. The prevalence of risk factors was further compared between recently registered AMI patients and an age-matched general population.

**Methods**

**Study Population**

Yamagata Prefecture is located in the northern part of the main island of Japan. In the 2005 census, the population was 1,216,000 and the proportion of people ≥65 years old was higher than the average for Japan (25.5% vs. 20.1%). Since 1993, a multicenter project on the surveillance of AMI has been conducted as the Yamagata AMI Registry. The clinical characteristics of AMI patients admitted to all hospitals belonging to the Yamagata Medical Association between 1993 and 2007 were investigated. A diagnosis of AMI required that the “definite criteria of AMI”, as described in the World Health Organization MONICA Project, be satisfied. Of the 6,957 consecutive patients who were registered in Yamagata Prefecture from 1993 to 2007, 6,222 patients with a first-ever AMI were included in the present study. The observation period of 15 years was sub-divided into three intervals, 1993–1997 (n=1,827), 1998–2002, (n=1,999) and 2003–2007 (n=2,396). In addition, the enrolled patients were categorized into three groups by age at onset of AMI (younger, <65 years old; early elderly, 65–74 years old; late elderly, ≥75 years old).

**Data Collection**

Standard data were collected prospectively and entered into a computer database. These data included details of clinical presentation (age, gender, date and time of onset of AMI, time of admission to hospital), personal and family medical history, as well as coronary risk factors. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m²). Obesity was defined as BMI ≥25 kg/m² for both genders. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or current use of antihypertensive drugs. Hypercholesterolemia was defined as a serum total cholesterol concentration ≥220 mg/dL and/or current use of lipid-lowering drugs. Diabetes mellitus was defined as a fasting blood glucose concentration ≥126 mg/dL, a non-fasting blood glucose concentration ≥200 mg/dL, and/or the use of antidiabetic drugs (any oral hypoglycemic agent or insulin). A family history of CHD and current cigarette smoking status were verified by a self-reported questionnaire and by interviewing the family.

Fasting blood samples were obtained during hospitalization. Low-density lipoprotein (LDL) cholesterol concentrations were calculated using the Friedwald formula when the triglyceride concentration was 400 mg/dL or less. Hypertriglyceridemia was defined as a triglyceride concentration ≥150 mg/dL and low high-density lipoprotein (HDL) cholesterol was defined as a HDL cholesterol concentration <40 mg/dL if male or <50 mg/dL if female. Metabolic syndrome was defined according to the modified National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines and criteria. Patients were deemed to have metabolic syndrome if three or more of the following five criteria were satisfied: obesity, hypertriglyceridemia, low HDL cholesterol, high blood pressure, and high fasting glucose, as previously reported. In this study, BMI was used to define obesity because waist circumference measurements were not available.

**Statistical Analysis**

To calculate the incidence rates for AMI per 100,000 person-years during the three time intervals, the annual population of Yamagata Prefecture was used as the denominator. To adjust for patient age, the Japanese population, as determined by the 2005 census, was used as the standard population. In addition, a case-control study was performed, comparing coronary risk factors during 2003–2007 between AMI patients and 2,400 age-matched control subjects who were enrolled in the Takahata study in 2005. The Takahata study has been described in detail elsewhere. To adjust for the age of subjects, we used standardized incidence ratios.
Categorical variables were analyzed using the chi-square test. Continuous variables are presented as the means ±SD. Differences among groups were analyzed by analysis of variance (ANOVA) with the Scheffe post hoc test. Multivariate logistic regression analysis was used to evaluate the relationship between coronary risk factors and the development of AMI. A value of $p<0.05$ was considered significant.

### Results

The clinical characteristics of the 6,222 patients enrolled in the study are summarized in Table 1. The female patients were, on average, about 10 years older than the male patients, and the age at onset of AMI was also significantly higher in female patients. There were increases in the numbers of male patients and in the age-adjusted incidence rate of AMI among male patients. Although the incidence rate of AMI increased with advancing age, it was not increased in elderly patients during the three time periods; in contrast, there was a significant increase among younger male patients.

As shown in the lower panel of Table 1, significant increases in the prevalence of hypertension and diabetes mellitus were observed in both genders. In contrast, there were significant increases in the prevalence of obesity and hypercholesterolemia among males, but not among females. A decrease in the proportion of AMI patients with a family history was observed in both genders during the third period (2003–2007) (Table 1). While the prevalence of treatment for hypertension was relatively high in both genders, the prevalence of the control of diabetes and hypercholesterolemia was still insufficient (Table 1). In males, the prevalence of treatment for each risk factor was approximately 10% lower than in females. Despite decreases in the proportion of current smokers among male patients, the proportion of male smokers was about six times greater than the proportion of female smokers (Table 1).

To evaluate the prevalence of coronary risk factors among AMI patients, the prevalence of each risk factor was compared between AMI patients during the third period (2003–2007) and the Japanese general population. AMI patients had a higher prevalence of...
Table 2. Comparison of clinical risk factors between patients with AMI in the third period (2003–2007) and age-adjusted control subjects

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Male 3rd (03'–07)</th>
<th>Takahata 3rd (03'–07)</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p value</th>
<th>Female 3rd (03'–07)</th>
<th>Takahata 3rd (03'–07)</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity, BMI ≥25 (%)</td>
<td>31.6</td>
<td>28.7</td>
<td>1.15</td>
<td>0.96-1.37</td>
<td>0.1235</td>
<td>29.2</td>
<td>30.9</td>
<td>0.92</td>
<td>0.73-1.15</td>
<td>0.4735</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>58.3</td>
<td>47.2</td>
<td>1.56</td>
<td>1.33-1.83</td>
<td>&lt;0.0001</td>
<td>69.2</td>
<td>46.0</td>
<td>2.63</td>
<td>2.17-3.19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>30.3</td>
<td>9.1</td>
<td>4.34</td>
<td>3.42-5.49</td>
<td>&lt;0.0001</td>
<td>33.0</td>
<td>6.0</td>
<td>7.65</td>
<td>5.81-10.06</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>34.6</td>
<td>22.1</td>
<td>1.87</td>
<td>1.56-2.23</td>
<td>&lt;0.0001</td>
<td>39.1</td>
<td>33.2</td>
<td>1.29</td>
<td>1.06-1.57</td>
<td>0.0091</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>55.4</td>
<td>31.3</td>
<td>2.73</td>
<td>2.31-3.22</td>
<td>&lt;0.0001</td>
<td>8.9</td>
<td>1.6</td>
<td>6.26</td>
<td>3.76-10.42</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Multivariate analysis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension (%)</td>
<td>1.32</td>
<td>1.10-1.60</td>
<td>0.0035</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>4.02</td>
<td>3.06-5.29</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypercholesterolemia (%)</td>
<td>1.64</td>
<td>1.33-2.02</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>3.25</td>
<td>2.66-3.96</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Age-adjusted control subjects were enrolled in the Takahata study in 2005. Multivariate logistic regression analysis adjusted for patient age.

Hypertension, diabetes, hypercholesterolemia and current smoking were more prevalent among women. Although obesity (BMI ≥25) increased among male patients during the third period, obesity was not a significant risk factor either in males or females. In multivariate logistic regression analysis adjusted for patient age, hypertension, diabetes, and current smoking were independent risk factors for AMI in both genders. Hypercholesterolemia was an independent risk factor for AMI among men, but not among women.

Surprisingly, more than 70% of younger male patients were current smokers, and the proportion of smokers was unchanged, except among early elderly men (Fig. 1). Younger female patients were also more likely to be smokers than elderly female patients. Younger male patients showed increases in the prevalence of hypertension and diabetes, increases in BMI and a decrease in the proportion with a family history of MI. Younger male patients showed a greater increase in triglyceride levels, while HDL and LDL cholesterol levels were unchanged. An increase in the prevalence of diabetes was observed for most patients, except younger female patients.

As shown in Fig. 1, younger men showed significant increases in the prevalence of hypertension and diabetes, as well as in BMI and triglyceride levels during the third period (2003–2007). Consequently, the number of risk factors associated with metabolic syndrome increased among younger and early elderly men (Table 3). In contrast, there was no significant change in the number of risk factors among women.

The prevalence of risk factors associated with metabolic syndrome was compared within each age group, between AMI patients during the third period (2003–2007) and the Japanese general population. Early elderly male patients had a higher prevalence of hypertension, diabetes, and low HDL cholesterolemia than control subjects (Table 4); however, younger male patients had a higher prevalence of all coronary risk factors associated with metabolic syndrome than control subjects. Multivariate regression analysis revealed that hypertension, diabetes and low HDL cholesterolemia were independent risk factors for AMI among younger and early elderly men. Further, BMI was an independent risk factor for AMI among younger men, but not among early elderly men. In contrast, BMI was not an independent risk factor for AMI among younger men, but not among early elderly men. In addition, male patients with AMI aged <40 years showed significant increases in BMI (Fig. 2) and the prevalence of obesity during the third period. In addition, male patients with AMI aged <40 years showed significant increases in BMI (Fig. 2) and the prevalence of obesity during the third period. Consequently, there was an accumulation of risk factors associated with metabolic syndrome among younger men. Furthermore, there were differences between younger and early elderly male patients in the proportion receiving medical treatment. Fig. 3 demonstrates that the prevalence of treatment for hypertension and diabetes was significantly lower among younger men and, in contrast to the changes observed for elderly patients, this did not improve at all during the three time periods.
Fig. 1. Trends in coronary risk factors and lipid profiles among AMI patients.
Bars indicate the prevalence of coronary risk factors and the lipid profiles during hospitalization in the three age groups (<65, 65-74, ≥75 years old), for both genders, during the three time periods. Continuous variables are presented as the mean ± SE. *p<0.05, **p<0.01 compared with 1st period; †p<0.05, ††p<0.01 compared with 2nd period.
Comparison of risk factors associated with metabolic syndrome between younger and early elderly male patients with AMI

Trends in the number of risk factors associated with metabolic syndrome

<table>
<thead>
<tr>
<th>Group</th>
<th>1st (93’–97”)</th>
<th>2nd (98’–02”)</th>
<th>3rd (03’–07”)</th>
<th>p value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;64 years old</td>
<td>1.60 ± 1.18</td>
<td>1.74 ± 1.19</td>
<td>1.87 ± 1.19**</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>65–74 years old</td>
<td>1.71 ± 1.23</td>
<td>1.97 ± 1.24*</td>
<td>2.02 ± 1.26**</td>
<td>0.0017</td>
</tr>
<tr>
<td>&gt;75 years old</td>
<td>1.54 ± 1.17</td>
<td>1.57 ± 1.14</td>
<td>1.94 ± 1.13**!</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;64 years old</td>
<td>2.04 ± 1.10</td>
<td>2.08 ± 1.14</td>
<td>2.12 ± 1.20</td>
<td>0.6639</td>
</tr>
<tr>
<td>65–74 years old</td>
<td>2.02 ± 1.07</td>
<td>1.93 ± 1.09</td>
<td>1.98 ± 1.29</td>
<td>0.9013</td>
</tr>
<tr>
<td>&gt;75 years old</td>
<td>2.13 ± 1.09</td>
<td>2.07 ± 1.20</td>
<td>2.15 ± 1.27</td>
<td>0.8721</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01 compared with 1st period; †p < 0.05 compared with 2nd period.

Table 3. Trends in the number of risk factors associated with metabolic syndrome

Table 4. Comparison of risk factors associated with metabolic syndrome between younger and early elderly male patients with AMI during the third period (2003–2007) and control subjects

Discussion

The present study showed that the age-adjusted incidence of AMI increased in male patients. Younger men in particular showed a significant increase in the incidence of AMI during 2003–2007. In contrast, there was no increase in the incidence of AMI among females during the observation periods. There was a significant increase in the prevalence of metabolic syndrome among younger male patients compared with other age groups, as well as a greater increase in the number of risk factors associated with metabolic syndrome. These results suggested that an increase in the prevalence of risk factors associated with metabolic syndrome may be related to the increased incidence rate for AMI among younger men.

Increased Incidence of AMI Among Male Patients

An increased number of AMI was observed among male patients (Table 1). In contrast, the number of AMI did not increase and the age at onset increased significantly among women. There was no significant change in the age-adjusted incidence rate of AMI among women in the present study, which is consistent with the findings of the Hisayama study7. Another AMI registry study reported that the age-adjusted incidence rate increased by 7.6% among men and by 8.3% among women, between 1990 and 20018. In contrast, the present study demonstrated that the age-adjusted incidence rate for AMI increased
only among men and was much higher than in women. Younger men in particular showed a significant increase in the incidence rate of AMI, which was seven times greater than in women during 2003–2007 (Table 1). These findings are not likely to be explained only by the influence of aging of the general population. We hypothesized that changes in the prevalence of risk factors, due to the westernization of dietary habits and changes in lifestyle, may have influenced the recent incidence rates of AMI.

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

There were differences in the trends in coronary risk factors between men and women. Both showed a similar magnitude of increase in the prevalence of hypertension and diabetes; however, only younger men showed a significant increase in the prevalence of obesity and in serum triglyceride levels during 2003–2007 (Fig. 1). Consequently, the proportion of patients with metabolic syndrome increased among younger and early elderly men (Table 3). Several studies have demonstrated that metabolic syndrome is a significant risk factor for the development of AMI[18-24], but it had a weak or no association with CHD in the elderly[31], which is consistent with the findings of the present study.

In the present study, AMI patients of both genders showed a higher prevalence of hypertension, diabetes and hypercholesterolemia, and a higher incidence of current smoking than age-adjusted control subjects, which was consistent with the findings of the Framingham study[32]. Recently, a large Japanese case-control study demonstrated that hypertension, diabetes, current smoking, family history, and hypercholesterolemia were all independent risk factors for AMI[12]; however, only current smoking, diabetes and, hypertension were identified as independent risk factors in women in their study. Therefore, it was suggested that

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Table 5. Comparison of risk factors associated with metabolic syndrome between younger and early elderly female patients with AMI during the third period (2003–2007) and control subjects

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Younger women</th>
<th>Early elderly women</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Takahata</td>
<td>3rd (03–07)</td>
<td>3rd (03–07)</td>
</tr>
<tr>
<td>54.1 ± 7.9y</td>
<td>(n = 87)</td>
<td>69.6 ± 2.8y</td>
</tr>
<tr>
<td>54.9 ± 6.4y</td>
<td>(n = 692)</td>
<td>69.4 ± 2.8y</td>
</tr>
<tr>
<td>odds ratio</td>
<td>2.91</td>
<td>2.80</td>
</tr>
<tr>
<td>95% CI</td>
<td>1.37–5.40</td>
<td>1.11–5.77</td>
</tr>
<tr>
<td>p value</td>
<td>0.004</td>
<td>0.017</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>2.14</td>
<td>1.14–3.90</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>1.82</td>
<td>1.41–2.39</td>
</tr>
<tr>
<td>Hypertriglyceridemia (%)</td>
<td>4.47</td>
<td>3.90–5.07</td>
</tr>
<tr>
<td>Low HDL cholesterolemia (%)</td>
<td>7.02</td>
<td>6.65–7.41</td>
</tr>
<tr>
<td>Metabolic syndrome (%)</td>
<td>1.85</td>
<td>1.43–2.90</td>
</tr>
</tbody>
</table>

BMI, body mass index; HDL, high density lipoprotein

Data represent odds ratio corresponding to 1SD increase in BMI level
hypercholesterolemia was an independent coronary risk factor in men, but not women, which is consistent with the results of the present study.

Previous studies reported that obesity and low HDL cholesterolemia were independent risk factors among younger male patients [33-35], which is consistent with our findings. In particular, male patients with AMI aged <40 years showed significant increases in BMI and the prevalence of obesity (Fig. 2).

Although the incidence of current smoking decreased during 2003–2007 in male patients (Table 1), it was significantly higher than in age-adjusted control subjects (Table 2). Surprisingly, the incidence of current smoking in female AMI patients was about six times higher than in age-adjusted control subjects, whereas it was lower than in male AMI patients. Thus, the prevalence of smoking has decreased in men, but not in women. Notably, the prevalence of smoking was significantly higher in younger women than in elderly patients. These results suggest that current smoking is an important risk factor for AMI, which is consistent with the findings from a previous study [12, 32, 36].

During 2003–2007, there was a significant decrease among both genders in the proportion of AMI patients with a family history (Table 1). This does not mean there was a decrease in the number of AMI patients with a family history, but rather that there was an increase in the number without a family history. In addition, the impact of lifestyle-related factors on the development of AMI may have become relatively more important in recent years [14-17, 29].

**Insufficient Treatment of Coronary Risk Factors**

Female AMI patients were 8–10 years older than male patients (Table 1). A previous study also reported that women develop CHD about 10 years later than men [37]. In general, menopause is a risk factor among females, which contributes to gender differences [38, 39]; however, it has been suggested that the difference in the age at onset is largely explained by the higher number of risk factors at younger ages in men than women [37]. The age at onset increased significantly in women in the present study. Since the number of female patients did not increase, despite an increase in the aging population, it is suggested that medical treatment may have partly contributed to suppressing the incidence of AMI in women. In fact, the proportion of patients receiving medical treatment for each risk factor was approximately 10% higher in women than men (Table 1). Although the proportion of patients receiving treatment for hypertension reached 94% in female patients, the proportions receiving treatment for diabetes and hypercholesterolemia remained suboptimal at 78% and 59%, respectively.

In order to reduce the age-adjusted incidence of AMI in women, improved rates of treatment for diabetes and hypercholesterolemia, as well as increased rates of smoking cessation, are required.

In contrast to women, there was an accumulation of coronary risk factors and an increased incidence of AMI in male patients. Particular attention should be paid to the increased incidence of AMI among younger men, who showed a greater increase

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**Fig. 3.** Comparison of the proportions of male patients receiving medical treatment.

Bars indicate the proportions of male patients in the three age groups (<65, 65–74, ≥75 years old), receiving medical treatment for hypertension and diabetes during the three time periods. *p < 0.05, **p < 0.01 compared with late elderly patients; †p < 0.05, ††p < 0.01 compared with early elderly patients.
in the prevalence of the metabolic syndrome than other age groups (Table 4), and also had a markedly high incidence of current smoking (Fig. 1), which did not decrease over the three time periods. Furthermore, the proportion of patients receiving treatment for each coronary risk factor was significantly lower in younger male patients than other age groups (Fig. 3). Therefore, control of the risk factors associated with metabolic syndrome, in addition to conventional risk factors, such as hypercholesterolemia, and increased rates of smoking cessation, are required to decrease the incidence of AMI among men.

In conclusion, the age-adjusted incidence of AMI increased in male patients, but not in female patients. In particular, younger men have shown a significant increase in the incidence of AMI recently. The control of conventional coronary risk factors is still thought to be insufficient, in both men and women, to contribute to a decrease in the incidence of AMI. In addition, preventive care for metabolic syndrome may be required in younger men.

Acknowledgements

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