Comparison of Clinical Characteristics of Acute Myocardial Infarction Between Young (< 55 Years) and Older (55 to < 70 Years) Patients

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Summary

Although the incidence of acute myocardial infarction (AMI) has been decreasing in the elderly, it has been increasing in the young, especially in Japan. A social impact of AMI would be greater in the young, because loss of the young directly influences social activities such as business, child-raising, and tax payment. The aim of this study was to identify the specific characteristics of young AMI patients. We retrospectively included 408 consecutive AMI patients < 70 years of age, divided into a young group (< 55 years: n = 136) and an older group (55 to < 70 years: n = 272). The prevalence of overweight was greater in the young group (58.5%) than in the older group (40.7%) (P = 0.001). The frequency of current smokers was higher in the young group (67.6%) than in the older group (44.9%) (P < 0.001). Although the prevalence of hypertension was lower in the young group (66.7%) than in the older group (77.2%) (P = 0.017), that of untreated hypertension was greater in the young group (40.4%) than in the older group (27.2%) (P = 0.007). Furthermore, the prevalence of untreated dyslipidemia was greater in the young group (45.0%) than in the older group (26.6%) (P < 0.001). In conclusion, the young AMI patients had more modifiable risk factors such as obesity, smoking, untreated hypertension, and untreated dyslipidemia than the older patients. There is an unmet medical need for the prevention of AMI in the young generation.

Key words: Risk factor, Untreated, Obesity, Smoking, Hypertension, Dyslipidemia, Diabetes mellitus

Coronary artery disease (CAD) is the leading cause of death in the world.11) Recently, the incidence of acute myocardial infarction (AMI) has been decreasing in western countries, partly because of public efforts to reduce coronary risk factors.2-5) However, the incidence of AMI has been increasing in Asian countries such as Taiwan and Korea.4-6) Furthermore, the incidence of AMI is increasing in the young in Japan.9) A social impact of AMI would be greater in the young than in the elderly, because loss of the young directly influences social activities such as business, child-raising, and tax payment.9) Therefore, for a better future, it is important to prevent AMI in the young generation. For the prevention of AMI, it is necessary to appreciate the real-world characteristics of young patients with AMI and take a specific approach for the young population. Although CAD is increasing in the young population, the absolute number of CAD is less in the young population than in the elderly population.43) As a result, most research has focused on identifying the risk factors in the elderly population.10) The aim of this study was to identify the clinical characteristics of young AMI patients in comparison with older AMI patients.

Methods

Study design: We reviewed consecutive AMI patients from hospital records in our medical center from January 2015 to December 2018. The inclusion criteria were (1) first-time AMI and (2) patients aged less than 70 years. The exclusion criteria were (1) AMI caused by trauma, (2) AMI caused by cardiovascular surgery, and (3) AMI patients who did not undergo coronary angiography. The final study population was divided into a young group (< 55 years) and an older group (55 to < 70 years). The definition of “young” with respect to AMI varied widely according to the literature, and cut-off ages of 45 or 55 have been used in most studies.10-15) Spatz, et al. and McManus, et al. defined young as < 55 years of age,14,15) and considering the Japanese life expectancy, which is the longest in the world,16) we adopted 55 years as the upper limit of the young group. Clinical characteristics were compared between the young and older groups. We also examined major adverse cardiovascular events (MACE) until September 30, 2019. MACE represented a composite
of all-cause death, no fatal myocardial infarction (MI), target vessel revascularization (TVR), and re-admission for heart failure. We defined the admission day as the index day in this analysis. This study was approved by the institutional review board, and written informed consent was waived because of the retrospective study design.

**Definitions:** AMI was defined as a rise in a cardiac biomarker (preferably cardiac troponin with a ≥ 1 value above the 99th percentile upper reference limit) and with one or more of the following: (1) symptoms of ischemia; (2) new or presumed new significant ST-segment T-wave changes or new left bundle branch block; (3) development of pathological Q waves on an electrocardiogram; (4) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality; and (5) identification of an intracoronary thrombus on angiography, according to the universal definition.23 Hypertension was defined as systolic blood pressure (SBP) > 140 mmHg, diastolic blood pressure (DBP) > 90 mmHg, or medical treatment for hypertension.18 Untreated hypertension was defined as SBP > 140 mmHg or DBP > 90 mmHg without medical treatment for hypertension. Diabetes mellitus was defined as hemoglobin A1c (HbA1c) ≥ 6.5% or treatment for diabetes mellitus.19,20 Untreated diabetes mellitus was defined as HbA1c ≥ 6.5% without medical treatment for diabetes mellitus. Dyslipidemia was defined as total cholesterol ≥ 220 mg/dL, low-density lipoprotein (LDL) cholesterol ≥ 140 mg/dL, or treatment for dyslipidemia.19,20 Untreated dyslipidemia was defined as total cholesterol ≥ 220 mg/dL or LDL cholesterol ≥ 140 mg/dL, without medical treatment for dyslipidemia. We used the laboratory data at admission. As we could not measure some laboratory data such as HbA1c or LDL cholesterol levels during off-hours (nights or holidays), we substituted the earliest HbA1c or LDL cholesterol levels since admission for the laboratory data at admission. However, we used the earliest LDL cholesterol levels only when they were tested before the administration of statins. Overweight was defined as body mass index > 25 kg/m². We also calculated estimated glomerular filtration rate (eGFR) using serum creatinine (Cr), age, weight, and gender according to the following formula: eGFR = 194 × Cr⁻¹.094 × age⁻₀·₈⁵ (male) or eGFR = 194 × Cr⁻¹.094 × age⁻₀·₈³ × 0.739 (female).21 Peripheral artery disease (PAD) was defined as an ankle-brachial index of < 0.90 or medical treatment for PAD.19,22 Shock was defined as SBP < 90 mmHg, vasopressors required to maintain blood pressure, or attempted cardiopulmonary resuscitation.19,20 We investigated whether patients had regularly received medical prescriptions for any lifestyle diseases before AMI admission. When patients remembered the results of a regular medical check-up, we regarded them as having a medical check-up. Left ventricular ejection fraction (LVEF) was measured using a modified Simpson method. LVEF measured by the Teichholz method was adopted only when a modified Simpson method was not available. Echocardiography was evaluated during the index hospitalization.

**Statistical analysis:** Data are presented as a percentage for categorical variables and the mean ± SD for continuous variables. Categorical variables were compared using Pearson’s χ² test or Fisher’s exact test. The Shapiro-Wilk test was conducted to determine whether the continuous variables were normally distributed. Normally distributed continuous variables were compared between the groups using the unpaired Student’s t-test. Otherwise, continuous variables were compared using the Mann-Whitney U test. Kaplan-Meier survival analysis was performed with respect to MACE, all-cause death, no fatal MI, TVR, and re-admission for heart failure. The difference between the two survival curves was compared by the log rank test. We also performed multivariate Cox regression analysis to investigate the association between the young group and MACE after controlling known clinical confounders such as eGFR,21 ST elevated myocardial infarction (STEMI),21 single-vessel disease,21 and percutaneous coronary intervention (PCI) to the culprit lesion.21 Hazard ratios (HR) and the 95% confidence intervals (CI) were calculated. All reported P values were determined by two-sided analysis, and P values < 0.05 were considered significant. All analyses were performed with IBM SPSS statistics version 25 (Chicago, IL, USA).

**Results**

Among 1089 patients admitted to our medical center from January 2015 to December 2018, 408 patients were included as the final study population and were divided into a young group (n = 136) and an older group (n = 272) (Figure 1).

The comparisons of patients’ characteristics are shown in Table I. The frequency of current smokers was significantly higher in the young group (67.6%) than in the older group (44.9%) (P < 0.001), whereas the frequency of former smokers was significantly higher in the older group than in the young group (P < 0.001). The prevalence of hypertension was significantly lower in the young group (66.7%) than in the older group (77.2%) (P = 0.017), whereas that of untreated hypertension was significantly higher in the young group (40.4%) than in the older group (27.2%) (P = 0.007). Furthermore, the prevalence of untreated dyslipidemia was significantly higher in the young group (45.0%) than in the older group (26.6%) (P < 0.001). Patients who had a primary care doctor before admission were significantly less in the young group (48.5%) than in the older group (70.1%) (P < 0.001).

Table II shows the comparisons of angiographic lesion and procedural characteristics between the young and older groups. Single-vessel disease was more common in the young group (55.9%) than in the older group (41.9%) (P = 0.008). Thrombectomy was more frequently performed in the young group (27.0%) than in the older group (17.1%) (P = 0.029).

The comparisons of clinical outcomes between the young and older groups are shown in Table III. The length of hospital stay was shorter in the young group (9.6 ± 9.9) than in the older group (11.5 ± 13.5) (P = 0.041). Median follow-up duration was 352 days (Q1: 209 days - Q3: 662 days). The Kaplan-Meier curves for MACE are shown in Figure 2. There was no significant difference in MACE between the 2 groups. Multivariate
Cox hazard analysis was performed in Table IV. The young group was not significantly associated with MACE (HR 0.94, 95% CI 0.606-1.461, \( P = 0.786 \)) after controlling gender, eGFR, STEMI, single-vessel disease, and PCI to the culprit lesion.

Discussion

The present study included 408 AMI patients aged < 70 years, who were divided into a young group (< 55 years) and an older group (55 to < 70 years). The prevalence of overweight and current smoking was significantly greater in the young group than in the older group. Although the prevalence of hypertension was significantly lower in the young group than in the older group, the prevalence of untreated hypertension was significantly higher in the young group than in the older group. Similarly, although the prevalence of dyslipidemia was comparable between the 2 groups, the prevalence of untreated dyslipidemia was significantly higher in the young group than in the older group. Patients who had a primary care doctor before admission were significantly less in the young group than in the older group even after abnormal findings were pointed out at the medical check-up. These results suggest that risk factors such as smoking, hypertension, and dyslipidemia were not sufficiently modified in the young group.

Several groups have reported that smoking and obesity are common risk factors among “young” MI patients.\(^{36,25}\) Our results also showed that the prevalence of overweight and current smoking was higher in the young group than in the older group, consistent with earlier literature. As overweight and current smoking are influenced by individual lifestyle, the young generation should pay more attention to their body weight and smoking habit to prevent AMI. However, even if a young person was both overweight and a current smoker, the young person might have no contact with physicians, because overweight and smoking are not considered as an illness among the young generation. It is important to educate the young generation that overweight or smoking can be a cause of fatal diseases such as AMI.

Incalcaterra, et al. reported that the prevalence of hypertension was lower in “young” MI patients than in older MI patients,\(^ {20} \) consistent with our results. Interestingly, we demonstrated that the prevalence of untreated hypertension was higher in the young group than in the older group. Untreated hypertension is known to be associated with hemorrhagic stroke or in-hospital death in patients with intracerebral hemorrhage.\(^ {29,30} \) However, the association between untreated hypertension and AMI, especially in the young generation, has not been reported. Although our results did not prove the direct association between untreated hypertension and AMI in the young generation, future studies to investigate such an association are warranted.

Regarding dyslipidemia, some groups reported a lower prevalence of dyslipidemia among “young” MI patients than among older patients, whereas other groups reported opposite results.\(^ {8,25,31} \) In the present study, although there was no significant difference in the prevalence of dyslipidemia between the young group and the older group, the prevalence of untreated dyslipidemia was higher in the young group than in the older group. Although the association between dyslipidemia and AMI is well known in the literature,\(^ {4,20} \) the difference between treated and untreated dyslipidemia has not been focused on to date. Our results suggest the possible association between untreated dyslipidemia and AMI among the young generation.

From the coronary angiographic findings, the prevalence of single-vessel disease was greater in the young group than in the older group, consistent with earlier literature.\(^ {11,31,32} \) This is not surprising, because atherosclerosis progresses with aging.\(^ {33} \) Interestingly, thrombectomy was more frequently performed in the young group than in the older group, suggesting that thrombotic occlusion might occur more frequently in the young group than in
Data were expressed as mean ± SD or numbers (percentages). A Student’s t-test was used for normally distributed continuous variables, and the Mann–Whitney U test was used for abnormally distributed continuous variables. A chi-square test was used for categorical variables. ACE indicates inhibitors angiotensin-converting enzyme inhibitor; ARBs, angiotensin receptor blockers; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; and PCI, percutaneous coronary intervention.
### Table II. Comparison of Lesion and Procedural Characteristics Between the Young and the Older Groups

|                      | All (n = 408) | Young group (n = 136) | Older group (n = 272) | P value |
|----------------------|---------------|-----------------------|-----------------------|---------|
| Coronary spastic angina, n (%) | 21 (5.1)      | 10 (7.4)              | 11 (4.0)              | 0.154   |
| Number of narrowed coronary arteries, n (%) | 190 (46.6)    | 76 (55.9)             | 114 (41.9)            | 0.008   |
| Left main trunk stenosis > 50%, n (%) | 37 (9.1)      | 9 (6.6)               | 28 (10.3)             | 0.223   |
| Chronic total occlusion in other vessels, n (%) | 51 (12.5)     | 12 (8.8)              | 39 (14.3)             | 0.112   |
| Number of intervention artery, n (%) | 361 (88.5)    | 115 (84.6)            | 246 (90.4)            |         |
| CABG                  | 10 (2.5)      | 3 (2.2)               | 7 (2.6)               |         |
| PCI                   | 37 (9.1)      | 18 (13.2)             | 19 (7.0)              |         |
| Infarct-related artery, n (%) | 20 (5.4)      | 15 (11.2)             | 5 (1.9)               | 0.226   |
| Left main trunk       | 19 (4.7)      | 4 (2.9)               | 15 (5.5)              |         |
| Left anterior descending artery | 183 (44.9)   | 66 (48.5)             | 117 (43.0)            |         |
| Left circumflex artery | 55 (13.5)    | 11 (8.1)              | 44 (16.2)             |         |
| Right coronary artery | 120 (29.4)    | 42 (30.9)             | 78 (28.7)             |         |
| Approach site, n (%) | 108/361 (29.9) | 31/115 (27.0) | 77/246 (31.3) |         |
| Final TIMI flow grade | 0.355         |                      |                      |         |
| 0                    | 169 (41.4)    | 65 (47.8)             | 104 (38.2)            | 0.253   |
| 1                    | 43 (10.5)     | 15 (11.0)             | 28 (10.3)             |         |
| 2                    | 58 (14.2)     | 16 (11.8)             | 42 (15.4)             |         |
| 3                    | 138 (33.8)    | 40 (29.4)             | 98 (36.0)             |         |
| Size of guide catheter, n (%) | 0.324         |                      |                      |         |
| 6 Fr                 | 237/357 (66.4) | 79/114 (69.3) | 158/243 (65.0) |         |
| 7 Fr                 | 116/357 (32.5) | 35/114 (30.7) | 81/243 (33.3) |         |
| 8 Fr                 | 4/357 (1.1)   | 0/114 (0.0)           | 4/243 (1.6)           |         |
| Final PCI procedures | 0.217         |                      |                      |         |
| POBA, n (%)          | 11/361 (3.0)  | 1/115 (0.9)           | 10/246 (4.1)          |         |
| Thrombectomy, n (%)  | 3/361 (0.8)   | 0/115 (0.0)           | 3/246 (1.2)           |         |
| Thrombectomy and POBA, n (%) | 4/361 (1.1)  | 2/115 (1.7)           | 2/246 (0.8)           |         |
| Drug-coated balloon, n (%) | 10/361 (2.8) | 3/115 (2.6)           | 7/246 (2.8)           |         |
| Drug-eluting stent implantation, n (%) | 326/361 (90.3) | 109/115 (94.8) | 217/246 (88.2) |         |
| Bare metal stent implantation, n (%) | 6/361 (1.7)  | 0/115 (0.0)           | 6/246 (2.4)           |         |
| Wire did not cross the lesion, n (%) | 1/361 (0.3)   | 0/115 (0.0)           | 1/246 (0.4)           |         |
| Length of stents or drug-coated balloons, mm | 27.0 ± 13.0 (342/342) | 27.4 ± 13.5 (112/112) | 26.8 ± 12.8 (230/230) | 0.710 |
| Diameter of stents or drug-coated balloons, mm | 2.9 ± 0.4 (342/342) | 2.9 ± 0.4 (112/112) | 2.8 ± 0.4 (230/230) | 0.013 |
| Actual stent type deployed at culprit lesions, n (%) | 0.312         |                      |                      |         |
| BMS                  | 6/342 (1.8)   | 0/112 (0.0)           | 6/230 (2.6)           |         |
| DES                  | 324/342 (94.7) | 109/112 (97.3) | 215/230 (93.5) |         |
| DCB                  | 11/342 (3.2)  | 3/112 (2.7)           | 8/230 (3.5)           |         |
| DES + DCB            | 1/342 (0.3)   | 0/112 (0.0)           | 1/230 (0.4)           |         |
| Fluoroscopy time, minutes | 25.2 ± 16.8 (335/361) | 23.9 ± 18.2 (106/115) | 25.9 ± 16.2 (229/246) | 0.103 |
| Amount of contrast agent, mL | 135.8 ± 49.2 (344/361) | 135.6 ± 50.0 (100/115) | 135.9 ± 49.0 (235/246) | 0.934 |

Data were expressed as mean ± SD or numbers (percentages). A Student’s t-test was used for normally distributed continuous variables, and the Mann–Whitney U test was used for abnormally distributed continuous variables. A chi-square test was used for categorical variables. BMS indicates bare metal stent; CABG, coronary artery bypass grafting; DCB, drug-coated balloon; DES, drug-eluting stent; PCI, percutaneous coronary intervention; POBA, percutaneous old balloon angioplasty; and TIMI, thrombolysis in myocardial infarction.
the old group. It may be important, especially for the young generation, to avoid dehydration. Although the length of hospital stay was shorter in the young group, there was no significant difference in the other clinical outcomes such as in-hospital death or MACE between the 2 groups. In general, the long-term follow-up studies show a greater incidence of all-cause death in the old generation than in the young generation, because the life span is limited. Moreover, the incidence of re-admission for heart failure was not significantly different between the groups, even though the usage rate of diuretics at discharge was significantly greater in the older group than in the young group. Our follow-up period might not be long enough to find the difference of mortality or other events.

We should discuss why patients who had their primary care doctor were less in the young group. First, the young generation tends to be overconfident regarding their health. They might not think seriously that lifestyle diseases lead to life-threatening diseases such as AMI. Second, the young generation has multiple responsibilities not only for their business matters but also for their family. As compared to the older generation, the young generation has a greater role in social activities such as employment or childcare; hence, it might be difficult for them to find the time to see a primary care doctor. Furthermore, the work environment might be related to the smoking habit. In Japan, many companies still have a smoking area in their office, which gives young workers more opportunities to smoke. It may be important to build up a better social system, in which the young generation can make the time to see a primary care doctor or to think about their health more seriously. In 2020, we experienced the COVID-19 pandemic all over the world. In this “With-Corona” era, telemedicine has been developed rapidly, which may give the young another opportunity to improve their health.

**Study limitations:** Because our study was designed as a single-center, retrospective observational study, there is a risk of selection bias. Our study has some missing values in the laboratory data, such as LDL cholesterol, HDL cholesterol, and HbA1c, which were not measured on admission when patients presented to our hospital during off-hours. As familial hypercholesterolemia (FH) is known to be one of the most important factors for AMI in the young, there could be several FH patients in our study population, considering its epidemiological prevalence. However, we could not specify FH patients, because we administered high-dose statins to our AMI patients on admission and did not conduct screening tests for FH such as X-rays of the Achilles tendons. Therefore, the exact number of FH patients in this study was unclear. Moreover, we did not measure specific lipid markers such as lipoprotein-A in our daily practice. Detailed physical findings such as abdominal girth were not available in this retrospective study. Furthermore, because we could not perform a statistical power analysis, there is a possibility of beta errors. Finally, the cause-and-effect relationship between untreated risk factors and AMI needs to be confirmed in future prospective studies.

**Conclusions**

Young AMI patients had more modifiable risk factors, such as obesity, smoking, untreated hypertension, and untreated dyslipidemia, than older AMI patients. Moreover, patients who had their primary care doctor were less in the young AMI patients than in the older AMI patients. Our results suggest the unmet medical need to prevent serious diseases such as AMI in the young generation.

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| Table III. Comparison of Clinical Outcomes Between the Young and the Older Groups |
|---------------------------------------------------------------|
| **All events**                                               | **All (n = 408)** | **Young group (n = 156)** | **Older group (n = 272)** | **P value** |
| In-hospital outcomes                                         |                  |                        |                          |             |
| Peak CK, mg/dL                                               | 2115.0 ± 3459.0  | 2472.8 ± 4085.5        | 1936.1 ± 3091.7          | 0.139       |
| Peak CK-MB, mg/dL                                            | 171.5 ± 220.7    | 195.6 ± 238.6          | 159.4 ± 210.6            | 0.289       |
| Left ventricular ejection fraction, %                        | 54.3 ± 13.7 (387/408) | 54.5 ± 13.6 (132/136) | 54.1 ± 13.9 (255/272)    | 0.777       |
| In-hospital death, n (%)                                     | 12 (2.9)         | 3 (2.2)                | 9 (3.3)                  | 0.534       |
| Length of hospital stay, days                                | 10.9 ± 12.4      | 9.6 ± 9.9              | 11.5 ± 13.5              | 0.041       |
| Length of CCU stay, days                                     | 3.3 ± 3.1        | 3.2 ± 2.4              | 3.4 ± 3.4                | 0.684       |
| Long-term clinical outcomes                                  |                  |                        |                          |             |
| Follow-up duration                                           | 492 ± 396        | 433 ± 349              | 520 ± 415                | 0.093       |
| MACE, n (%)                                                  | 109 (26.7)       | 29 (21.3)              | 80 (29.4)                | 0.082       |
| All-cause death, n (%)                                       | 30 (7.4)         | 6 (4.4)                | 24 (8.8)                 | 0.108       |
| Re-admission for heart failure, n (%)                        | 14 (3.4)         | 3 (2.2)                | 11 (4.0)                 | 0.336       |
| No fatal MI, n (%)                                           | 27 (6.6)         | 7 (5.1)                | 20 (7.4)                 | 0.398       |
| TVR, n (%)                                                   | 66 (16.2)        | 19 (14.0)              | 47 (17.3)                | 0.392       |

Data were expressed as mean ± SD or numbers (percentages). A Student’s t-test was used for normally distributed continuous variables, and the Mann–Whitney U test was used for abnormally distributed continuous variables. A chi-square test was used for categorical variables. CCU indicates coronary care unit; CK, creatine kinase; CK-MB, creatine kinase-myoglobin binding; MACE, major adverse cardiovascular events; MI, myocardial infarction; and TVR, target vessel revascularization.
Figure 2. Kaplan–Meier curves for MACE (A), all-cause death (B), no fatal MI (C), TVR (D), and re-admission for heart failure (E) between the young and the older AMI groups. MACE indicates major adverse cardiovascular events; and TVR, target vessel revascularization.

Disclosure

Conflicts of interest: Dr. Sakakura has received speaking honoraria from Abbott Vascular, Boston Scientific, Medtronic Cardiovascular, Terumo, OrbusNeich, Japan Lifeline, Kaneka, and NIPRO; he has served as a proctor for Rotablator for Boston Scientific, and he has served as a consultant for Abbott Vascular and Boston Scientific. Prof.
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