Acute Myocardial Infarction in Young Japanese Adults

— Clinical Manifestations and In-Hospital Outcome —

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Background The prevalence and clinical manifestations of acute myocardial infarction (AMI) in young patients in Japan have not been fully investigated.

Methods and Results In the present study, 1651 AMI patients were enrolled in the AMI-Kyoto Multi-Center Risk Study between January 2000 and June 2004. Of these, the clinical background, risk factors, angiographic findings, acute results of primary percutaneous coronary intervention (PCI) and in-hospital outcomes for 27 young patients <40 (young group), and 338 non-young patients 60 ≤, <70 years old (non-young group) were retrospectively compared. The young AMI patients were all male. Current smoking, hypercholesterolemia and family history were the most common risk factors in young patients, while hypertension and diabetes mellitus were more prevalent in non-young patients. Young patients had a higher prevalence of single-vessel disease and a lesser incidence of left circumflex coronary artery as a culprit lesion. The young group had high acquisition rates of Thrombolysis In Myocardial Infarction 3 flow just after primary PCI (95.8%) and no in-hospital deaths, which was not significantly different from the non-young group.

Conclusions These results suggest that young AMI patients have different clinical characteristics from those in non-young AMI patients, and acute results of primary PCI and in-hospital prognosis in young AMI patients are comparable to those in non-young AMI patients in Japan. (Circ J 2005; 69: 1454–1458)

Key Words: Acute myocardial infarction; Japan; Percutaneous coronary intervention; Smoking; Young adults

Young adults are a relatively small portion of those having acute myocardial infarction (AMI). However, they are an important group to examine with regard to risk factor modification and secondary prevention. Previous studies have estimated that young patients of less than 40 years old make up between 2% and 6% of all AMI. AMI in young patients has different characteristics from that in older. Coronary angiography (CAG) performed in young patients with a history of myocardial infarction has identified a relatively high incidence of normal coronary arteries, non-obstructive stenosis or single-vessel disease. Risk factor analysis in young AMI patients has revealed a high prevalence of current smoking, hyperlipidemia and family history. In addition, non-classical risk factors such as vasospastic tendencies, thrombophilic conditions and a history of Kawasaki disease have also been proposed as the causes of AMI in young patients. However, the data on the prevalence and clinical characteristics in young Japanese patients with AMI, aged <40 years, are still lacking.

Primary percutaneous coronary intervention (PCI) is now widely accepted as a therapeutic strategy for older patients with AMI. Early, complete revascularization can salvage myocardium at risk and improve survival rates. However, on the basis of the difference in etiology of AMI, there is a possibility that the clinical effectiveness of PCI for young adults with AMI might be different from that for older patients. Moreover, there has been no data on the primary PCI in young Japanese patients with AMI. The AMI-Kyoto Multi-Center Risk Study, a large multicenter observational study in which 15 collaborating hospitals in Kyoto Prefecture have collected demographic, procedural and outcome data on AMI patients, was established in 2000 in order to analyze this data and establish an emergency-hospital network for heart diseases in Kyoto.

The purpose of the present study is therefore to examine retrospectively the clinical background, angiographic findings, acute results of PCI and in-hospital outcome in young adults with AMI in Japan.

Methods

Patient Population

From January 2000 to June 2004, 1651 consecutive patients with a diagnosis of AMI, who were admitted to AMI-Kyoto Multi-Center Risk Study Group Hospitals within 1 week after the onset of AMI, were enrolled in the present study. Of these, 27 patients <40 years of age at the time of infarction were assigned to the young group. In an attempt to exclude an influence of high age itself on acute...
results of primary PCI and in-hospital outcome as far as possible, we selected 338 patients aged 60–70 years old at the time of infarction as the non-young group. We retrospectively compared the clinical background, coronary risk factors, angiographic findings, acute results of primary PCI and in-hospital outcome in the young group and the non-young group. The diagnosis of AMI required the presence of 2 of the following 3 criteria: (1) characteristic clinical history; (2) serial changes on the ECG suggesting infarction (Q-waves) or injury (ST-segment elevations); and (3) a transient increase in cardiac enzymes to more than 2-fold the normal laboratory value.

Data Collection

The patients’ demographic information, cardiovascular history and risk factors (ie, smoking, hypercholesterolemia, hypertension, diabetes mellitus, and family history) were recorded. Hypercholesterolemia was defined as total cholesterol greater than or equal to 220 mg/dl or the use of cholesterol-lowering agents by patient; hypertension was defined as systemic blood pressure $\geq 140/90$ mmHg or a history of previous treatment; diabetes mellitus was defined as fasting blood sugar $\geq 120$ mg/dl or the use specific treatment. A family history of coronary artery disease in siblings, parents’ siblings or grandparents was registered. After informed consent to participate in the AMI-Kyoto Multi-Center Risk Study was confirmed by each patient, all in-hospital data were transmitted to the center located at the Department of Cardiology and Vascular Regenerative Medicine in Kyoto Prefectural University School of Medicine for analysis. The study protocol was approved by each hospitals’ ethics committee.

Emergency Coronary Arteriography, Reperfusion Therapy and Outcome

Emergency CAG was performed using the standard technique. The coronary flow in the infarct-related artery was graded according to the classification used in the Thrombolysis In Myocardial Infarction (TIMI) trial. Significant coronary artery stenosis was defined as at least a 75% reduction in the internal diameter of the right, left anterior descending or left circumflex coronary arteries and their major branches, or a 50% reduction in the internal diameter of the left main trunk. Non-significant stenosis was defined as coronary arterial narrowing less than a significant stenosis. Patients with either angiographically normal coronary arteries or non-significant stenosis were classified as having zero-vessel disease. After the culprit

### Table 1 Clinical Characteristics of the Study Patients

<table>
<thead>
<tr>
<th></th>
<th>Young group, n=27</th>
<th>Non-young group, n=338</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean years±SD)</td>
<td>33.2±5.1</td>
<td>64.2±2.9</td>
<td></td>
</tr>
<tr>
<td>Range (years)</td>
<td>20–39</td>
<td>60–69</td>
<td></td>
</tr>
<tr>
<td>Men (%)</td>
<td>27 (100)</td>
<td>268 (79.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Previous MI (%)</td>
<td>1 (3.7)</td>
<td>51 (15.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Previous PCI/CABG (%)</td>
<td>1 (3.7)</td>
<td>32 (9.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>20 (74.1)</td>
<td>156 (46.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>16 (59.3)</td>
<td>125 (37.0)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>6 (22.2)</td>
<td>176 (52.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>4 (14.8)</td>
<td>116 (34.3)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Family history (%)</td>
<td>5 (18.5)</td>
<td>14 (4.1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Elapsed time (h)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;24 (%)</td>
<td>27 (100)</td>
<td>290 (85.8)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;24 (%)</td>
<td>0 (0)</td>
<td>25 (7.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0)</td>
<td>23 (6.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Killip 3/4 (%)</td>
<td>1 (3.7)</td>
<td>42 (12.4)</td>
<td>NS</td>
</tr>
</tbody>
</table>

### Table 2 Angiographic Findings of the Study Patients

<table>
<thead>
<tr>
<th></th>
<th>Young group, n=27</th>
<th>Non-young group, n=338</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency CAG (%)</td>
<td>26 (96.3)</td>
<td>316 (93.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Culprit lesions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (%)</td>
<td>1 (3.8)</td>
<td>1 (0.3)</td>
<td>NS</td>
</tr>
<tr>
<td>RCA (%)</td>
<td>12 (46.2)</td>
<td>97 (30.7)</td>
<td>NS</td>
</tr>
<tr>
<td>LAD (%)</td>
<td>13 (50.0)</td>
<td>145 (45.9)</td>
<td>NS</td>
</tr>
<tr>
<td>LCX (%)</td>
<td>0 (0)</td>
<td>54 (17.1)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LMT (%)</td>
<td>0 (0)</td>
<td>9 (2.8)</td>
<td>NS</td>
</tr>
<tr>
<td>SVG (%)</td>
<td>0 (0)</td>
<td>1 (0.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Multivessel (%)</td>
<td>0 (0)</td>
<td>9 (2.8)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 (%)</td>
<td>1 (3.8)</td>
<td>2 (0.6)</td>
<td>NS</td>
</tr>
<tr>
<td>1 (%)</td>
<td>20 (76.9)</td>
<td>179 (56.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2 (%)</td>
<td>4 (15.4)</td>
<td>84 (26.6)</td>
<td>NS</td>
</tr>
<tr>
<td>3 (%)</td>
<td>1 (3.8)</td>
<td>44 (13.9)</td>
<td>NS</td>
</tr>
<tr>
<td>LMT (%)</td>
<td>0 (0)</td>
<td>7 (2.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

CAG, coronary angiography; RCA, right coronary artery; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; LMT, left main trunk; SVG, saphenous vein graft.
lesions were ascertained by CAG, PCI was subsequently performed. Successful reperfusion was defined as the establishment of TIMI grade 3 flow in the infarct-related artery on the final CAG. Each in-hospital death was categorized as cardiac or non-cardiac. Death ascribed to AMI, heart failure or arrhythmia were included in cardiac death, while those attributed to cerebral vascular disease, pneumonia, decrepitude and so on were included in non-cardiac death.

Statistics
Data are expressed as mean±SD. The young and non-young groups were compared using the chi-square test and unpaired Student’s t-test according to standard statistical methods using a computer-based program. In all analyses, significance was accepted at p<0.05.

Results

Patient Characteristics and Risk Factors
The clinical characteristics and risk factors in the young and the non-young patients with AMI are summarized in Table 1. Approximately 1.6% of AMI patients were less than 40 years of age. The young patients were all male and there was a significantly higher prevalence of smoking, hypercholesterolemia and family history in the young group. In contrast, hypertension and diabetes mellitus were risk factors that were more frequent among the non-young group. Elapsed time and Killip grade ≥3 at admission did not differ between the 2 groups.

Angiographic Data
Table 2 shows the emergency coronary angiographic data in the young and the non-young groups. Emergency CAG was performed in 26 of all young patients (96%) and 316 of all non-young patients (94%). Young patients were more likely to have single-vessel disease, compared to non-young patients. As a culprit lesion, the prevalence of left circumflex coronary arteries was less frequent among the young group.

Results of Coronary Intervention
Table 3 shows the results of coronary intervention in the young and non-young groups. After CAG, PCI was subsequently performed in 24 of the young patients (89%) and 289 of the non-young patients (86%). The distributions of TIMI grade before and after primary PCI did not differ significantly between the 2 groups. The use of distal protection or aspiration was significantly higher in the young patients, while the rates of stent usage did not differ significantly between the 2 groups.

In-Hospital Outcome
Table 4 shows the in-hospital prognosis in the young and the non-young patients. There was no significant difference in in-hospital survival rates between the young group.
(100%) and the non-young group (93%). The cause of death was cardiovascular in 79% of the non-young group. The length of hospital stay and the maximal creatine kinase level (maxCK) did not differ between the 2 groups.

### Discussion

The major findings of the present multicenter study are: all young patients with AMI were male, and cigarette smoking, hypercholesterolemia and family history were the most common risk factors among young patients. Young patients had a higher frequency of single vessel disease and a lower frequency of left circumflex coronary arteries as culprit lesions. The young patients had high acquisition rates of TIMI 3 flow just after primary PCI and there no in-hospital deaths that were comparable to those in the non-young patients.

In the present study, approximately 1.6% of AMI patients were less than 40 years of age, which is smaller than those of young Westerners in the previous studies. The male preponderance and high incidences of smoking, hypercholesterolemia and family history in the young AMI patients we found in the present study were consistent with the results in previous reports. Cigarette smoking is an established and correctable major risk factor for coronary artery disease in young patients as well as in older patients. Previous studies have shown high rates of smoking among young AMI patients, with percentages ranging from 70% to 90%, that are consistent with our present report. In addition, persistent smoking is associated with an increased long-term mortality after AMI. Smoking is associated with increased fibrinogen concentrations, enhanced platelet aggregability, impaired fibrinolytic activity, decreased coronary flow reserve and increased vasospasm. These observations support the current emphasis on cigarette smoking cessation to prevent young adult coronary heart disease. However, there is a possibility that the prevalence of smoking and hypercholesterolemia might be also high in young healthy subjects and the frequent risk factors in the young such as smoking and hypercholesterolemia did not play a critical role in the pathogenesis of young AMI. Therefore, a controlled case study is more suitable design than the comparison of young and elderly patients with AMI.

In agreement with previous reports, the present study has also shown that young AMI patients had a higher frequency of single coronary vessel disease compared to non-young AMI patients, indicating that coronary sclerosis is less severe in young AMI patients. However, in the present study, the incidence of total occlusion (TIMI 0) in the young group is relatively high at the initial CAG, compared to that in the non-young group, implying acute thrombosis of a single-lesion as a cause of AMI in young patients. The predilection for involvement of the left anterior descending coronary artery followed by the right coronary and left circumflex coronary arteries has been documented in other reports on young AMI patients. The present analysis also indicates a high prevalence of the left anterior descending coronary artery and the right coronary artery as an infarct-related artery, while there were no cases with left circumflex coronary arteries as culprit lesions. Although we cannot explain the discrepancy precisely, we cannot rule out the possibility that AMI with left circumflex coronary arteries as a culprit lesion might have a tendency to be misdiagnosed in young adults, because these AMI do not usually show a typical ST wave change in electrocardiogram.

Taking the higher prevalence of smoking and the higher frequency of single coronary vessel disease into consideration, coronary obstruction in young patients might be more thrombogenic, more spasmogenic and less atherosclerotic, and therefore interventions such as aspiration and distal protection might be more effective in young AMI patients. In the present study, the distribution of TIMI grade before and after primary PCI, as well as the acquisition rates of successful reperfusion, did not differ between the 2 groups. Regarding facilitated PCI, a recent report has demonstrated that the efficacy and safety of PCI do not differ between young and elderly patients with AMI. Previous studies concerning young patients with stable angina, unstable angina and AMI showed that the balloon angioplasty in younger populations has a high immediate success rate with relatively few complications. In contrast, as to long-term outcome of PCI, young patients with angina have a high need for repeat revascularization and many of them suffer an AMI in follow-up period while young patients with AMI have a low re-stenosis rate. The present study suggests that primary PCI for young Japanese adults with AMI can be safe and effective in the short term. However, the long-term efficacy of PCI for young Japanese adults with AMI is unknown and long-term follow-up is needed.

In the present study, there was no in-hospital death in young AMI patients. In addition, length of hospital stay, maxCK and in-hospital survival rates did not differ between the 2 groups. Previous studies have indicated that the rate of in-hospital complications, such as congestive heart failure, cardiogenic shock and death, were lower in young AMI patients. As to the short- and long-term prognosis, most previous reports have shown a favorable prognosis after discharge in young AMI patients. It has been speculated that young patients have an improved survival rate compared with old patients, because of their less severe coronary involvements. However, recent reports have demonstrated that the long-term prognosis of young AMI patients is not benign, especially when low ejection fraction, previous myocardial infarction, previous bypass surgery or peripheral atherosclerotic disease is present.

### Study Limitations

First, this is a retrospective analysis of a relatively small number of patients. Second, the present study population consisted of AMI patients who were admitted to collaborating hospitals in Kyoto Prefecture, therefore it might not reflect the manifestations of the entire Japanese population. Third, the data for maxCK were not available for all patients. Further prospective studies or controlled case studies are needed to ascertain the pathogenesis in young Japanese patients with AMI.

### Conclusion

The present study provides evidence that young Japanese patients with AMI have a high prevalence of being male, cigarette smoking, hypercholesterolemia and family history, a higher frequency of single vessel disease and a lower frequency of left circumflex coronary arteries as culprit lesions compared with older patients. Moreover, we demonstrate for the first time that the initial results of primary PCI and in-hospital outcome in young patients...
with AMI are comparable to those in non-young patients with AMI in Japan. However, the long-term prognosis for young Japanese adults with AMI is uncertain and a long-term follow-up study is needed. In addition, the small sample size of our report is a major limitation and a larger study should be performed to confirm our findings.

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References


Appendix