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Original Article

Clinical Features of Acute Myocardial Infarction in Elderly Patients

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The aim of this study was to clarify the prevalence of coronary risk factors in order to characterize the prognostic factors in elderly patients and to also identify any factors beneficial for the prevention of further cardiac events and death. We studied 888 patients with ST-elevation acute myocardial infarction who were admitted within 48 h of symptom onset. The patients were divided into 3 groups according to age for comparison of variables: a younger group (n = 99) aged ≤ 50, a middle-aged group (n = 435) ≥ 51 years but < 70 years and an elderly group (n = 354) aged ≥ 71 years. The elderly group had higher rates of female gender, pulmonary congestion, in-hospital mortality, and atrial fibrillation and a higher plasma concentration of high-sensitivity CRP (hs-CRP) ($p < 0.05$). Hypertension, diabetes mellitus, and dyslipidemia were more common in the middle-aged group ($p < 0.05$). The prevalence of smokers and the plasma level of total cholesterol, LDL-cholesterol and triglycerides were lower in the elderly group ($p < 0.05$). The grade of collateral circulation was highest in the elderly group, but the success rate of reperfusion therapy was lowest. Multiple regression analysis showed that age, pulmonary congestion, CKD and hs-CRP were predictors of in-hospital mortality. This investigation indicated that elderly patients with acute myocardial infarction have different clinical characteristics than younger patients. A specific algorithm might be needed in elderly patients, and could use hs-CRP, eGFR and atrial fibrillation as factors.

Key words: acute myocardial infarction, coronary risk factor, elderly

The recent developments in the treatment of acute myocardial infarction (MI), such as coronary recanalization therapy, and the increased availability of CCUs have significantly improved the acute prognosis and reduced the hospital mortality rate of these events. However, when analyzed by age of onset, the prognosis for elderly patients is still poorer than that for young and middle-aged patients.

Major advances are also being made in preventive care for patients demonstrating acute MI, as its pathogenesis and the associated risk factors have also been clarified. It is, however, unclear whether reducing the same risk factors for all patients is beneficial, especially in the elderly.

The objective of this study was to examine acute MI patients by age group and compare them with regard to the prevalence of coronary risk factors and prognostic factors in order to characterize such factors in elderly patients and identify any factors that might be able to potentially prevent MI and MI-related death.

Materials and Methods

Study patients. This study was retrospectively

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conducted using data obtained from 888 patients who were admitted to Iwakuni Clinical Center, National Hospital Organization from January 1, 1998 to December 31, 2006 due to acute MI, and who were admitted within 48 h after the onset of symptoms.

The diagnosis of acute MI was established by the presence of at least 2 of the following 3 criteria: 1) elevation of serum creatine kinase more than twice the upper limit of normal values, 2) characteristic chest pain lasting at least 30 min, or 3) ECG ST-T wave changes with evolution of abnormal Q waves. The patients' clinical history, physical examination, laboratory data, standard 12-lead ECG and chest roentgenograms were obtained on admission. ECG leads CM5 and NASA were continuously monitored for at least the following 2 days. Laboratory examinations followed on the 2nd, 3rd and 6th days of admission. The patients were divided into 2 groups based on the location of infarction using standard 12-lead ECG. When an abnormal Q wave was observed in any of the leads V1 through V4 with a characteristic ST elevation, the infarction was defined as an "anterior infarction". If the abnormal Q wave was not in any of these anterior chest-leads and was found in leads II, III and/or a VF with significant ST elevation, the infarction was considered an "inferior infarction". Patients in whom an abnormal Q wave was observed in neither the anterior nor inferior leads were excluded from this study. Patients with non-Q-wave infarctions were also excluded from this study, because it was difficult to estimate the region of their infarction by ECG. Pulmonary congestion due to left ventricular failure was categorized according to Killip's classification, and patients were grouped into 2 further groups: those with (Killip's criteria ≥ 2) and those without (Killip's criteria $= 1$) congestion. In this study, in-hospital death included patients who died during admission due to cardiac disorders, and patients who showed cardiac arrest on admission but whose symptoms and ECG were recorded before they arrived at our hospital and who demonstrated typical acute MI. The laboratory data on admission were adopted for analysis. Hypertension was considered to be present if there was an apparent history of high blood pressure, regardless of medication, or if physical examination showed elevated systolic and/or diastolic blood pressure (persistently $\geq 140/90$ mmHg). Diabetes mellitus was diagnosed in patients who had previously been diagnosed with diabetes regardless of treatment, and/or whose fasting blood glucose level was frequently higher than 110 mg/dl. Patients in whom the serum lipid levels met any of the following criteria were defined as having "dyslipidemia": a total-cholesterol level ≥ 220 mg/dl, HDL-cholesterol ≤ 40 mg/dl, LDL-cholesterol ≥ 140 mg/dl and triglycerides ≥ 150 mg/dl, which were respectively defined as hypercholesterolemia, hypo-HDL cholesterolemia, hyper-LDL cholesterolemia and hypertriglycemia. The smoking history was defined as "Yes" if the patient had smoked within 3 months before the present MI. Patients were defined as having chronic kidney disease (CKD) if their estimated glomerular filtration rate (eGFR), calculated from their serum creatinine on admission using the Modified Diet in Renal Disease (MDRD) equation, was less than 60 ml/min/1.73m^2.

Patients were then divided into 3 groups according to age (younger, middle-aged and elderly), and variables were compared among groups. The younger group consisted of patients ≤ 50 years, the middle-aged group included patients from 51 to 70 years, and the elderly group included those older than 70 years. Coronary arteriograms and percutaneous coronary intervention (PCI: thrombolysis, coronary angioplasty and/or coronary stenting) were performed within 90 min after patient arrival at the hospital. The success of the PCI was defined as achieving a Thrombolysis in Myocardial Infarction (TIMI) flow grade of 3 [1]. Collateral circulation was graded using a semiquantitative scale depending on the angiographic findings of the occluded artery using the best injection [2]. Grades 1 to 3 defined that the collateral circulation was present.

Data analysis. The SAS software program (SAS Institute Inc., Cary, NC, USA) was used for data analysis. An analysis of variance and then Bonferroni's modified *t*-test were applied to compare group means for continuous variables, and the chi-square test with Yates' correction was used to compare the incidence of discrete variables with a normal distribution, and the Mann Whitney U test was used for abnormally distributed variables. Multivariate logistic regression analysis was performed to evaluate the independent importance of the variables for predicting in-hospital death.

The research protocol was approved by the ethics committee of Iwakuni Clinical Center and all patients

gave informed consent.

Results

Of the 888 patients, 99 belonged to the younger group, 435 to the middle-aged group and 354 to the elderly group. The clinical characteristics of the 3 patient groups on admission are represented in Tables 1–3. Almost 60% of patients were male in the elderly group, with progressively higher rates of males in each of the younger groups.

Pulmonary congestion (Killip's criteria 2–4) was observed in half of the elderly patients, which was significantly higher than the number observed in the younger and middle-aged groups ($p = 0.005$ and $p < 0.001$, respectively).

Patient history. About 5% of the patients in each group had experienced a previous MI. Hypertension, diabetes mellitus and dyslipidemia, including hypercholesterolemia and hypertriglyceridemia were less frequently observed in the elderly group than in the middle-aged group, but the elderly group suffered from previous cerebrovascular accidents more frequently than the other 2 groups. Thirty-five percent of the elderly patients smoked, which was significantly less than the percentage in the other 2 groups. CKD was more common in the elderly group than in the other 2 groups, and the rate of CKD increased with age.

ECG and coronary arteriographic findings. Atrial fibrillation appeared most frequently in the elderly group (Table 2). The incidence of arrhythmia in the elderly group was almost double and 5 times that of the middle-aged and young groups, respectively.

Table 1 Patient characteristics

	Younger group (n = 99)	Middle-aged group (n = 435)	Eldery group (n = 354)
Age (mean ± SD)	44 ± 5	62 ± 5	78 ± 5
Gender, male	91 (92%)†	326 (75%)*	211 (60%)
Pulmonary congestion	36 (36%)*	154 (35%)*	186 (53%)
Previous myocardial infarction	5 (5.1%)	22 (5.1%)	15 (4%)
Hypertension	33 (33%)	171 (39%)*	132(37%)
Diabetes mellitus	10 (10%)‡	106 (24%)*	59 (17%)
Dyslipidemia	46 (46%)	232 (53%)*	143(40%)
Hyper cholesterolemia	22 (22%)*	78 (18%)*	39(11%)
Hyper LDL cholesterolemia	17 (17%)	57 (13%)	39 (11%)
Hypo HDL cholesterolemia	39 (39%)	178 (41%)	152 (43%)
Hyper triglycerolemia	32 (32%)†	87 (20%)*	28 (8%)
Smoking	85 (86%)†	262 (60%)*	125 (35%)
Previous cerebral infarction	0 (0%)†	31 (7%)*	47(13%)
CKD	9 (9%)†	100 (23%)*	181 (51%)
Death	4 (4%)*	35 (8%)*	85 (24%)

CKD, chronic kidney disease. *$p < 0.05$ vs. elderly group, †$p < 0.05$ vs. elderly group and middle-age group, ‡$p < 0.05$ vs. middle-age group.

Table 2 Findings of ECG on admission and coronary angiography

	Younger group (n = 99)	Middle-aged group (n = 435)	Elderly group (n = 354)
Anterior wall involvement	51 (52%)	201 (46%)*	184 (52%)
Atrial fibrillation	2 (2%)*	23 (5%)*	34 (10%)
RBBB	9 (9%)	47 (1%)*	60 (17%)
LAD involvement	50 (51%)	186 (43%)	146 (41%)
Significant collateral	10 (10%)*	71 (16%)	57 (16%)
Successful PCI	92 (94%)*	343 (88%)*	221 (81%)

RBBB, right bundle branch block; LAD, left anterior descending coronary artery; PCI, percutaneous coronary intervention.
*$p < 0.05$ vs. elderly group

Table 3 Laboratory data on admission

	Younger group (n = 99)	Middle-aged group (n = 435)	Elderly group (n = 354)
Peak CK (IU/l)	1,526 ± 2,062*	1,222 ± 1,408	1,027 ± 1,172
Total cholesterol (mg/dl)	201.8 ± 37.1*	198.2 ± 41.3*	184.8 ± 37.7
LDL cholesterol (mg/dl)	133.4 ± 33.8*	132.4 ± 38.2*	122.6 ± 34.6
HDL cholesterol (mg/dl)	44.0 ± 13.3	43.1 ± 12.1*	44.9 ± 11.7
Triglyceride (mg/dl)	124.9 ± 57.4*	114.9 ± 64.3*	89.9 ± 40.6
Uric acid (mg/dl)	5.1 ± 1.5	5.3 ± 2.0	5.5 ± 1.9
C-reactive protein (mg/dl)	0.48 ± 0.70*	0.45 ± 068*	0.65 ± 0.74
eGFR (ml/min/1.73m^2)	96.7 ± 62.3†	75.7 ± 33.8*	62.8 ± 37.6

Data are represented by means ± standard deviations.
CK, creatine kinase; LDL, low-density lipoprotein; HDL, high-density lipoprotein; eGFR, estimated glomerular filtration ratio.
*$p < 0.05$ vs. elderly group, †$p < 0.05$ vs. elderly group and middle-age group.

The incidence of anterior wall involvement on the ECG was not different between the elderly (52%) and young (52%) groups, and was slightly lower in the middle-aged patients (46%, $p < 0.001$ vs. the elderly group).

Coronary arteriography was conducted in 273 (77%) out of the 354 elderly patients, 388 (89%) of the 435 middle-aged, and 98 (99%) of the 99 younger patients. Almost half of the patients examined in each group showed involvement of the anterior descending coronary artery (LAD), and successful PCI was achieved in 81% of the elderly patients. This success rate was significantly lower than those in the middle-aged (88%) and younger (93%) groups.

Laboratory examinations. The serum peak CK level varied widely in each group (Table 3). The mean value of the peak CK of the elderly group was significantly lower than that in the younger group, but compared to the middle-aged group, the peak serum level of this enzyme did not show any significant difference. The serum levels of total cholesterol, LDL cholesterol and triglycerides on admission in the elderly group were significantly lower than each lipid level in the middle-aged and younger groups ($p < 0.05$); these variables were not significantly different between the middle-aged and younger groups. The serum HDL cholesterol level was higher in the elderly group than in the other 2 patient groups.

The high-sensitivity C-reactive protein (CRP) level was less than 1.0 mg/dl on average in all 3 patient groups, but was significantly higher in the elderly group than in the other 2 groups. The eGFR was significantly lower in the elderly group, and there was a decrease in eGFR with increasing age.

In-hospital prognosis and factors affecting in-hospital death. Twenty-four percent of the elderly patients died during their stay in the hospital. The incidence of death in the elderly group was 3 times higher than in the middle-aged group and 6 times higher than in the younger group. When limiting the data to cardiac death, however, the in-hospital death of the elderly group decreased from 24.0% to 12.2%, which was slightly, but still significantly, higher than that in the middle-aged group (Table 1).

A multivariate logistic regression analysis applied to the data from all 888 patients revealed that 4 variables including age, pulmonary congestion, CKD and the high-sensitivity serum CRP level independently predicted an adverse in-hospital prognosis. Signs of pulmonary congestion in chest X-ray examination were related to an in-hospital mortality rate 29.3 times higher than that in patients without pulmonary congestion. Being older than 71 years of age was also a strong predictor for in-hospital death. The presence of CKD was related to about triple the risk of in-hospital death compared to that in patients without CKD.

When the data analysis was limited to each of the 3 age groups, significant independent variables for predicting in-hospital death were as follows: none in the younger group, pulmonary congestion and a high uric acid level in the middle-aged group and pulmonary congestion and a high CK level in the elderly group.

Discussion

This investigation represents the different clinical characteristics of elderly patients with acute myocar-

dial infarction compared to middle-aged and younger patients. Goch *et al.* previously demonstrated a high prevalence of diabetes and hypertension and a low prevalence of smoking and dyslipidemia in elderly MI patients [3]. Zimmermann *et al.* also reported a high prevalence of hypertension and diabetes in elderly MI patients, and reported that more elderly than younger patients had a previous history of cerebral infarction, in agreement with the present study [4]. Scoenenberger *et al.* suggested that dyslipidemia and smoking are prevalent in younger MI patients [5]. Our results also showed patterns of dyslipidemia and smoking similar to those observed in other studies, although the prevalence of hypertension and diabetes were lower in elderly than in younger patients. A national nutrition survey has revealed that the elderly have lower serum total cholesterol levels and smoking rates than young and middle-aged adults [6]. The present findings may thus also reflect the characteristics of the entire population of MI patients. The national nutrition survey also showed that the prevalence of hypertension and diabetes increases with age, and is highest in the elderly aged 85 years or older. It remains unclear why the present findings did not reflect the characteristics of the entire MI population with regard to diabetes and hypertension. Given that many non-ST-elevation MI patients are diabetic and/or hypertensive, the inclusion of only ST-elevation MI patients in the present study might explain the discrepancy.

The in-hospital mortality rate was higher in the elderly group than in the other groups in this study. This is probably because many of the elderly patients had experienced a previous infarction, and the success rate for coronary artery intervention was relatively low in the elderly group, consistent with the findings reported by Scoenenberger *et al.* [4]. Collateral blood flow was well developed in elderly MI patients, but did not affect their prognosis. A low degree of early CK washout due to the low rate of success of PCI and well-developed collateral blood flow might have been responsible for the low peak CK level in the elderly group.

Other factors may have been associated with the poor prognosis in elderly MI patients. Elderly patients have ambiguous symptoms, and may thus require a longer time before arrival at the hospital, resulting in a lower rate of coronary angiography (CAG) being performed, and with a prolonged time from onset of symptoms before it is performed [3]. In addition, multivessel disease is common in elderly MI patients [4]. Studies have suggested that even in elderly patients, successful PCI should provide prognostic results comparable to those achieved in younger patients [7]. However, the difficulty of obtaining vascular access and the high frequency of poor renal function in the elderly often leads to difficulty in performing PCI and a high incidence of post-procedural complications, suggesting the need for patient-specific measures [8–10].

Our study demonstrated that the eGFR was significantly higher and the CKD level was significantly lower in the elderly group. These findings may also reflect the known decrease in GFR associated with increased age, and the greater ratio of females in the elderly group in our study [11]. Renal failure is known to be a sign of poor prognosis in both the short and long term for patients with ischemic heart disease [12]. In our study, CKD was found to be an independent predictor of a poor outcome after acute MI. Oldgren suggested that the increase in cardiovascular risk for people with renal disease is only partially explained by the presence of concomitant classic risk factors, since the association between renal dysfunction and adverse cardiovascular outcomes persists after statistical adjustment for these covariates [13]. The serum phosphate concentration was found to be inversely related to kidney function when the GFR was $< 60\,ml/min/1.73m^2$ [14]. Vascular calcification has been postulated as the link between hyperphosphatemia and adverse outcomes in the setting of kidney disease, and may be accelerated by abnormal calcium levels and hyperparathyroidism [15].

The present study found a higher prevalence of atrial fibrillation (AF) in the elderly group than in the other groups. Scoenenberger *et al.* also reported a low prevalence of AF in younger patients, without mentioning the significance of this observation [5]. The prevalence of AF has been shown to increase with age [16]. The high AF prevalence in elderly MI patients in the present study might thus also reflect the prevalence of AF in the entire population. Takahashi *et al.* have demonstrated that patients with AF exhibit decreases in exercise-induced, endothelium-dependent vasodilatation resulting from reduced production or activity of NO on exertion [17]. NO has been shown

to exert anti-thrombotic activity by reducing coronary arterial tonus. This suggests that the presence of AF in elderly MI patients not only increases their risk of thrombosis, but also promotes arteriosclerosis and thrombus formation.

Since MI in the elderly is associated with poor prognosis, prevention is important. In young to middle-aged adults, active intervention to correct coronary risk factors, such as dyslipidemia, results in the primary prevention of cardiovascular events [18]. In the elderly, on the other hand, active use of lipid-lowering therapies leads to secondary prevention of cardiovascular events [19]. The advantage of performing early intervention to correct coronary risk factors is supported by the suggested importance of the duration of exposure to these factors. At the same time, it is still unclear whether therapeutic intervention to correct coronary risk factors would lead to primary prevention of cardiovascular events in the elderly who are receiving such intervention for the first time, as reports have been published where the mortality rate conversely increased in elderly patients with hypertension [20]. With regard to intervention for dyslipidemia, since lipid levels were generally lower in the elderly group than in other groups, it is difficult to set a threshold lipid level for determining whether to perform intervention. A recent report has suggested the effectiveness of intervention with a lipid-lowering therapy for the primary prevention of cardiovascular events in normolipidemic patients with high serum CRP levels [21]. Badran *et al.* have also suggested that differences exist in the significance of increased hCRP levels between young or middle-aged patients and elderly patients [22]. More specifically, elderly patients exhibited a greater increase in CRP than young and middle-aged patients at the onset of AMI. Given these findings, they speculated that the CRP levels are related to the degree of extension of coronary lesions; younger patients tended to exhibit rapid extension of small lesions, while elderly patients tended to have slower-growing extensive coronary lesions. These observations suggest that providing therapeutic intervention after estimating the degree of extension of coronary lesions based on the CRP levels, instead of lipid levels, may also be beneficial for elderly patients. Prudence is needed in making clinical judgments based on a single measurement of CRP, which is affected by various pathological conditions and can rapidly change within a short period of time. Further studies of prevention of cardiovascular events should be conducted in elderly patients in a prospective fashion.

Study limitation. Our data did not include information on the patient's prior treatment with aspirin, statins, β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists, all factors shown to influence mortality from AMI and the laboratory data on admission.

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