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In-hospital Outcome in Octogenarians with Acute Coronary Syndrome Undergoing Emergent Coronary Angiography

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SUMMARY

Very elderly patients have higher mortality rates than younger patients after acute coronary syndrome (ACS). However, the mechanism by which increasing age contributes to such mortality remains unclear. In addition, the efficacy and safety of invasive coronary procedures for octogenarians with ACS have not been well established.

We compared the clinical characteristics and in-hospital outcome of 193 octogenarians (mean age, 83 years) with those of 1,462 younger patients (mean age, 64 years) with ACS who underwent emergent coronary angiography. Octogenarians included a greater number of females, had higher rates of cerebrovascular disease and multivessel disease, a higher Killip class, a higher Forrester class, and lower rates of smoking, diabetes, and hypercholesterolemia than the younger subjects. Interventions, including percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG), were performed less frequently in octogenarians than in younger patients (88.0% versus 90.8%). The procedural success rate in octogenarians did not differ from that in younger patients. However, the in-hospital mortality rate for the octogenarians was about three times higher than for the younger patients (19.2% versus 6.9%). Multivariate analysis revealed that the predictors of in-hospital mortality in the octogenarians were a higher Killip class and a higher Forrester class.

Octogenarians with ACS had fewer coronary risk factors and a similar success rate for the intervention, but had more greatly impaired hemodynamics and higher in-hospital mortality than the younger patients. Therefore, impaired myocardial reserve may contribute to a large portion of in-hospital deaths in octogenarians with ACS. (Jpn Heart J 2003; 44: 11-20)

Key words: Acute coronary syndrome, Octogenarian, Coronary angiography

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INCREASING age is associated with higher mortality following acute coronary syndrome (ACS).¹⁻⁴⁾ However, the mechanism by which increasing age contributes to mortality remains unknown. In addition, the therapeutic strategies for elderly patients have not been well established. Although thrombolytic therapy has been shown to improve survival in the elderly,^{5,6)} several studies have shown that primary percutaneous transluminal coronary angioplasty (PTCA) is superior for elderly patients.^{1-3,7)} However, the safety and efficacy of invasive coronary procedures (angiography, PTCA, and coronary artery bypass grafting (CABG)) are unclear in very elderly patients. As life expectancy continues to increase, we expect to encounter a significant increase in the number of patients with ACS who are at least 80 years old. Therefore, we investigated the clinical characteristics and in-hospital outcome in octogenarians with ACS who had undergone emergent coronary angiography.

METHODS

Patients: We retrospectively analyzed the data of 1,655 consecutive patients who presented with ACS, including myocardial infarction and unstable angina, and had undergone emergent coronary angiography between January 1995 and December 1999 at the hospitals participating in this study. Electrocardiographic criteria included persistent or transient ST elevation or a depression of more than 0.5 mm. Acute myocardial infarction (AMI) was considered to have occurred if the level of creatine kinase MB isoenzyme was above normal and comprised at least 3 percent of the total creatine kinase level. If the creatine kinase MB level had not been measured, the total creatine kinase level had to be more than twice the upper limit of the normal range. Significant stenosis was defined as a $\geq 75\%$ reduction in coronary artery diameter. Procedural success of PTCA was defined as achieving stenosis of less than 75% of the residual diameter with Thrombolysis In Myocardial Infarction (TIMI) trial grade 3 flow. A bleeding complication was defined as an intracranial hemorrhage or severe bleeding requiring a blood transfusion.

Statistical analysis: The clinical characteristics and in-hospital outcome were compared between the octogenarian cohort and patients less than 80 years old. In-hospital mortality was the primary end-point. Statistical testing was performed using the chi-square test for categorical variables and the *t* test for continuous variables. We subsequently performed multivariate logistic regression analysis for in-hospital deaths along with variables that were significant in the univariate analysis. A *P* value < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics: The baseline clinical characteristics of the patients are presented in Table I. Of the 1655 consecutive patients, 1,462 (88%) were less than 80 years old (mean 63 years) and 193 patients (12%) were greater than 80 years old (mean 83 years). Octogenarians were more likely to be women and had a higher rate of prior cerebrovascular disease, a higher Killip class, and a higher Forrester class at presentation (Table I). Coronary risk factors such as diabetes, smoking, and hypercholesterolemia were less common and diastolic blood pres-

Table I. Baseline Characteristics of Patients Studied

| | Age≥80 (n=193) | Age<80 (n=1462) | P value |
|------------------------------------|-------------------|--------------------|---------|
| Age (year) | 83.4±2.8 | 63.5±10.2 | <0.0001 |
| Female sex | 56.5 | 21.5 | <0.0001 |
| Myocardial infarction (%) | 86.9 | 81.4 | NS |
| Unstable angina (%) | 13.1 | 18.6 | |
| ST elevation (%) | 78.9 | 72.6 | NS |
| Hypertension (%) | 52.9 | 44.4 | NS |
| Diabetes (%) | 27.6 | 34.1 | 0.0146 |
| Smoking (%) | 28.6 | 59.5 | <0.0001 |
| Hypercholesterolemia (%) | 25.3 | 36.9 | 0.0062 |
| Prior myocardial infarction (%) | 13.2 | 10.4 | NS |
| Prior angina (%) | 36.1 | 38.3 | NS |
| Prior congestive heart failure (%) | 6.3 | 3.8 | NS |
| Cerebrovascular disease (%) | 17.3 | 9.4 | 0.0035 |
| Prior CABG (%) | 1.1 | 2.3 | NS |
| Prior PTCA (%) | 2.1 | 7.3 | 0.0245 |
| Peripheral vascular disease (%) | 3.7 | 2.7 | NS |
| Heart rate (beats/min) | 78.3±20.5 | 77.8±19.7 | NS |
| Systolic blood pressure (mmHg) | 128.6±29.7 | 129.5±27.4 | NS |
| Diastolic blood pressure (mmHg) | 68.5±14.5 | 74.6±29.6 | 0.0062 |
| Killip class (%) | | | 0.0010 |
| 1 | 116 (60.1) | 1009 (69.0) | |
| 2 | 16 (8.3) | 77 (5.3) | |
| 3 | 8 (4.1) | 31 (2.1) | |
| 4 | 19 (9.89) | 63 (4.3) | |
| unknown | 34 (17.6) | 282 (19.3) | |
| | | | <0.0001 |
| Forrester class (%) | | | |
| 1 | 47 (24.4) | 472 (32.3) | |
| 2 | 21 (10.9) | 140 (9.6) | |
| 3 | 17 (8.8) | 38 (2.6) | |
| 4 | 15 (7.8) | 23 (1.6) | |
| unknown | 93 (48.2) | 789 (54.0) | |

sure was lower in the octogenarians. On the other hand, heart rate and systolic blood pressure did not differ between the two groups.

Angiographic characteristics and intervention: The octogenarians had a higher rate of multivessel disease. There were no significant differences in the prevalence of left main lesions or culprit lesions between the two groups (Table II). Interventions, including PTCA and CABG, were performed in 88.0% of the octogenarians and 90.8% of the younger patients. Thus interventions were performed less frequently in octogenarians than in younger patients ($P=0.0104$). The rate of procedural success was 89.8% in the octogenarians and 93.2% in the younger patients, which did not differ significantly (Table III).

Outcome: The older the patient, the higher the rate of in-hospital mortality (Figure 1). The in-hospital mortality rate was about three times higher in the octogenarians than in the younger patients (19.2% versus 6.9%), and the rate of bleeding complications was six times higher (3.9% versus 0.6%). The rate of recurrent

Table II. Angiographic Characteristics of Patients Studied

| | Age \geq 80 (n=193) | Age<80 (n=1462) | P value |
|--------------------------------|--------------------------|--------------------|---------|
| No. of diseased vessels (%) | | | 0.0296 |
| 0 | 1.0 | 2.3 | |
| 1 | 38.3 | 47.7 | |
| 2 | 30.1 | 27.8 | |
| 3 | 29.5 | 20.9 | |
| unknown | 1.0 | 1.3 | |
| Left main coronary disease (%) | 4.7 | 3.5 | NS |
| Culprit lesion * (%) | | | |
| Anterior descending | 44.3 | 53.4 | NS |
| Circumflex | 18.2 | 12.6 | |
| Right | 37.5 | 34.0 | |

* Culprit lesions were assessed when patients had one vessel disease.

Table III. Clinical Outcome

| Outcome | Age \geq 80 (n=%) | Age<80 (n=%) | Odds Ratio (95% CI) | P value |
|--------------------------|------------------------|-----------------|---------------------|---------|
| Death | 37/193 (19.2) | 101/1462 (6.9) | 3.20 (2.12-4.82) | <0.0001 |
| Procedural success | 123/137 (89.8) | 967/1038 (93.2) | 0.65 (0.35-1.18) | NS |
| Bleeding complication | 6/154 (3.9) | 7/1113 (0.6) | 6.45 (2.14-19.61) | 0.0022 |
| Recurrent ischemic event | 16/154 (10.4) | 83/1115 (7.4) | 1.44 (0.82-2.53) | NS |

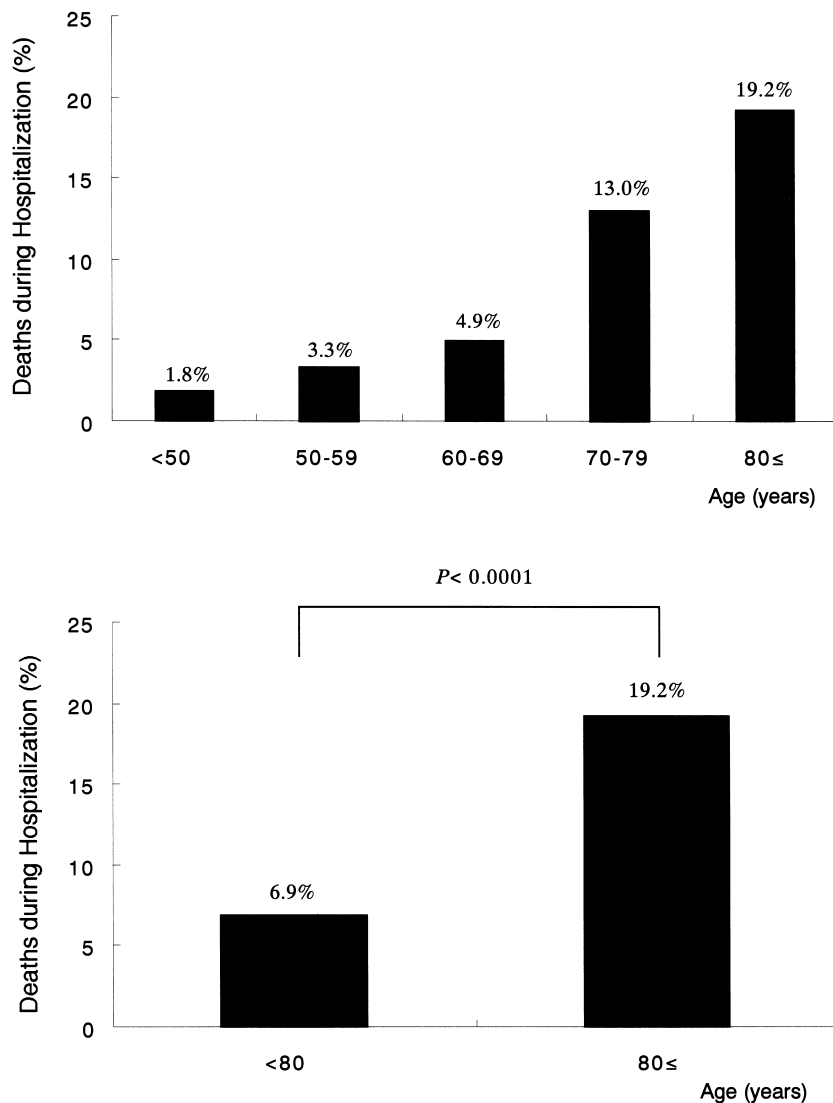


Figure 1. Rates of death during hospitalization for acute coronary syndrome according to age.

ischemic events between the two groups did not differ (Table III). The octogenarians had a higher in-hospital mortality rate with any type of ACS than the younger patients (Figure 2). Of the deaths, 60.6% occurred within 7 days, 85.6% within 35 days, and the others after 35 days.

Cause of death: Of the deaths, about half were due to heart failure, and the causes of death were not different between the two groups (Table IV). Other

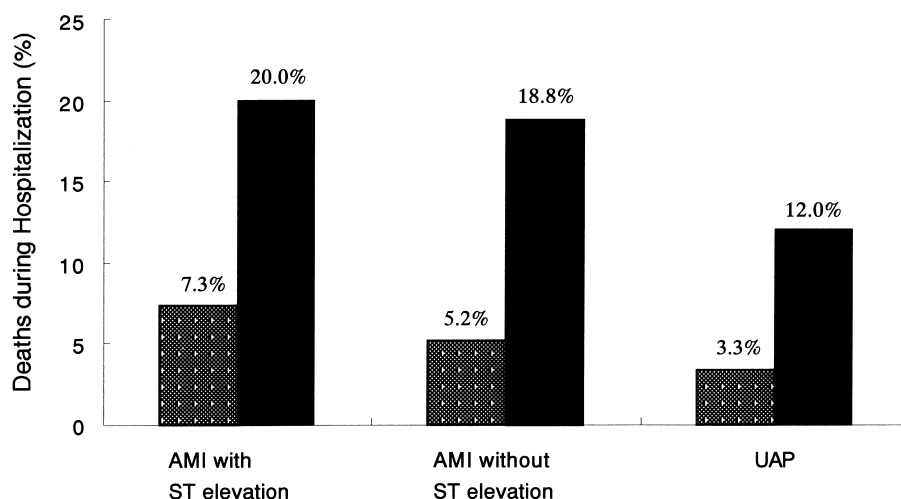


Figure 2. Rates of death during hospitalization for acute coronary syndrome (ACS) among octogenarians and younger patients, according to type of ACS. Gray bar, younger patients; black bar, octogenarians. AMI=acute myocardial infarction; UAP=unstable angina pectoris.

Table IV. Cause of Death

| | Age \geq 80 (n=193) | Age<80 (n=1462) | P value |
|----------------------|--------------------------|--------------------|---------|
| Cause of death-n (%) | NS | | |
| Heart failure | 18 (48.6) | 53 (52.5) | |
| Arrhythmia | 3 (8.1) | 10 (9.9) | |
| Other | 5 (13.5) | 15 (14.9) | |
| Unknown | 11 (29.7) | 23 (22.8) | |

causes of death included cardiac rupture (8 cases), pneumonia (6 cases), renal failure (2 cases), cardiac tamponade with unknown cause (1 case), hepatic failure (1 case), mesenteric artery embolus (1 case), and disseminated intravascular coagulation (1 case).

Predictors of in-hospital mortality among octogenarians: Among the octogenarians, univariate analysis revealed that predictors of in-hospital mortality were greater age, lower systolic blood pressure, higher Killip class, and higher Forrester class (Table V). In multivariate analysis, only a higher Killip class ($P=0.003$) and higher Forrester class ($P=0.046$) remained as independent predictors of in-hospital mortality.

Table V. Univariate Predictors of In-hospital Mortality

| Variables | Odds Ratio (95% CI) | P value |
|-----------------|---------------------|---------|
| Age (/year) | 1.17 (1.03-1.32) | 0.0138 |
| SBP (/mmHg) | 0.98 (0.97-0.99) | 0.0016 |
| Killip class | | |
| I | 1 | |
| II | 8.10 (2.34-28.02) | |
| III | 4.50 (0.78-26.01) | <0.0001 |
| IV | 29.25 (8.78-97.59) | |
| Forrester class | | |
| I | 1 | |
| II | 4.84 (0.41-56.65) | |
| III | 19.17 (2.04-179.91) | 0.0005 |
| IV | 23.00 (2.42-219.00) | |

SBP=systolic blood pressure

DISCUSSION

Previously reported reasons for increased mortality among elderly patients were multifactorial, including a high prevalence of comorbidity,^{8,9)} more diffuse multivessel disease,^{4,8,10)} delayed presentation,¹¹⁾ greater risk of cardiac rupture,¹²⁾ insufficient use of beta-blocker¹³⁾ and aspirin,¹⁴⁾ and less aggressive treatment.¹⁵⁾ In this study, in-hospital mortality in the octogenarians with ACS was about three times higher than in the younger patients in spite of a similar rate of successful intervention. This suggests that impaired myocardial reserve and other comorbid conditions contributed to the worse prognosis among the octogenarians. There were no differences in the causes of in-hospital death between the two groups, suggesting that octogenarians have higher mortality from both cardiac decompensation and noncardiac multisystem dysfunction. The greater prevalence of multivessel disease and impaired myocardial reserve may be the cause of the more greatly impaired hemodynamics among the older patients. The major factors contributing to dysfunction of the aging heart are a decreased beta-sympathetic response and increased impedance to left ventricular ejection.¹⁶⁾ Moreover, the aging heart with its modest hypertrophy and consequent prolonged relaxation is perhaps more sensitive to ischemic injury with more profound consequences.¹⁶⁾

Although reperfusion therapy reduces the infarction area and preserves left ventricular function, most clinicians are reluctant to use thrombolytic therapy in the elderly for fear of serious hemorrhagic complications.¹¹⁾ Primary angioplasty has higher rates of vessel patency and TIMI grade 3 flow relative to thrombolytic therapy.¹⁷⁾ Therefore, to preserve cardiac function and improve prognosis, angioplasty should be the treatment of choice in octogenarians with ACS. In fact, sev-

eral studies have shown a lower mortality rate when elderly patients are treated with primary PTCA compared with thrombolytic therapy.^{1-3,7)} The Fibrinolytic Therapy Trialists (FTT) overview¹⁸⁾ showed that the rate of death during days 0 - 35 in patients ≥ 75 years old with AMI was 24.3% in the fibrinolytic group and 25.3% in control patients. Other previous studies reported that mortality reaches $\geq 30\%$ in octogenarian patients with AMI.^{2,9,12)} In this study, in-hospital mortality of the octogenarians with AMI was 19.9%. This suggests that emergent coronary angiography and subsequent intervention may be superior to thrombolysis and routine therapy with antiplatelet agents and heparin alone.

In this study, the octogenarians had about a six times higher rate of bleeding complications than the younger patients (3.7% versus 0.6%), which was higher than that reported in the FTT overview (fibrinolytic group, 1.1%; control, 0.5%).¹⁸⁾ However, we suppose that most of the bleeding complications were access site complications and invasive coronary procedures (angiography and intervention) are relatively safe even in octogenarians.

There is a prevailing notion that the strength of the association of cardiovascular risk factors with the development of coronary heart disease diminishes with advancing age.¹⁹⁾ Consistent with this notion, octogenarians in this study had fewer coronary risk factors, including diabetes, smoking, and hypercholesterolemia. This suggests that very great age in itself is a risk factor of coronary artery disease, and the cause of poor hemodynamics. In this study, poor hemodynamics strongly predict in-hospital death in octogenarians. Therefore, octogenarians who have a high Killip class or high Forrester class require more careful management.

Study limitations: This study has several limitations. First, it was not randomized, and information on the octogenarians for whom emergent coronary angiography was not performed is lacking. Therefore, octogenarians in this study may have had fewer comorbid conditions than those in whom emergent coronary angiography was not performed. Second, we did not determine the prevalence of thrombolytic therapy among these patients, which is a principal therapy for AMI in Western populations. Although the exact prevalence is not known, we feel that the number of patients who received thrombolytic therapy was very small in this study. Third, the prevalence of aspirin, beta-blocker, and angiotensin converting enzyme inhibitor use, which reduces the mortality after AMI,²⁰⁾ was not determined. Fourth, we did not consider PTCA and CABG separately, but rather combined them as one intervention type. Therefore, the prevalence of each therapy among these patients is unknown.

Conclusions: Although there were no significant differences in the rate of success of the intervention, the octogenarians had more greatly impaired hemodynamics and higher in-hospital mortality than the younger patients. We suppose that impaired myocardial reserve contributes to a large portion of in-hospital

deaths and aggressive recanalization strategies (emergent coronary angiography and subsequent intervention) may be effective in improving the prognosis of octogenarians with ACS.

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