Incidence and Mortality of Acute Myocardial Infarction

A Population-Based Study Including Patients With Out-of-Hospital Cardiac Arrest

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Summary

The in-hospital mortality rate of acute myocardial infarction (AMI) is improving. In Japan, little information exists concerning the incidence and mortality of AMI. Therefore, our population-based analysis examined the incidence and mortality rate in AMI cases in individuals that lived in the Matsumoto region in 2002. We studied 169 AMI patients who were admitted within 14 days after a non-out-of-hospital cardiac arrest (non-OHCA group) and 63 patients with an AMI-related out-of-hospital cardiac arrest (OHCA group). The in-hospital mortality rate of the non-OHCA group was 9.5% (reperfusion therapy [+] 3.4%, [-] 22.7%, $P < 0.0001$). The rate of return of spontaneous circulation and the survival rate were 21% and 1.6%, respectively, in the OHCA group. The incidence of AMI in the non-OHCA and OHCA groups combined was 55.2 to 63.1 events/100,000 people annually and the mean age of AMI patients was 70 ± 13 years. The population-based mortality rate of AMI was 34% to 42%. The mortality rate of AMI remains high, and most deaths occur outside of the hospital. Prehospital care may lower the mortality rate of AMI. (Int Heart J 2011; 52: 197-202)

Key words: Acute myocardial infarction, Mortality, Out-of-hospital cardiac arrest, Population-based study

During the past 25 years, the mortality rate of coronary heart disease (CHD) has declined substantially in many Western countries because of successful prevention efforts and improved treatment of CHD and acute coronary syndromes.[1-3] The in-hospital mortality rate of acute myocardial infarction (AMI) has dramatically decreased because of progress in reperfusion therapy and in treating arrhythmias and pump failure. Epidemiological studies and clinical trials show that the 28-day fatality rate of MI among patients that are alive when they reach the hospital has declined to 10% or less.[4,5]

However, the mortality rate is still high for patients in which AMI occurs outside the hospital. Only a few longitudinal studies have analyzed trends in sudden or out-of-hospital cardiac deaths.[6-8] The majority of all CHD deaths are out-of-hospital deaths and are therefore of considerable public health significance. Thus, relatively little is known about trends in sudden out-of-hospital AMI deaths in light of the recent decline in the AMI mortality rate.

In the current study, we analyzed all AMI cases in the Matsumoto region of Japan during a 1-year period. The aim of this study was to investigate and clarify the incidence and mortality rate of all cases of AMI, including out-of-hospital cardiac arrest due to AMI, using a population-based analysis.

Methods

Study populations: We conducted the study in the Matsumoto region (area 1,750 km^2, 420,000 residents) in Nagano prefecture. First, we mailed a letter describing the purpose and procedure of the survey to all 20 general hospitals in the Matsumoto region and we requested the case reports of patients with AMI or patients with out-of-hospital cardiac arrest. Second, we visited all 20 hospitals to identify and examine the data of patients with AMI or patients with out-of-hospital cardiac arrest. Six of these hospitals have coronary arteriographic facilities and are equipped for acute coronary care. We included in the registry all patients examined from January 1, 2002, to December 31, 2002.

Non-OHCA group: We studied all patients admitted within 14 days after the onset of AMI. Patients who had AMI during their hospital stay due to another disease were also included. We combined and analyzed the data of 2 or more hospitals for patients that had been transferred to another hospital. AMI was defined as acute chest pain lasting less than 12 hours with new ST-segment elevation greater than 1 mm noted in 2 contiguous leads or new left branch bundle block and levels of cardiac enzymes (total creatinine kinase [CK] or CK-MB) that were at least twice the upper limit of the reference range.

OHCA group: We investigated cases of AMI from all out-of-hospital cardiac arrests events. We defined cardiac arrest as the cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation. We excluded patients with out-of-hospital cardiac arrest caused by trauma, drowning, drug overdose, asphyxia, or exsanguination. We collected data retrospectively and included all core data recommended in the Utstein-style reporting guidelines for cardiac arrests. The core

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data were sex, age, initial cardiac rhythm, time course of resuscitation, type of bystander-initiated cardiopulmonary resuscitation (CPR), return of spontaneous circulation, hospital admission, and in-hospital mortality.[9] We determined the cause of cardiac arrest on the basis of the medical chart filled out by the attending physician in collaboration with emergency medical service rescuers.

We made a diagnosis of AMI in the OHCA group by using the criteria of the WHO-MONICA project.[10] AMI patients in the OHCA group were classified as Fatal 1 (F1) if they had a definite AMI and as Fatal 2 (F2) if they had a possible AMI or coronary death for definition 2. Collectively, F1 and F2 patients and patients who were unclassifiable were classified as Fatal 9 (F9) for definition 1. Definition 2 was more restrictive and excluded the unclassifiable cases.

Incidence and mortality of AMI: We estimated the incidence and mortality of AMI by combining the non-OHCA and OHCA groups. We calculated the event rates for definition 1 and for definition 2. We used the data of definition 2 to analyze seasonal and circadian differences in the onset of AMI.

Data analysis: All continuous data are expressed as the mean ± the standard deviation (SD), and discrete variables are expressed as the number and percentage. We used the unpaired Student's *t* test for statistical analyses of the 2 groups. Differences among the 3 groups were analyzed by ANOVA. We compared dichotomous variables using the chi-square test. Statview for Macintosh was used for statistical analysis. We considered a probability (P) value of less than 0.05 statistically significant.

Results

Non-OHCA group: The non-OHCA group was composed of 169 patients (male 121, female 48). Table I lists the baseline characteristics of patients in the non-OHCA group. The median time from onset to admission was 150 minutes. Seventy-nine percent of patients had Killip's classification I and the in-hospital mortality rate was 9.5%. The factors that influenced AMI mortality in the non-OHCA group are shown in Figure 1. The mortality rate in patients with Killip's classification III and IV was significantly higher than the mortality rate in patients with Killip's classification I. It was unknown whether 6 patients out of 169 had undergone revascularization treatment. Among the remaining 163 cases, 119 patients (73%) received prompt revascularization treatment. Of the 16 patients (9.5%) that died of AMI, there were 4 patients treated with reperfusion therapy, and 10 were treated without revascularization. It is unclear whether the remaining 2 patients were treated with revascularization. The mortality rate of patients that were treated with reperfusion therapy was significantly lower than patients without revascularization treatment (3.4% versus 22.7%, $P < 0.0001$). There were no significant differences in the mortality rate between different methods of admission or between genders.

OHCA group: An out-of-hospital cardiac arrest occurred in 227 patients. The rate of return of spontaneous circulation was 16% and the survival rate, which refers to successful discharge from hospital to home, was 1%. Figure 2 shows the clinical diagnosis of 227 patients with an out-of-hospital cardiac arrest. Of these 227 patients, 63 (28%) were diagnosed with definite or possible AMI (definition 2 in WHO-MONICA criteria), 36 patients (17%) were diagnosed with congestive heart failure caused by diseases other than AMI, and 33 patients (15%) had an out-of-hospital cardiac arrest of undetermined cause. Thus, we enrolled 96 patients that met WHO-MONICA project definition 1 in the OHCA group and 63 of these patients met WHO-MONICA project definition 2. The rate of return of spontaneous circulation and the survival rates of the 227 out-of-hospital cardiac arrest patients are shown in Figure 3. In the AMI patients, the rate of return of spontaneous circulation was 21% and the survival rate was 1.6%. Patients hospitalized for causes other than arrhythmia had a poor prognosis and the survival rate was very low.

The type of electrocardiogram, such as ventricular fibrillation and/or tachycardia (VF/VT), pulseless electrical activity (PEA), or asystole did not significantly affect the prognosis of out-of-hospital cardiac arrest patients (Figure 4). Among the 227 patients with an out-of-hospital cardiac arrest, the event was witnessed in 51% patients and 31% of these patients received bystander-initiated CPR. The rate of return of spontaneous circulation (ROSC) and the survival rate were significantly higher in patients whose AMI was witnessed. Bystander CPR did not significantly influence either the ROSC or survival rate.

Table I. Baseline Characteristics of Patients in the Non-OHCA Group

n (male/female)	169 (121/48)
Age (years)	70 ± 12
Method of admission (%)	
Directly	57
Indirectly	43
Time from onset to admission (minutes)	282 ± 480
Killip classification (I/ II/ III/ IV) (%)	79/6/9/9
Treatment with revascularization (%)	73 (PCI 98%, CABG 1%, Thrombolysis 1%)
In-hospital mortality rate (%)	9.5

Values of age and time from onset to admission are mean ± SD. OHCA indicates out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; and CABG, coronary artery bypass grafting.

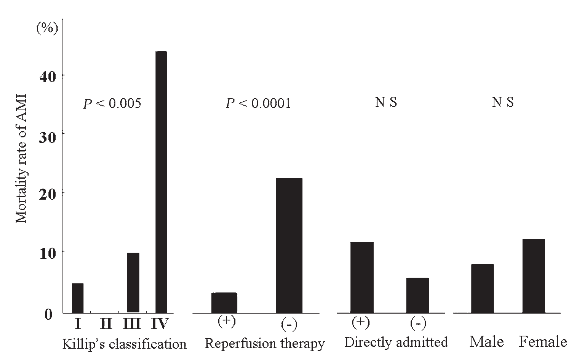

Figure 1. Factors that influenced the AMI mortality rate in the non-OHCA group. The mortality rate in patients with Killip classification III and IV was significantly higher than in patients with Killip classification I. The mortality rate of patients treated with revascularization therapy was significantly lower than that of patients not treated with revascularization. AMI indicates acute myocardial infarction and NS, not significant.

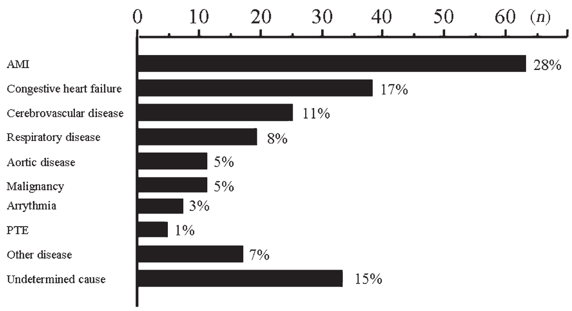

Figure 2. Clinical diagnosis of 227 out-of-hospital cardiac arrest patients. Of 227 patients, 63 (28%) were diagnosed with an AMI and enrolled in the OHCA group. We presumed that 33 patients (15%) had an out-of-hospital cardiac arrest. AMI indicates acute myocardial infarction and PTE, pulmonary thromboembolism.

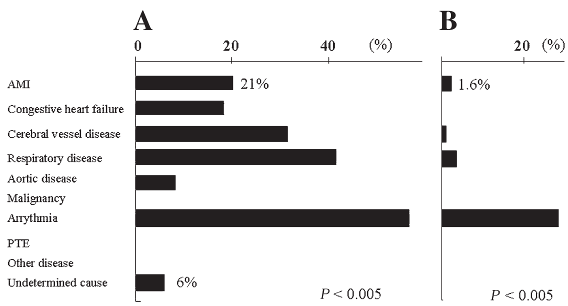

Figure 3. The prognosis of an out-of-hospital cardiac arrest. The rate of return of spontaneous circulation (**A**) in patients with an AMI (ie, the OHCA group) was 21% and the survival rate (**B**) was 1.6%. The survival rate of patients hospitalized for causes other than arrhythmia was very low. AMI indicates acute myocardial infarction and PTE, pulmonary thromboembolism.

Table II. Incidence and Mortality of AMI (the Non-OHCA and OHCA Groups Combined)

A

	definition 2	definition 1
Population (*n*)	420,000	420,000
Non-OHCA group (*n*)	169	169
OHCA group (*n*)	63	96
Rate of incidence of AMI	55.2/100,000/year	63.1/100,000/year

B

	definition 2	definition 1
Death in Non-OHCA group (*n*)	16	16
Death in OHCA group (*n*)	62	95
Mortality rate (%)	(16 + 62)/(169 + 63) = 34%	(16 + 95)/(169 + 96) = 42%

AMI indicates acute myocardial infarction and OHCA, out-of-hospital cardiac arrest.

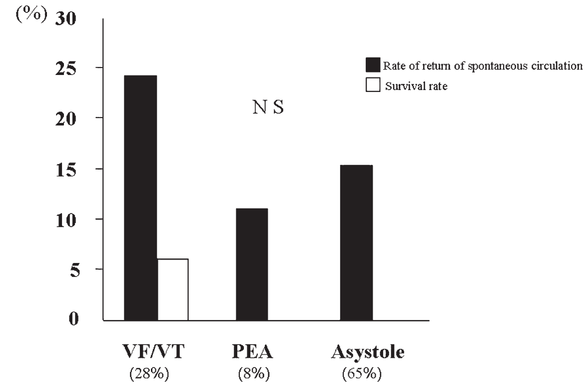

Figure 4. The prognosis of out-of-hospital cardiac arrest across different types of electrocardiogram. There were no significant differences in prognosis across the different types of electrocardiogram such as VF and/or VT, PEA, and asytole. VT indicates ventricular tachycardia; VF, ventricular fibrillation; PEA, pulseless electrical activity; and NS, not significant.

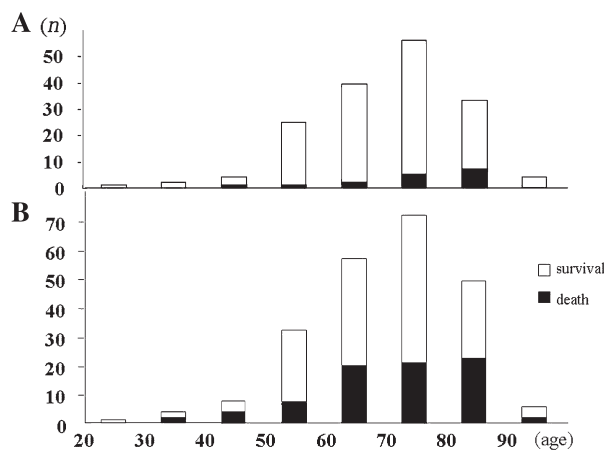

Figure 5. Age distribution and mortality rate of AMI. Slightly higher mortality rates were observed in elderly patients in both the non-OHCA group (**A**) and all AMI patients (**B**). OHCA indicates out-of-hospital cardiac arrest.

However, the AMI was both witnessed and received bystander-CPR in all survivors.

Incidence and mortality rate of AMI: We calculated the incidence and mortality rate of AMI by combining the non-OHCA and OHCA groups. The incidence of AMI was 55.2 to 63.1 events/100,000 people per year (Table IIA) with a mean age of 70 ± 13 years. The population-based mortality rate of AMI was 34% to 42% (male 31%, female 41%) (Table IIB). The mortality rate was slightly higher in the elderly patients in the non-OHCA group, but this was not significant (Figure 5). When data were standardized using the World Standard Population for the 35-64 year old age group,[11] the annual event rates according to definition 2 and 1 were 41.0 and 46.6 events/100,000 people per year, respectively. Mortality rates were 33.9% and 37.3%, respectively.

Seasonal and circadian differences in AMI onset: Figure 6 shows the seasonal and circadian distribution of AMI onset.

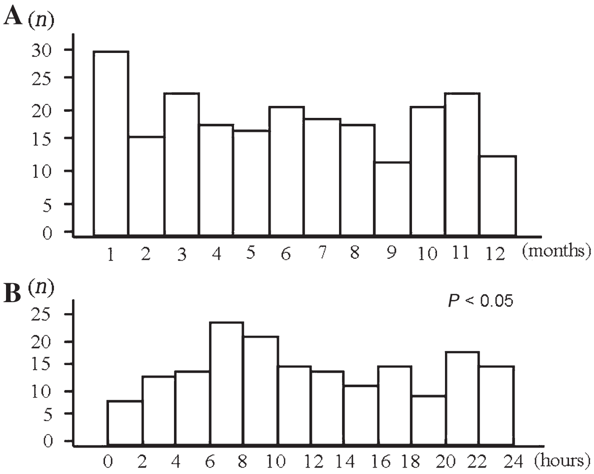

Figure 6. Seasonal and circadian differences in AMI onset. Although the onset of most AMIs occurs in January and in the early morning, there were no significant differences in AMI onset between the months (**A**) or each circadian time (**B**).

There was no significant difference in the onset of AMI between months of the year. The frequency of onset showed a bimodal circadian variation distribution with a primary peak frequency between 6:00 AM and 10:00 AM and with a secondary smaller peak in the evening hours.

Discussion

In this study, the incidence of AMI was 55.2 to 63.1 events/100,000 people per year and the AMI mortality rate was 34% to 42% in all patients. The mortality rate was lower in the non-OHCA group (9.5%) than in the OHCA group. In addition the mortality rate was especially lower in patients treated with reperfusion therapy than in patients without this therapy. Our study demonstrates that the mortality rate of AMI is high, especially in the OHCA group and that prehospital care is important for lowering AMI mortality.

Few studies have reported population-based data on the incidence and mortality of AMI in Japan. A population-based study performed in the cities of Niigata and Nagaoka demonstrated an AMI incidence of 45.8 events/100,000 people per year when data were standardized using the World Standard Population for the 35 to 64 year old age group.[12] According to a 5-year investigation of 9 small to medium workplaces in Osaka, the annual incidence of AMI among men aged 40 to 59 years was 72.0 events/100,000 people per year. A report from Okinawa revealed an annual incidence of 26 per 100,000 in the standard population of Japan, and 31 per 100,000 among individuals aged 35 to 64 years, adjusted for the World Standard Population.[13]

Hirobe, *et al* studied MI and coronary death in 257,440 workers from 76 workplaces in Japan.[14] They found that the age-standardized annual event rate and case fatality rate for men, aged 35 to 64 years, were 40.2 per 100,000 persons and 22.2%, respectively. This analysis was not performed for women because there were so few cases.

Most studies on the incidence and outcome of AMI have been performed in referral hospitals equipped with angiographic facilities and a coronary care unit. It is possible that AMI patients with severe conditions, advanced age, or comorbidities (eg, cerebrovascular disease or malignancy) were not transferred from small clinics or general hospitals to referral hospitals. Thus, these previous studies could have been slightly biased in patient selection. Furthermore, few AMI studies have included both hospital admission patients and out-of-hospital cardiac arrest patients.

In the current study, we studied the outcome of all AMI and OHCA patients in all 20 hospitals in the Matsumoto region. Fourteen of the 20 hospitals did not have angiographic facilities or a coronary care unit, and these hospitals usually transfer acute coronary patients to referral hospitals. We investigated all AMI patients in the region, including patients who were too severely ill for transfer, of advanced age, or with severe comorbidities. Incomplete case ascertainment in our study depended on the rate of admission of AMI patients in the community. Because the Matsumoto region is geographically isolated, almost all AMI patients are admitted into hospitals in this region. Furthermore, because every person in Japan has medical insurance, the rate of patients seeking treatment and admission is extremely high. The hospital referral rate for AMI is also high. Thus, we believe that we detected nearly 100% of all AMI patients with the exception of OHCA patients. We additionally detected all OHCA cases and attempted to precisely diagnose AMI in the OHCA group. Therefore, we believe that our population-based study precisely reflects the incidence and mortality of AMI in Japan.

The incidence of AMI in our study is similar to the incidences in the Niigata and Nagaoka studies. In the WHO-MONICA project, the annual event rates for MI and coronary deaths per 100,000 persons for men aged 35 to 64 years were 500 to 800 in Northern Europe and the United Kingdom and approximately 500 in the United States, and for women, 130 to 250 in Northern Europe and the United Kingdom and approximately 500 in the United States.[15,16] Thus, our data confirm that the incidence of AMI is considerably lower in Japan than in western countries.

The prognosis of patients who undergo reperfusion therapy was significantly better than patients who did not undergo this therapy in the non-OHCA group. Our results confirmed that early reperfusion therapy improves the prognosis for patients with AMI. Fourteen of 20 hospitals in the Matsumoto region do not have angiographic facilities or a coronary care unit. Therefore, it is possible that the survival rates were influenced by differences in the quality of intensive care in each hospital rather than by the effect of reperfusion therapy alone. The most common reasons that patients did not undergo reperfusion therapy were conditions too severe for transfer, advanced age, or comorbidities such as cerebral disease and malignancy. Thus, the differences in survival rates between patients with and without reperfusion therapy may have resulted not only from the effect of reperfusion therapy but also from the patient's baseline characteristics.

Sudden cardiac arrest due to AMI is a leading cause of death in the industrialized world.[17] A strong chain of survival measures (early activation of emergency medical services, early CPR, early defibrillation, and early advanced life support measures) has substantially improved outcomes in several smaller cities such as Seattle (Washington, USA),[18] Goteborg (Sweden),[19] and Rochester (Minnesota, USA).[20] However, the survival rate of out-of-hospital sudden cardiac arrests, including AMI, in large urban populations is generally less than 3%.[21-23] Relatively little is known about trends in sudden out-of-hospital AMI deaths in light of the recent decline in AMI mortality rate.

Consistent with other epidemiological studies, our study confirms that the majority of AMI deaths take place outside of the hospital. A recent study showed that advanced cardiac life support with endotracheal intubation and the administration of intravenous drugs by paramedics did not improve the rate of survival of OHCA patients. The SOS-KANTO study indicated that bystander-initiated CPR appears to prolong VF or pulseless VT after a cardiac arrest.[24]

The Utstein Osaka study demonstrated that bystander-initiated CPR, either with cardiac only resuscitation or conventional CPR, improves the outcome of a witnessed cardiac arrest of less than 15 minutes duration. The effectiveness of each type of bystander CPR depends on the duration. Cardiac-only resuscitation may be superior to conventional CPR within 5 minutes of the cardiac arrest, but rescue breathing may be helpful for a prolonged cardiac arrest (greater than 15 minutes from collapse to emergency medical service resuscitation). These findings suggest that the optimal survival rate for an OHCA resulting from an AMI will be achieved by training Japanese citizens in basic life support and in the use of automated external defibrillators (AED).

Limitations: First, although we attempted to diagnose AMI in the OHCA group as precisely as possible, there were limitations when diagnosing AMI in OHCA patients that had not been successfully resuscitated. Second, our data is based on 1 year and can not reflect a temporal trend. In Japan, the survival rate of out-of-hospital cardiac arrest patients has been improving because of the use of defibrillation therapy under the comprehensive directions by rescue crews since April 2003. Therefore, it is possible that the mortality rate of AMI has further declined since completion of this investigation. Further investigation is necessary to clarify temporal trends in the incidence and mortality rate of AMI.

Conclusions: In conclusion, the mortality rate of AMI is still high and most deaths occur outside the hospital. Prehospital care is important for further lowering the mortality of AMI. A well-developed, monitored, layperson-enacted CPR-response plan may be enhanced by adding AEDs and AED training. This can improve the mortality rate of AMI by increasing the number of survivors whose out-of-hospital cardiac arrest occurs in public locations.

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