Follow-up of 2,733 Japanese Patients with Myocardial Infarction

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Two thousand, seven hundred and thirty-three patients with acute myocardial infarction (AMI) who were admitted to our 11 institutions between 1983 and 1988, examined by coronary arteriography and discharged alive, were followed for an average of 2.9 years. During the follow-up period, 212 patients (7.6%) died.

The factors that governed the prognosis of myocardial infarction after discharge were advanced age, female gender, obesity, previous infarction, angina pectoris more than 1 month before the onset of AMI, post-infarction angina, multiple-vessel diseases, advanced stage by Killip's and/or Forrester's classification on admission, elevated pulmonary capillary arterial pressure, decreased cardiac index, decreased left ventricular ejection fraction, increased left ventricular end-diastolic volume and left ventricular aneurysm before hospital discharge. Patients with ventricular tachycardia or ventricular fibrillation during hospitalization showed a poor prognosis.

In contrast, patients who received intracoronary thrombolysis, or emergent and/or elective percutaneous transluminal coronary angioplasty showed a favorable prognosis.
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THE mortality rate in acute myocardial infarction (AMI) has been reduced by the use of intracoronary thrombolysis (ICT) and other treatment in the coronary care unit (CCU)¹. However, additional efforts are needed to improve the prognosis of such patients with myocardial infarction (MI) after discharge. Little information is available concerning the post-hospital prognosis of MI

patients in Japan, much less the efficacy of ICT, percutaneous transluminal coronary angioplasty (PTCA) and bypass surgery of the coronary artery (CABG).

The present study included all of the patients who were discharged after treatment in the CCU and who were examined by coronary arteriography (CAG). To eliminate regional characteristics, this study was designed as a multicenter investigation with the participation of institutions in Hokkaido, Tohoku, Kanto, Kansai and Kyushu.

Key words:

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Fig.1. The relationship between age, sex and long-term prognosis of in patients with MI. The mortality rate increased in patients of advanced age, starting in the 60s. The mortality rate in females was significantly higher than that in males.

Fig.2. Relationship between obesity mass index and long-term prognosis of patients with MI. The long-term prognosis of patients with MI was progressively unfavorable as the obesity index increased.

METHODS

The subjects consisted of all of the patients with AMI who were admitted to our institutions between 1983 and 1988, examined by coronary arteriography and discharged alive.

The admission survey forms gave the histories of the subjects on admission. The information consisted of risk factors, previous infarction, angina pectoris, acute pump failure, ventricular arrhythmias, results of stress testing and coronary arteriography, details of medicinal treatment, ICT, PTCA and CABG during hospitalization.

Patients who had not had previous infarction were described as first AMI. Patients

whose electrocardiograms showed old abnormal Q waves, and who had a previous history of short-term chest pain, were described as probable previous infarction.

The pressures in the right side of the heart were measured using a Swan-Ganz catheter and the pressure of the left ventricle was measured using a pigtail catheter. Six or more successive ventricular premature beats was considered ventricular tachycardia.

After registration, the information collected during the follow-up period was entered on follow-up forms in 1986 and 1988. These forms also contained information regarding the prognosis, the occurrence of re-infarction and details of the therapies.

Continuous variables and discrete variables were assessed by the t-test and the χ^2 -test, respectively, to determine the significance of differences between groups. To evaluate some of the risk factors, such as smoking, the mortality rates obtained from life insurance tables² were applied to assess the significance of our results. This mortality rate represents the ratio of the number of observed deaths divided by the number of expected deaths corresponding to age and sex.

RESULTS

1. Number of Enrolled Subjects

A total of 2,803 subjects were enrolled in this study. The regional distribution of subjects showed that 160 cases enrolled in Hokkaido, 202 in Tohoku, 905 in Kanto, 954 in Kansai and 582 in Kyushu. When classi-

Fig.3. Relationship between long-term prognosis and previous infarction or angina pectoris before and after AMI. The prognosis of patients with previous infarction or angina pectoris before or after AMI was unfavorable.

Fig.4. Relationship between the number of involved coronary vessels and the long-term prognosis of patients with MI. The long-term prognosis was progressively unfavorable as the number of involved vessels increased.

fied by year, 348 patients were enrolled in 1983, 475 in 1984, 501 in 1985, 603 in 1986, 540 in 1987, and 336 in 1988. Seventy of the 2,803 patients died after re-infarction during hospitalization and were excluded from this study.

The remaining 2,733 patients were followed for an average of 2.9 ± 1.8 years after discharge. There were 2,232 males and 501 females, with an average age of 58.8 ± 11.3 years. During follow-up, 172 subjects

(6.3%) developed re-infarction and 212 (7.6%) died.

2. Age and Sex

The prognosis in each age group is shown in the left panel of Fig. 1. As is clear from this figure, the mortality rate increased in patients of advanced age, starting in the 60s. The mortality rate was 9.1% in patients in their 60s, 13.8% in those in their 70s, and 31.4% in those in their 80s or older. Advanced age was one of the factors which determined the long-term prognosis of MI ($p < 0.001$).

As shown in the right panel of Fig. 1, the mortality rate of females was 11.0%, which was significantly higher than that (7.0%) in males ($p < 0.005$). However, females had a greater average age than males. Therefore, age- and sex-related differences were adjusted using mortality rates obtained from life insurance tables. The mortality rate of males was 180.9% and that of females was 394.8%. Thus, the mortality rate of females was significantly higher than that of males.

3. Risk Factors

Total cholesterol, HDL cholesterol, smoking, previous hypertension and diabetes mellitus, obesity mass index and family history were studied as risk factors in the long-term prognosis of MI.

Only smoking and the obesity mass index

Fig. 5. Relationship between the severity of Killip's or Forrester's classification on admission and the prognosis of patients with MI during follow-up. There was a significant relationship between the severity of Killip's and/or Forrester's classification on admission and the prognosis of patients with MI during follow-up.

were related to the long-term prognosis of MI. The mortality rate of non-smokers was, unexpectedly, the highest, at 11.2% and their prognosis was significantly unfavorable ($p < 0.001$), when significance was assessed using the t-test. However, the non-smoking group included many older females. Therefore, the difference was evaluated using the mortality rate obtained from life insurance tables. The mortality rate was 201.9% in non-smokers and 160.7% in heavy smokers (more than one pack per day), with no significant difference between the two groups.

As shown in Fig. 2, the mortality rate was 8.0% for patients with an obesity mass index of less than 100%, 6.2% for those with 100% to 119%, 12.2% for those with 120% to 139% and 21.4% for those with an obesity mass index of more than 140%. Briefly, the long-term prognosis of MI was progressively unfavorable with an increasing obesity mass index ($p < 0.0025$).

When total cholesterol was classified into 4 grades (<200, 200–249, 250–299, and 300 mg/dl) and HDL cholesterol into 3 grades (<35, 35–49, and 50 mg/dl), there was no significant relationship between the prognosis and total cholesterol or HDL cholesterol.

There was also no significant relationship

between the prognosis and other risk factors, ie, hypertension, diabetes mellitus, and family history (MI, angina pectoris, or both).

4. Previous Infarction and Angina Pectoris

The long-term prognosis in patients with previous infarction is shown in the left panel of Fig. 3. The mortality rate was 6.2% for patients without previous infarction, and 14.3% for those with previous infarction. Thus, the long-term prognosis of patients with previous infarction was significantly poor ($p < 0.001$). Seventy seven patients were classified as probable previous infarction, and their mortality rate was 14.3%. The prognosis of the patients with probable previous infarction was also significantly unfavorable ($p < 0.001$).

The middle panel in Fig. 3 shows the long-term prognosis in patients with angina pectoris that had occurred more than one month before the onset of AMI. While the mortality rate for the patients without previous angina pectoris was 6.5%, the mortality rate for those with previous angina pectoris was 9.7%. Thus, patients with previous angina pectoris showed a significantly unfavorable prognosis ($p < 0.005$).

The right panel in Fig. 3 shows the long-term prognosis in patients with angina pecto-

Fig.6. The relationship between hemodynamic parameters obtained just before discharge and the prognosis of patients with MI during follow-up. The mortality rate during follow-up was significantly high for patients with high pulmonary capillary pressure or a low cardiac index.

ris after the onset of AMI. While the mortality rate for patients without post-infarction angina pectoris was 6.6%, the mortality rate for those with post-infarction angina pectoris was 11.2%. Patients with post-infarction angina pectoris showed a significantly unfavorable prognosis ($p < 0.001$).

There was no significant relationship between Q wave infarction or non-Q wave infarction and the long-term prognosis in this study.

5. Number of Involved Coronary Vessels

Long-term prognosis in cases with a different numbers of involved coronary vessels is shown in Fig. 4. The mortality rate was 5.3% for subjects with zero-vessel disease, 4.6% for those with single-vessel disease, 9.0% for those with double-vessel disease, 12.6% for patients with triple-vessel disease, and 20.0% for patients with stenosis of the left main truncus of the left coronary artery (LMT). The long-term prognosis of MI was progressively unfavorable as the number of involved vessels increased ($p < 0.001$). Among the patients with stenosis of the LMT, 18 had zero-vessel disease, 18 had single-vessel disease, 32 had double-vessel disease, and 32 had triple-vessel disease. There was no significant relationship be-

tween the number of involved vessels and the long-term prognosis in patients with stenosis of the LMT.

There was also no relationship between a positive treadmill exercise test and the long-term prognosis of MI in this study.

6. Severity of Heart Failure on Admission

The prognosis during follow-up according to the severity of Killip's classification on admission is shown in the left panel of Fig. 5. The mortality rate was 5.8% for patients in stage I, 11.7% for those in stage II, 21.7% for those in stage III, and 31.9% for those in stage IV. The mortality rate during follow-up progressively increased with an increasing severity of Killip's classification on admission ($p < 0.001$).

The prognosis during follow-up according to the severity of Forrester's classification on admission is shown in the right panel of Fig. 5. The mortality rate was 5.4% for patients in stage I, 11.5% for those in stage II, 13.7% for those in stage III, and 28.9% for those in stage IV. Again, the mortality rate during follow-up progressively increased with an increasing severity of Forrester's classification on admission ($p < 0.001$).

7. Cardiac Function just before Discharge

Fig. 7. The relationship between left ventricular function data and long-term prognosis of patients with MI. The mortality rate during follow-up was significantly high for patients with low LVEF, large LVEDVI or left ventricular aneurysm.

Fig. 8. The relationship between ventricular tachycardia and/or ventricular fibrillation during hospitalization and long-term prognosis of patients with MI. The mortality rate during follow-up was higher for patients with ventricular tachycardia and/or ventricular fibrillation during hospitalization.

Just before discharge, 2,370 patients were catheterized to evaluate their cardiac function. The long-term prognosis in patients with a high pulmonary capillary pressure is shown in the left panel of Fig. 6. The mortality rate was 7.1% for the patients with a pulmonary capillary pressure of less than 18 mmHg, but was significantly higher (17.8%) for patients with a pressure of greater than 18 mmHg ($p < 0.001$). However, no relationship was found between the prognosis and a left ventricular end-diastolic pressure (LVEDP). While the mortality rate was

5.0% for patients with a cardiac index of more than 2.2 l/min/m^2 , it was significantly higher (13.2%) for patients with a cardiac index of less than 2.2 l/min/m^2 ($p < 0.001$) (Fig. 6).

The long-term prognosis in patients with a low left ventricular ejection fraction (LVEF) is shown in the left panel of Fig. 7. The mortality rate was 3.7% for patients with a LVEF of more than 50%, but was significantly higher (5.4%) for those with a LVEF of 40–49% and for those with a LVEF of less than 40% (7.7%) ($p < 0.001$).

Fig.9. The relationship between interventional therapy and long-term prognosis of patients with MI.

The mortality rate during follow-up was lower in patients who had received intracoronary thrombolysis (ICT), or emergent or elective percutaneous transluminal coronary angioplasty (PTCA).

The long-term prognosis in patients with a large left ventricular end-diastolic volume index (LVEDVI) is shown in the middle panel of Fig. 7. While the mortality rate was 4.5% for patients with a LVEDVI of less than 100 ml/m², it was significantly higher (8.4%) for those with an index of more than 100 ml/m² ($p < 0.001$).

The long-term prognosis in patients with a left ventricular aneurysm is shown in the right panel of Fig. 7. While the mortality rate was 4.7% for patients without a left ventricular aneurysm, it was significantly higher (11.1%) for those with a left ventricular aneurysm ($p < 0.001$).

8. Arrhythmias during Hospitalization

Fig. 8 shows the long-term prognosis in patients with ventricular tachycardia (VT) and/or ventricular fibrillation (Vf) during hospitalization. While the long-term mortality rate was 6.8% for patients without VT during hospitalization, it was significantly higher (12.0%) for those with VT ($p < 0.001$). Similarly, while the long-term mortality rate was 7.1% for patients without Vf during hospitalization, it was significantly higher (19.0%) for those with Vf ($p < 0.001$).

9. The Therapies during Hospitalization

Fig. 9 shows the prognosis during post-hospital follow-up in patients who received interventional therapies. In the acute phase

of AMI, 685 patients received ICT. There were no significant differences between cases with and without ICT according to age and gender. While the mortality rate during the follow-up was 5.3% for all of the patients who had received ICT, regardless of whether or not it was effective, it was significantly higher (8.6%) for those who had not received ICT ($p < 0.005$).

In the acute phase of AMI, 413 patients underwent direct PTCA. While the mortality rate during follow-up was 3.1% for all of the patients who had received direct PTCA, regardless of whether or not it was effective, it was significantly higher (8.6%) for those who had not received the procedure ($p < 0.001$). The mortality rate was very low (1.3%) for 157 patients who underwent elective PTCA, regardless of whether or not it was effective, while it was significantly higher (8.2%) for those who did not undergo the procedure ($p < 0.005$). Patients with and without PTCA were similar with respect to age, but females received PTCA significantly more often than males ($P < 0.025$).

Conversely, while the mortality rate was high (11.5%) for 218 patients who underwent CABG, it was significantly low (7.4%) for those who did not undergo CABG ($p < 0.05$). There were no significant differences between the patients with and without CABG with regard to age and gender.

DISCUSSION

MI patients who were discharged after hospitalization in the acute phase of the disease were investigated to determine factors that governed their long-term prognosis.

1. Age and Sex

The age on admission is one of the factors that govern the long-term prognosis of MI patients. The present study showed that the mortality rate began to increase in patients in their 60s, and accelerated in the 70s, 80s and more advanced ages. These findings are consistent with those of many other investigators^{3,4}

Females showed a worse prognosis than males, which has also been recognized in many recent studies^{3,5}

2. Risk Factors

Since risk factors for AMI are considered to give rise to re-infarction and degrade the prognosis of MI patients, the long-term prognosis was investigated in patients with risk factors.

There is little information available regarding the association between obesity and the long-term prognosis of MI. In this study, the long-term prognosis was progressively unfavorable with increasing obesity.

On the other hand, there was no relationship between serum total cholesterol or HDL cholesterol and prognosis after MI. However, secondary prevention, including post-hospital dietary guidance and antihyperlipidemic drug therapy, was not evaluated in the present study. The relationship between family history, previous hypertension or diabetes mellitus and the prognosis of MI was not clear.

3. Previous Infarction and Angina Pectoris

Patients with a history of MI showed an unfavorable prognosis, since they showed several unfavorable conditions such as severe cardiac dysfunction and multiple vessel disease^{3,4}

Patients who had experienced angina pectoris more than one month before the onset of AMI and/or angina pectoris after the onset of AMI had a poor prognosis, which may be accounted for by the fact that most of them had severe coronary artery disease^{3,4}

4. Number of Involved Vessels

The mortality rate increased as the number of involved vessels increased^{3,4}. It was particularly high in patients with triple-vessel disease⁶ or stenosis of the LMT⁷. This tendency has also been observed in studies of subjects, including MI patients, in Western countries. The prognosis of multiple-vessel disease is so poor that PTCA, CABG or other interventional therapies may be indicated for patients with this condition.

There have been several reports that patients with a positive exercise test show an unfavorable prognosis³. However, there was no significant relationship between a positive treadmill exercise test and the prognosis of MI in the present study.

5. Severity of Heart Failure on Admission and Cardiac Function evaluated just before Discharge

It is well known that patients who present in an advanced stage on admission according to Killip's or Forrester's classification show a poor prognosis in the acute phase of AMI! The present study has revealed that such patients also show an unfavorable prognosis during post-hospital follow-up^{3,4}. Patients who have acute pump failure on admission are also likely to have severe impairment of cardiac function in the acute phase of infarction so that they show a poor prognosis during post-hospital follow-up³.

The relationship between cardiac function evaluated immediately before discharge and the long-term prognosis was investigated. The mortality rate was high in patients with a high pulmonary capillary pressure, a low cardiac index, a low LVEF, a large LVEDVI and a left ventricular aneurysm. Many other investigators have noted that patients with diminished cardiac function have a poor prognosis. This is the most important of all of the prognosis-governing factors in patients with myocardial infarction during post-hospital follow-up^{3,6}.

6. Ventricular Tachycardia and Ventricular Fibrillation during Hospitalization

The occurrence of VT or Vf 2 weeks or more after the onset of AMI supposedly shows a positive relationship to the occurrence of these arrhythmias during post-hospital follow-up.

In the present study, we investigated whether there was a relationship between VT or Vf during hospitalization and the prognosis during post-hospital follow-up. We found that patients with such arrhythmia in the acute phase showed a poor long-term prognosis^{8,9}. One reason for a this poor prognosis may be that severe arrhythmia occurs during follow-up. However, it is also conceivable that patients with ventricular tachycardia or ventricular fibrillation in the acute phase also have impaired cardiac function.

7. Interventional Therapies during Hospitalization

The most important finding in this study is that ICT and/or PTCA were associated with a favorable prognosis for patients with MI during follow-up^{10,11}. This suggests that ICT and emergent PTCA have beneficial effects on the infarcted area. PTCA improves coronary stenosis, and thus improves the prognosis of MI patients. However, it should be noted that the present study is retrospective, and the backgrounds of patients who received interventional therapies were different than those of patients who did not. A final conclusion should be based on randomized studies.

CABG reportedly improves the prognosis of MI patients with two or more involved vessels, and its effect is particularly marked in patients with impaired cardiac function^{6,12}. However, the present study showed that CABG did not improve the prognosis of patients with MI. Again, no evaluation would be accurate unless the patients shared a common background.

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