Identification of Uncomplicated Patients With Acute Myocardial Infarction Undergoing Percutaneous Coronary Intervention

— Are These Patients Suitable for Early Discharge? —

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Background The hospital stay after acute myocardial infarction (AMI) is still extremely long in Japan and does not correspond with disease severity. The purpose of the present study was to identify a subgroup of AMI patients suitable for early discharge.

Methods and Results A total of 3,739 AMI patients treated with percutaneous coronary intervention (PCI) within 24 h after onset, who enrolled Osaka Acute Coronary Insufficiency Study between April 1998 and March 2004, were studied. Patients showing no complications within the first 7 days (n=1,786) were considered to be eligible for early discharge. In these patients, multivariate logistic regression analysis selected prior myocardial infarction, left anterior descending coronary artery disease and failed PCI as independent predictors of major complications from day 8 to discharge. Patients without any predictor had significant lower rates of major complications from day 8 to 6 months after discharge than those with 1 or more predictors. Furthermore, in the present study there were no deaths in patients without any predictors.

Conclusion Patients who either do not have serious complications during the first 7 days or any predictor are at very low risk of major complications from day 8 to 6 months after discharge. These carefully selected patients may be suitable for early (day 8) hospital discharge after AMI. (Circ J 2005; 69: 1163–1169)

Key Words: Acute myocardial infarction; Hospital stay; Japanese; Percutaneous coronary intervention

In Western countries, the length of hospital stay after acute myocardial infarction (AMI) has been reduced over the past 3 decades from several weeks to several days.^{1–16} Several factors have led to the reduction in the length of hospital stay, including the physical and psychological advantages of early mobilization, clinical innovations, and economic pressures to reduce medical costs. In contrast, although the length of hospital stay in Japan has gradually decreased, it is still extremely long, at approximately 4 weeks.^{17–22} In a recent study, we showed that the length of hospital stay did not correspond appropriately to the severity of AMI.²² These findings suggest that the hospital stay could be reduced without adverse effect for AMI patients in Japan. Furthermore, because the reduction of the

length of hospital stay has several advantages, it is necessary to adjust the length of hospital stay to correspond to disease severity by selecting candidates for early discharge. The purposes of the present study using a large hospital-based cohort were: (1) to discover independent predictors of in-hospital major complications; and (2) to identify a subgroup of Japanese AMI patients suitable for early discharge based on these predictors.

Methods

Patients

We registered 5,502 consecutive AMI patients in the Osaka Acute Coronary Insufficiency Study (OACIS) from April 1998 to March 2004. Of these patients, 3,739 who were treated with percutaneous coronary intervention (PCI) within 24 h of onset of AMI were included in this study. A detailed description of the OACIS has been published elsewhere.^{22–25} The OACIS is a prospective, multicenter observational study in which 25 collaborating hospitals in Japan recorded demographic, procedural and outcome data, and collected blood samples from patients with AMI. The registry was designed to collect uniform, prospective data on patients with AMI that could be used to assess clinical variables, therapeutic procedures and clinical events, and to

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Fig 1. Risk stratification of the total study population. Uncomplicated patients were defined as survivors with the absence of the following conditions or treatments: cardiogenic shock; CHF; reinfarction; angina; ventricular septal perforation; severe mitral regurgitation; cardiac rupture; thromboembolism; stroke; bleeding; VT/Vf; AV block; left main coronary artery disease or the need for coronary artery bypass grafting, percutaneous cardiopulmonary support, intra-aortic balloon pumping, or mechanical ventilation within the first 7 hospital days. Low-risk patients were defined as those who had neither serious complications during the first 7 days nor any independent predictor of late major complications (prior myocardial infarction, left anterior descending coronary artery disease and failed PCI). CHF, congestive heart failure; VT/Vf, ventricular tachycardia/fibrillation; AV, indicates second- or third-degree atrioventricular; PCI, percutaneous coronary intervention.

collect DNA samples from patients with AMI that could be used to investigate whether common genetic variations are involved in the pathogenesis of AMI.^{22–25} The present study protocol was approved by each of the hospitals' ethics committees.

Definitions

The diagnosis of AMI required the presence of 2 of the following 3 criteria: (1) a clinical history of central chest pressure, pain or tightness lasting for 30 min or more; (2) typical electrocardiographic changes (ie, ST segment elevation >0.1 mV in at least 1 standard or 2 precordial leads, ST segment depression >0.1 mV in at least 2 leads, abnormal Q wave or T wave inversion in at least 2 leads); and (3) an increase in the serum creatine kinase activity by 2-fold the normal laboratory value. All patients presenting within 1 week after the onset of AMI were registered prospectively, as soon as the diagnosis of AMI had been made.

Data Collection

Research cardiologists and specialized research nurses recorded data concerning sociodemographic variables, medical history, therapeutic procedures and clinical events during the patient's admission. Information was obtained from the hospital medical records and by direct interview with the patient, family members and the treating physician. After written informed consent for entering the OACIS was given by the patient, all in-hospital data were transmitted to the data collection center located in the Department of Cardiovascular Medicine in Graduate School of Medicine,

Osaka University for processing and analysis.

From patients who were discharged alive, we obtained follow-up clinical data at 3, 6 and 12 months after the onset of AMI and annually thereafter. We obtained data concerning subsequent cardiac events through visits to the research outpatient clinic or, in a few instances, by verbal or written contact with the patient's physician, the patient or family members.

Risk Stratification

Patients with complications within the first 7 days were considered to be ineligible for the early discharge strategy. In the present study, patients without complications within the first 7 days were the first candidates for early discharge. Uncomplicated patients were defined as those who did not have or require the following conditions or interventions: cardiogenic shock; congestive heart failure (CHF); reinfarction; angina; ventricular septal perforation; severe mitral regurgitation; cardiac rupture; thromboembolism; stroke; bleeding; ventricular tachycardia/fibrillation (VT/Vf); second- or third-degree atrioventricular (AV) block; left main coronary artery disease or requiring coronary artery bypass grafting; percutaneous cardiopulmonary support; intra-aortic balloon pumping; or mechanical ventilation within the first 7 hospital days. This group of uncomplicated patients was used to determine the factors predicting an uncomplicated course (absence of late major complications) from day 8 to hospital discharge. Late major complications were defined as death as well as CHF, reinfarction, angina, thromboembolism, stroke, bleeding, VT/Vf and

second- or third-degree AV block.

Statistical Analysis

Continuous variables between groups were compared using the t-test. Categorical variables were compared using the chi-square test. A multiple logistic regression analysis was used to identify independent predictors of major complications. Analyses of data were performed using SPSS statistical software (SPSS version 11.0, SPSS Japan Inc, Tokyo, Japan). For all analyses, significance was defined as $p < 0.05$.

Results

Early Complications

Fig 1 shows risk stratification of the total study population: 1,953 patients had complications within the first 7 days. Table 1 shows the frequency of complications within the first 7 days: 126 (3.4%) died; 737 (19.7%) had cardiogenic shock; 1,022 (27.3%) had CHF; and 92 (2.5%) had reinfarction. The remaining 1,786 patients were free of early complications. Using our definition of uncomplicated myocardial infarction (MI), 47.8% (1,786/3,739) of the total study population was classified as uncomplicated and therefore eligible for early discharge.

Predictors of Late Major Complications

Table 2 compares the clinical, angiographic and hospital characteristics between patients with and without late

Table 1 Frequency of Early Complications in the Total Study Population (n=3,739)

	n (%)
Death	126 (3.4)
Cardiogenic shock	737 (19.7)
CHF	1,022 (27.3)
Reinfarction	92 (2.5)
Angina	67 (1.8)
Ventricular septal perforation	18 (0.5)
Severe mitral regurgitation	20 (0.5)
Cardiac rupture	45 (1.2)
Thromboembolism	17 (0.5)
Stroke	28 (0.7)
Bleeding	150 (4.0)
VT/Vf	606 (16.2)
Second- or third-degree AV block	226 (6.0)
Left main coronary artery	82 (2.2)
Coronary artery bypass grafting	60 (1.6)
Percutaneous cardiopulmonary support	126 (3.4)
Intra-aortic balloon pumping	839 (22.4)
Mechanical ventilation	463 (12.4)
Any of the above	1,953 (52.2)

CHF, congestive heart failure; VT/Vf, ventricular tachycardia/fibrillation; AV, atrioventricular.

major complications. Patients with late major complications were less likely to have hyperlipidemia than those without. A history of MI was more likely in patients with late major complications. Patients with late major complications were less likely to be treated with coronary stenting

Table 2 Clinical, Angiographic, and Hospital Characteristics

	No late complication (n=1,709)	Late complication (n=77)	p value
<i>Clinical characteristics</i>			
Age, years	62.9	64.9	0.122
Male, %	79.4	80.5	0.813
Body mass index, kg/m ²	23.9	23.3	0.175
Diabetes mellitus, %	33.1	25.3	0.160
Hypertension, %	53.9	51.4	0.662
Hyperlipidemia, %	48.6	33.3	0.011
Current smoking, %	55.7	53.4	0.707
Prior myocardial infarction, %	10.5	19.5	0.013
Prior angina pectoris, %	26.7	31.2	0.384
Prior cerebrovascular disease, %	8.4	8.6	0.953
Time from onset to presentation <6 h, %	74.5	78.6	0.441
<i>Angiographic characteristics</i>			
Time to catheterization <6 h, %	66.0	68.9	0.604
Infarct-related artery, %			
Left anterior descending coronary artery	48.5	59.7	0.054
Left circumflex coronary artery	15.9	9.1	0.107
Right coronary artery	35.7	31.2	0.417
Bypass graft	0.1	0.0	0.832
Multivessel disease, %	25.1	31.2	0.233
Presence of collateral vessels, %	37.3	31.1	0.280
Preprocedural coronary artery stenosis ≥75%, %	99.3	98.3	0.422
Preprocedural TIMI flow grade ≤2, %	86.3	87.5	0.773
Thrombolysis, %	6.7	10.4	0.218
Intravenous	3.9	7.8	0.092
Intracoronary	2.8	2.6	0.899
Stent use, %	64.2	50.0	0.012
Successful PCI*, %	93.2	83.1	0.001
Time to reperfusion <6 h, %	61.5	66.7	0.496
<i>Hospital characteristics</i>			
Performance of PCI >200 procedures per year, %	83.6	77.9	0.194
AMI case load >50 patients per year, %	78.1	68.8	0.055

*Successful PCI was determined by coronary artery stenosis ≤25% and TIMI flow grade 3 on final angiography.

TIMI, Thrombolysis in Myocardial Infarction; PCI, percutaneous coronary intervention; AMI, acute myocardial infarction.

Table 3 Multivariate Predictors of Late Major Complications

	Chi-square*	Odds ratio (95% confidence interval)	p value
Age	1.13	1.03 (0.98–1.08)	0.287
Male	0.13	0.82 (0.27–2.44)	0.716
Body mass index $\geq 25 \text{ kg/m}^2$	1.48	1.76 (0.71–4.38)	0.224
Diabetes mellitus	0.37	1.33 (0.53–3.37)	0.542
Hypertension	0.05	0.90 (0.37–2.20)	0.824
Hyperlipidemia	2.64	0.46 (0.18–1.18)	0.104
Current smoking	0.20	1.24 (0.48–3.20)	0.651
Prior myocardial infarction	7.66	2.24 (1.27–3.98)	0.006
Prior angina pectoris	1.41	1.78 (0.69–4.61)	0.235
Prior cerebrovascular disease	0.40	1.59 (0.38–6.62)	0.526
Time from onset to presentation $< 6 \text{ h}$	0.02	0.87 (0.27–2.44)	0.883
Left anterior descending coronary artery disease	8.86	4.64 (1.69–12.7)	0.003
Multivessel disease	0.47	1.42 (0.53–3.83)	0.491
Presence of collateral vessel	0.06	0.89 (0.35–2.23)	0.800
Preprocedural coronary artery stenosis $\geq 75\%$	0.61	0.44 (0.06–3.44)	0.434
Preprocedural TIMI flow grade ≤ 2	0.17	1.42 (0.27–7.56)	0.166
Thrombolysis	1.16	2.13 (0.54–8.44)	0.282
Stent use	0.66	0.69 (0.28–1.69)	0.417
Failed PCI	4.13	3.51 (1.04–11.8)	0.023
Time to reperfusion $< 6 \text{ h}$	0.03	1.19 (0.13–10.8)	0.874
Performance of PCI > 200 procedures per year	2.45	0.38 (0.12–1.27)	0.117
AMI case load > 50 patients per year	1.34	2.25 (0.57–8.88)	0.248

*Wald's chi-square value. AMI, acute myocardial infarction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis in Myocardial Infarction.

Fig 2. Frequency of late major complications according to the number of predictors. 0 indicates patients with no predictors present; 1, with 1 predictor; 2, with 2 predictors; 3, with 3 predictors. The predictors are prior myocardial infarction, left anterior descending coronary artery disease and failed percutaneous coronary intervention.

and had lower rates of successful PCI than those without. Multivariate logistic regression analysis showed that prior MI, left anterior descending coronary artery disease and failed PCI were independent predictors of late major complications (Table 3).

Candidates for Early Discharge

To further identify the subgroup of patients suitable for early discharge, we identified the lowest risk group of late major complications. First, we examined the frequency of late major complications according to the number of predictors in patients without complications during the first 7 days. Fig 2 shows that patients without any independent predictors had significant lower rates of late major complications than those with 1 or more predictors. As shown in Fig 1, 742 patients (19.8%) were classified as low-risk and

1,044 patients were at high risk of late major complications; 64 (6.1%) of the 1,044 high-risk patients had late major complications: 4 died, 5 had reinfarction, 9 had angina, 3 had thromboembolism, 7 had bleeding, 2 had second- or third-degree AV block, 2 had a VT/Vf and 32 had CHF. However, 13 (1.8%) of the 742 low-risk patients had late major complications: none died, 1 had a reinfarction, 3 had angina, 1 had a bleeding, 1 had a second- or third-degree AV block, 1 had VT/Vf and 6 had CHF. To demonstrate the validity of early discharge in low-risk patients, we compared the frequency of clinical events (death, nonfatal MI, stroke, CHF and revascularization) 6 months after hospital discharge between low- and high-risk patients (Table 4). Low-risk patients had a lower risk of 6-month cardiovascular events than high-risk patients. Therefore, patients who had neither complications within the first 7

Table 4 Six-Month Clinical Events

	Low risk patients* (n=742) [‡]	High risk patients [†] (n=1,040) [‡]	p value
Clinical events, %	13.2	17.6	0.012
Death, %	0.0	0.4	0.088
Nonfatal myocardial infarction, %	1.1	2.5	0.027
Stroke, %	0.3	0.1	0.388
CHF, %	0.4	0.4	0.664
Revascularization, %	11.9	14.2	0.154

*Low risk patients were defined as those who had neither serious complications during the first 7 days nor any independent predictor of late major complications. [†]High risk patients were defined as those who had no serious complications during the first 7 days but had 1 or more independent predictors of late major complications. The predictors are prior myocardial infarction, left anterior descending coronary artery disease, and failed PCI. [‡]Sample numbers represent number of patients who were discharged alive in each group. CHF, congestive heart failure; PCI, percutaneous coronary intervention.

days nor any predictor were considered to be suitable for early discharge.

Discussion

The main finding of the present study is that patients who had neither serious complications during the first 7 days nor any independent predictor of late major complications (prior MI, left anterior descending coronary artery disease or failed PCI) had a very few major complications after day 8. This result suggests that these carefully selected patients may be suitable for early (day 8) hospital discharge after AMI.

In Western countries, the length of hospital stay after AMI was generally 2–3 weeks in the 1970s!^{–3} Because of recent clinical innovations, such as the routine use of aspirin, thrombolytic therapy and PCI, which reduce post-infarction complications, early discharge strategies became possible^{26–28} Several randomized studies of whether a more aggressive early discharge strategy was possible in uncomplicated patients with AMI showed that hospital discharge as early as 3–5 days was safe, feasible and cost effective.^{8–12} Recently, the hospital stay after AMI has been reduced to about 1 week in Western countries.^{13–16}

In contrast, although the length of hospital stay has gradually decreased, it is still extremely long, at approximately 4 weeks, in Japan!^{17–22} Furthermore, we previously reported that clinical variables, including demographic factors, coronary risk factors, medical history, infarct characteristics, procedures, medication and in-hospital complications, only explained 26% of the variation in the length of hospital stay²² which suggests that the length of hospital stay does not correspond appropriately with the severity of AMI and that it could be reduced without an adverse effect on the outcome. Furthermore, it is important to reduce the length of hospital stay after AMI to reflect the disease severity in order to improve the physical as well as the psychological status of the patient, as well as reducing medical costs. However, limited data exists on how Japanese AMI patients are identified as suitable for early hospital discharge.

In the present study, we first identified the candidates for early discharge as those without complications within the first 7 days (see Table 1). Next, we identified independent predictors of major complications from day 8 to hospital discharge in these uncomplicated patients, and risk stratification was performed according to these predictors (see Table 3). Third, patients who had neither complications within the first 7 days nor any predictor had the lowest risk of late major complications (see Fig 2). Finally, these

patients had very few complications and no deaths within 6 months of discharge (see Table 4). Therefore, patients who had neither complications within the first 7 days nor any predictors were considered suitable for early discharge. However, because the purpose of the present study was not to confirm the safety of early hospital discharge in low-risk patients, but to identify such patients, it was impossible to determine whether early hospital discharge strategy was safe. To determine the safety of early hospital discharge in low-risk patients, it is necessary to compare event rates between randomly assigned early discharge groups and late discharge groups. Because previous studies have shown that the 30-day major complication rate in low-risk patients for early discharge is 4–6%, 1.8% risk of non-fatal complications was thought to be relatively low and it seems ethically acceptable if the low-risk patients selected in this study were randomly assigned to an early or late discharge group!^{2,29}

In the present patient population, the mean length of hospital stay was 29.6 days in survivors. Furthermore, the mean hospital stay was 25.8 days in low-risk patients and 26.2 days in high-risk patients. If all low-risk patients were discharged at day 8, the mean hospital length of stay would be 25.9 days. However, early discharge (day 8) of 19.8% of all patients would reduce the total duration of all hospital stays for AMI by only 13%. The early discharge strategy for low-risk patients has only a limited impact on reduction of medical costs. Therefore, it is necessary to reduce the hospital stay in complicated patients with AMI. The present study could not determine the safety and feasibility of early discharge in complicated patients. A previous randomized controlled study in a Western county has shown that regardless of the presence or absence of complications, early discharge (day 12) had no more adverse events than late discharge (day 19).³ Therefore, further study is needed to determine whether early hospital discharge is safe in complicated patients in Japan.

Study Limitations

The present study was not a randomized controlled study but an observational study. Low-risk patients selected in the present study had only non-fatal complications after day 8. However, because the patients were actually hospitalized and were under rapid and better management, we consider that they were at very low risk of complications. Therefore, further randomized controlled studies are needed to examine the safety and feasibility of early discharge after AMI in Japan. Previous studies in Western countries of the safety and feasibility of early discharge in patients

with AMI treated with PCI have reported that an early discharge strategy (days 3–4) can be applied safely to low-risk patients^{10–12}. Although day 3–4 discharge is thought to be possible for Japanese AMI patients treated with PCI, the present study can not fully answer this question.

Conclusion

The present study suggests that patients who have neither serious complications during the first 7 days nor any independent predictor of late major complications are at very low risk of major complications after day 8 and that these carefully selected patients may be suitable for early hospital discharge after AMI. These results should be helpful in the development of guidelines, as well as clinical pathways, for management of Japanese AMI patients. However, because the present study has several limitations, randomized controlled studies are needed to examine the safety and feasibility of early discharge after AMI in Japan in order to standardize medical care.

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Appendix

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Osaka, Japan: Mishima M, Lim YJ; Higashi-Osaka City General Hospital, Higashi-Osaka, Japan: Kijima Y; Osaka National Hospital, Osaka, Japan: Kusuoka H, Koretsune Y, Yasumura Y; Osaka Minami Medical Center, Kawachinagano, Japan: Kinoshita N, Imai K; Osaka Kosei Nenkin Hospital, Osaka, Japan: Sasaki T; Kobe Ekisaikai Hospital, Kobe, Japan: Shimazu T, Fuji H; Yao Municipal Hospital, Yao, Japan: Hoshida S, Umemoto K; Osaka Railway Hospital of West Japan Railway Company, Osaka, Japan: Ezumi A; Kaizuka City Hospital, Kaizuka, Japan: Morita H, Lee JM; Kita-Osaka Hospital, Osaka, Japan: Ogitani N, Ikeda S;

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