Journal of Cardiology (2009) **54**, 1—9

JOURNAL of CARDIOLOGY
Official Journal of the Japanese College of Cardiology
www.elsevier.com/locate/jjcc

ELSEVIER

REVIEW ARTICLE

Modern state of acute myocardial infarction in the interventional era: Observational case—control study—Japanese acute coronary syndrome study (JACSS)

Hisao Ogawa (MD, PhD, FJCC)*, Sunao Kojima (MD, PhD)

Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto 860-8556, Japan

Received 8 April 2009; received in revised form 4 May 2009; accepted 7 May 2009
Available online 26 June 2009

KEYWORDS
Japanese acute coronary syndrome study (JACSS);
Retrospective study;
Myocardial infarction

Summary The Japanese acute coronary syndrome study (JACSS) is a retrospective and multicenter observational study conducted in 35 medical institutions across Japan. The JACSS database included 5325 consecutive patients hospitalized at the participating institutions within 48 h after the onset of symptoms of acute myocardial infarction (AMI) between January 2001 and December 2003. The JACSS data vividly displayed the modern state of AMI in the interventional era. Percutaneous coronary intervention (PCI) including balloon angioplasty and stent implantation was performed in 80% of the patients and approximately 90% of the treated patients had successful coronary recanalization during the acute phase of MI. The results showed very low rates of all-cause mortality and cardiovascular deaths during hospitalization. Various types of novel information have been produced from JACSS data by several leading clinical researchers in Japan and this may also be helpful in making plans for a prospective study.

Contents

* Corresponding author. Tel.: +81 96 373 5174/75; fax: +81 96 362 3256.
E-mail address: ogawah@kumamoto-u.ac.jp (H. Ogawa).

0914-5087/$ — see front matter
doi:10.1016/j.jjcc.2009.05.005

Introduction

The Japanese acute coronary syndrome study (JACSS) is a retrospective and multicenter observational study conducted in 35 medical institutions across Japan. The JACSS database included 5325 consecutive patients hospitalized at the participating institutions within 48 h after the onset of symptoms of acute myocardial infarction (AMI) between January 2001 and December 2003. Tables 1A and 1B show the clinical and angiographic characteristics of the patients and the state of AMI in the intervention era. Percutaneous coronary intervention (PCI) including balloon angioplasty and stent implantation was performed in 80% of the patients and approximately 90% of the treated patients had successful coronary recanalization (thrombolysis in myocardial infarction [TIMI] [1] III) during the acute phase of MI. The results showed very low rates of all-cause mortality (8%) and cardiovascular deaths (7%) during hospitalization. Several leading clinical researchers in Japan have used data of the JACSS in their analysis [2—14].

Table 1A Retrospective study on prognosis of patients with AMI-JACSS data-subjects: consecutive patients hospitalized within 48 h after the onset of symptoms of AMI from January 2001 to December 2003 (*n* = 5325).

Age	68 ± 12 (22—103) years
Sex:men	71%
Hypertension (SBP > 140 mmHg and/or DBP > 90 mmHg)	57%
Diabetes mellitus (FBS > 126 mg/dL or 75 g OGTT2 h > 200 mg/dL)	32%
Hyperlipidemia (total cholesterol > 220 mg/dL and/or triglyceride > 150 mg/dL)	34%
Smoking (active smoking or smoking within 2 years)	47%
Obesity (body mass index > 25 kg/m^2)	30%
Old myocardial infarction	13%
Time from onset to hospital admission	6.5 ± 8.6 h
Q wave myocardial infarction	71%
Preinfarction angina	
Sudden onset	69%
Effort angina	14%
Rest angina	17%
ST-T change on admission	
ST elevation	88%
ST depression	12%
Killip classification	
I	78%
II	7%
III	4%
IV	8%
Unknown	3%

AMI, acute myocardial infarction; DBP, diastolic blood pressure; FBS, fasting blood sugar; JACSS, Japanese acute coronary syndrome study; OGTT, oral glucose tolerance test; SBP, systolic blood pressure.

Risk factors for AMI in Japanese men and women

Current knowledge about the prevention of coronary heart disease and cardiovascular disease is mainly derived from studies in European populations [15]. However, the extent to which these findings apply worldwide is unknown. Some studies reported that risk factors for coronary artery disease vary in different geographic regions, especially Asian countries. For example, dyslipidemia is not a risk factor for coronary artery disease in India [16] and hypertension is more important in China [17]. In addition, the incidence of ischemic heart disease in Japan has been reported to be the lowest among the developed countries [18,19]. The differences between Japan and western countries may stem, in part, from genetic factors, but it is more likely that eating habits are the cause; for example, the average plant-based low-fat diet. Kawano et al. [9] clarified the risk factors for AMI in the Japanese population. Risk factors were assessed in patients with a first AMI and age- and sex-matched population-based controls. Hypertension, diabetes,

Table 1B Retrospective study on prognosis of patients with AMI-JACSS data-subjects: consecutive patients hospitalized within 48 h after the onset of symptoms of AMI from January 2001 to December 2003 (n = 5325).

Acute phase	
Coronary vessel involvement (n = 4827)	
0—vessel disease	1%
1—vessel disease	54%
2—vessel disease	29%
3—vessel disease	16%
Target lesion stenosis (n = 4707)	
AHA ≤ 75%	3%
AHA ≤ 90%	10%
AHA ≤ 99%	25%
AHA ≤ 100%	62%
Treatment	
Conservative	15%
Thrombolysis	4%
Percutaneous old balloon angioplasty	13%
(thrombolysis + balloon)	3%
Stent implantation	67%
(thrombolysis + stent)	8%
Coronary artery bypass graft	1%
Peak creatine kinase (n = 4916)	2896 ± 2938 IU/L
Final TIMI flow	
0	5%
1	1%
2	6%
3	88%
Left ventricular ejection fraction (n = 2022)	51 ± 12%
Chronic phase	
Left ventricular ejection fraction (n = 2602)	55 ± 13%
Target lesion stenosis (n = 3404)	
AHA ≤ 90% (50%)	90% (79%)
Prognosis (n = 5302)	
Prognosis during hospitalization	
All cause mortality	8%
Cardiovascular death	7%
Long-term prognosis (mean follow-up period after the onset of AMI: 412 ± 219 days)	
Cardiovascular death	9%
Reinfarction	2%
Unstable angina	2%
Ischemic heart failure	3%
Stroke	1%

AHA, American Heart Association; AMI, acute myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction.

current smoking, family history, and hypercholesterolemia were all independent risk factors for AMI (in both men and women) (Fig. 1A). However, obesity was not. Hypertension, current smoking, and diabetes were all independent risk factors for AMI in men. In contrast, only current smoking, diabetes, and hypertension were independent risk factors for AMI in women. Hypercholesterolemia was an independent risk factor for AMI in men, but not in women (Fig. 1B). In conclusion, hypertension, diabetes, current smoking, family history, and hypercholesterolemia are associated with AMI in Japanese patients. In addition, there are sex differences in the order of importance related to risk factors for AMI. Hypertension, current smoking, diabetes, and family history are the most important risk factors in men, whereas current smoking, diabetes, hypertension, and family history are the most important risk factors in women. Hypercholesterolemia is an independent risk factor for AMI in men, but not in women. This is the first clinical study that defines the relative importance of risk factors for AMI in Japanese patients.

Beneficial effects of preinfarction angina on in-hospital outcome

In experimental animals, brief episodes of ischemia before sustained coronary occlusion significantly decrease infarct size [20—22]. This phenomenon, known as ischemic preconditioning, also occurs in humans. Several clinical studies have demonstrated that angina attacks shortly before the onset of AMI limit infarct size and improve both short- and long-term outcomes [23—26]. However, the clinical significance of preinfarction angina in patients with AMI who undergo PCI is not known. Kosuge et al. [2] assessed the relationship between preinfarction angina, infarct size, and in-hospital outcome after PCI for AMI. They reported that preinfarction angina occurring ≤24 h before the onset of AMI was associated with lower peak creatine kinase levels (Fig. 2A) and lower in-hospital mortality in patients who underwent PCI for anterior infarction (Fig. 2B). This beneficial effect of preinfarction angina on in-hospital outcome was less obvious in patients with non-anterior infarction. A previous report described a favorable effect of preinfarction angina on in-hospital outcome in both anterior and non-anterior infarctions although only 19% of patients underwent PCI [27].

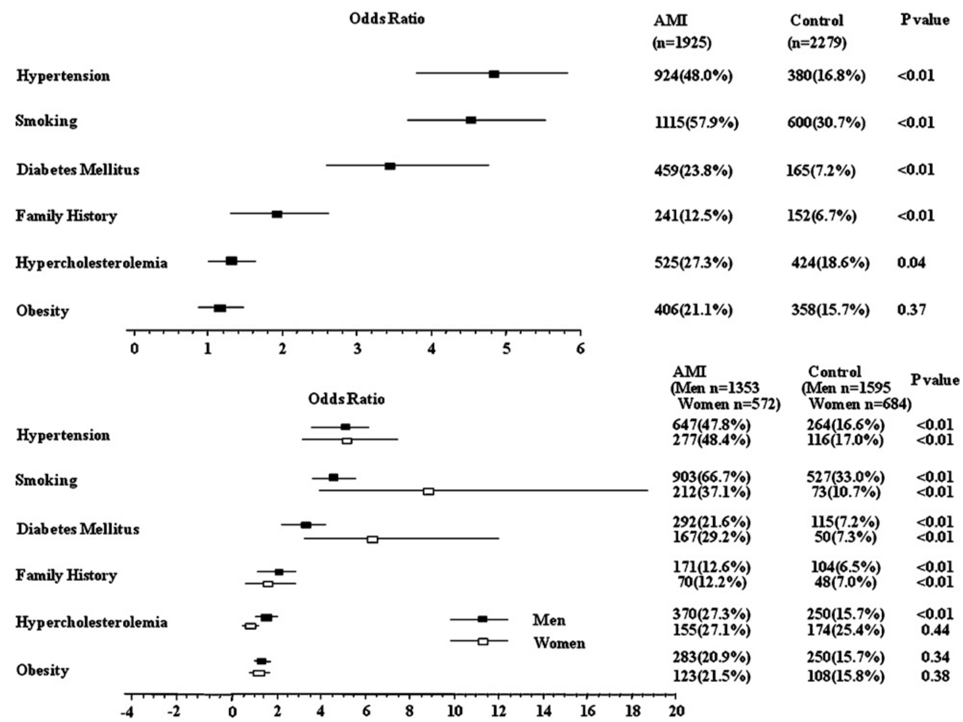

Figure 1 (A) Overall odds ratios for individual risk factors. (B) Sex differences in the odds ratios for individual risk factors. AMI, acute myocardial infarction.

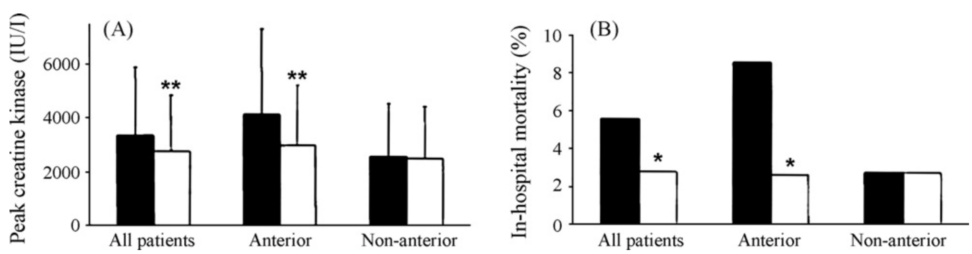

Figure 2 (A) Overall, peak creatine kinase was significantly lower in patients with (*white bars*) than without (*black bars*) preinfarction angina. In patients with anterior infarction, peak creatine kinase was significantly lower in those with (*white bars*) than without (*black bars*) preinfarction angina. In patients with non-anterior infarction, peak creatine kinase level did not differ significantly according to the presence (*white bars*) or absence (*black bars*) of preinfarction angina. **$P < 0.01$ versus patients without preinfarction angina. (B) Overall, in-hospital mortality was significantly lower in patients with (*white bars*) than without (*black bars*) preinfarction angina. In patients with anterior infarction, in-hospital mortality was significantly lower in those with (*white bars*) than without (*black bars*) preinfarction angina. In patients with non-anterior infarction, in-hospital mortality did not differ significantly according to the presence (*white bars*) or absence (*black bars*) of preinfarction angina. *$P < 0.05$ versus patients without preinfarction angina.

Leukocyte count and predictor of mortality

Inflammation is a significant risk factor for the development of coronary artery disease [28—30]. Recently, there has been a renewed interest in leukocyte count as a prognostic indicator of acute coronary syndrome [31]. The leukocyte count is a simple and universally available marker of inflammation and acute-phase reactants. Leukocytosis was also considered a high risk factor for adverse events following AMI in the era before coronary reperfusion therapy [32—34]. Kojima et al. [3] evaluated whether leukocyte count in the acute phase of MI predicts adverse in-hospital clinical outcomes and long-term prognosis in the coronary interventional era. Leukocyte count was significantly associated with smoking, sudden onset AMI, and the no-reflow phenomenon during PCI, as were age, peak creatine kinase level, and Killip class. Leukocytosis was significantly associated with higher risk of in-hospital mortality (Fig. 3). Patients in the

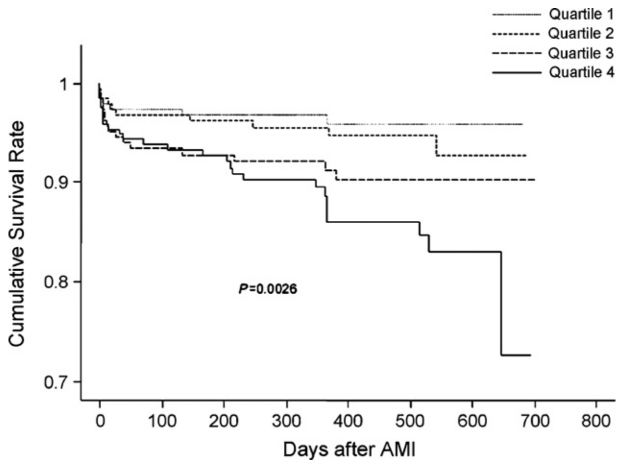

Figure 3 Event-free survival of patients after AMI by quartile of the leukocyte count. Quartile 1: leukocyte count ≤ 7800/mm^3; Quartile 2: 7800/mm^3 < leukocyte count ≤ 9750/mm^3; Quartile 3: 9750/mm^3 < leukocyte count < 12,100/mm^3; Quartile 4: 12,100/mm^3 < leukocyte count.

highest quartile of leukocyte count were about three times more likely to have a poor prognosis after AMI compared to those in the lowest quartile, after adjusting for independent factors which were closely associated with leukocyte count. They concluded that the leukocyte count is of great significance for stratifying patient risk and recommended its use as a marker for predicting future adverse events following treatment for AMI.

Hyperglycemia and adverse outcomes

An increase in plasma glucose concentration is often observed during the early hours after the onset of AMI not only in diabetic patients but also in patients free of diabetes mellitus [35]. It has been reported that both acute hyperglycemia and diabetes mellitus are independently associated with adverse outcomes after AMI in the pre-reperfusion era and in the thrombolytic era [36—41]. Ishihara et al. [7] assessed the association between acute hyperglycemia and in-hospital outcome after AMI in the contemporary PCI era. In addition, because acute hyperglycemia was often confused with chronic hyperglycemia, the association between diabetes mellitus and outcome after AMI in the PCI era was also investigated. The in-hospital mortality rate was significantly higher in patients with acute hyperglycemia than in patients without. However, there was no significant difference in mortality between diabetic and non-diabetic patients. Acute hyperglycemia was associated with a higher in-hospital mortality rate both in non-diabetic patients and in diabetic patients. The in-hospital mortality increased as plasma glucose increased (Fig. 4). Acute hyperglycemia was associated with a higher incidence of no-reflow during PCI but diabetes was not. They concluded that acute hyperglycemia, but not diabetes, was a predictor of in-hospital mortality after AMI in the PCI era. No-reflow occurred more frequently during PCI in patients with acute hyperglycemia, suggesting that microvascular dysfunction might contribute to the adverse outcome of such patients.

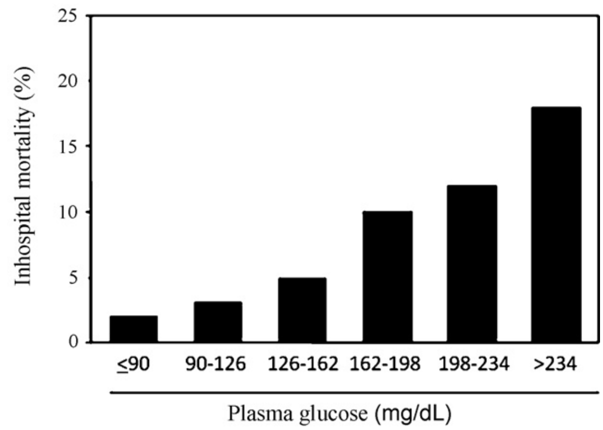

Figure 4 The in-hospital mortality rate increased as plasma glucose increased (2% in patients with plasma glucose ≤ 90 mg/dL, 3% in patients with plasma glucose 90—126 mg/dL, 5% in patients with plasma glucose 126—162 mg/dL, 10% in patients with plasma glucose 162—198 mg/dL, 12% in patients with plasma glucose 198—234 mg/dL, and 18% in patients with plasma glucose > 234 mg/dL; $P < 0.001$).

Other prognostic indicators of AMI

Other prognostic indicators of AMI in addition to leukocyte count and hyperglycemia were examined. Post-AMI hyperuricemia was associated with the development of heart failure [5]. Serum uric acid level on admission was a suitable marker for predicting AMI-related future adverse events (Fig. 5A), and the combination of Killip class and post-AMI serum uric acid level was a good predictor of mortality of patients with AMI (Fig. 5B) [5]. Leukocyte count and plasma glucose level were independently associated with in-hospital mortality suggesting that a simple combination of these two parameters might provide further information regarding prediction of outcome in patients with AMI (Fig. 6) [10]. In another study, risk stratification based on the combined use of leukocyte count,

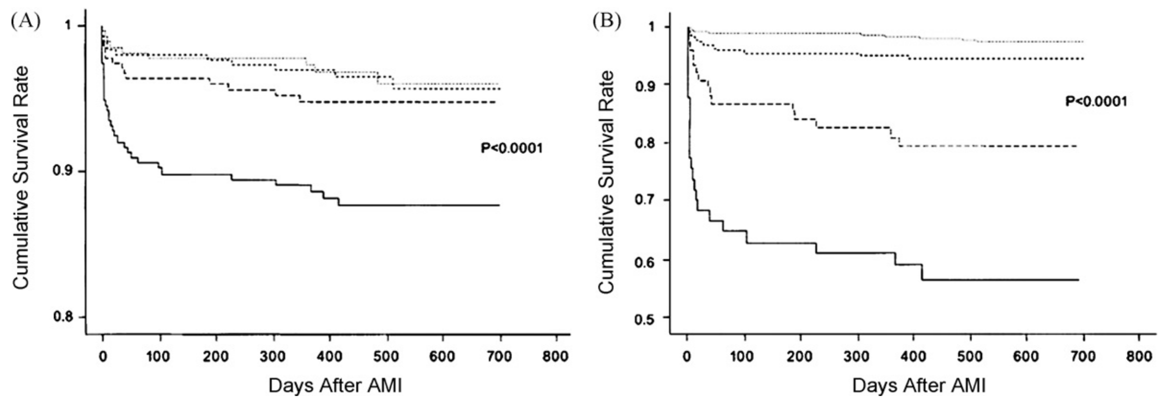

Figure 5 (A) Survival without all-cause mortality in patients after acute myocardial infarction based on serum uric acid concentrations of < 4.6 mg/dL in quartile 1 (*thin solid line*), 4.6 to 5.6 mg/dL in quartile 2 (*short-dash line*), 5.6—6.7 mg/dL in quartile 3 (*long-dash line*), and > 6.7 mg/dL in quartile 4 (*thick solid line*). (B) Survival without all-cause mortality in patients after acute myocardial infarction based on combinations of the best uric acid cut-off concentration of 7.5 mg/dl for predicting survival and Killip's class: Killip's classes I and II plus a uric acid concentration ≤ 7.5 mg/dl (*thin solid line*), Killip's classes I and II plus a uric acid concentration > 7.5 mg/dl (*short-dash line*), Killip's classes III and IV plus a uric acid concentration ≤ 7.5 mg/dl (*long-dash line*), and Killip's classes III and IV plus a uric acid concentration > 7.5 mg/dl (*thick solid line*). AMI, acute myocardial infarction.

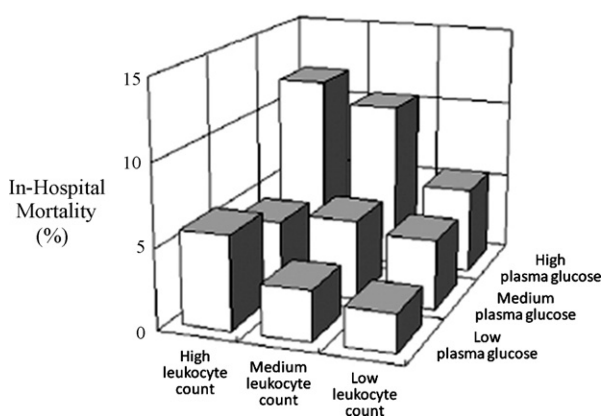

Figure 6 In-hospital mortality across tertiles of leukocyte count (low < 8300/mm^3, medium 8300—11,000/mm^3, high > 11,000/mm^3) and plasma glucose level (low < 133 mg/dl, medium 133—182 mg/dl, high > 182 mg/dl).

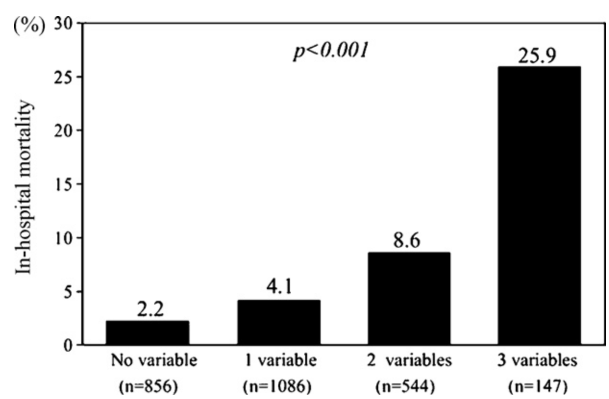

Figure 7 In-hospital mortality according to the number of variables of high leukocyte count (≥11,200/mm^3), high plasma glucose (>72.8 mg/dL), and low glomerular filtration rate (<60 mL/min/1.73 m^2).

plasma glucose, and glomerular filtration rate on admission provided important prognostic information and facilitated early risk stratification (Fig. 7) [14].

Patients with AMI on a weekday or on the weekend

Studies from North America report outcome differences between patients admitted to acute care hospitals on a weekday vs the weekend; that is, the mortality rate of patients admitted on weekends tended to be higher [42,43]. The difference was interpreted to be related to low staffing levels and availability of emergency procedures on the weekends compared with weekdays [44,45]. However, it is not clear whether this is also applicable to Japanese patients and hospitals. Matsui et al. [12] assessed the clinical outcomes for weekday and weekend admission to hospitals for patients with AMI in Japanese acute care hospitals. This study included AMI patients with weekday onset (Monday through Friday) and those with weekend onset (Saturday and Sunday). There were no significant differences between the 2 groups in patient background and clinical features. The proportions of patients who underwent emergency catheterization and reperfusion therapy were also similar. There were no differences between the 2 groups

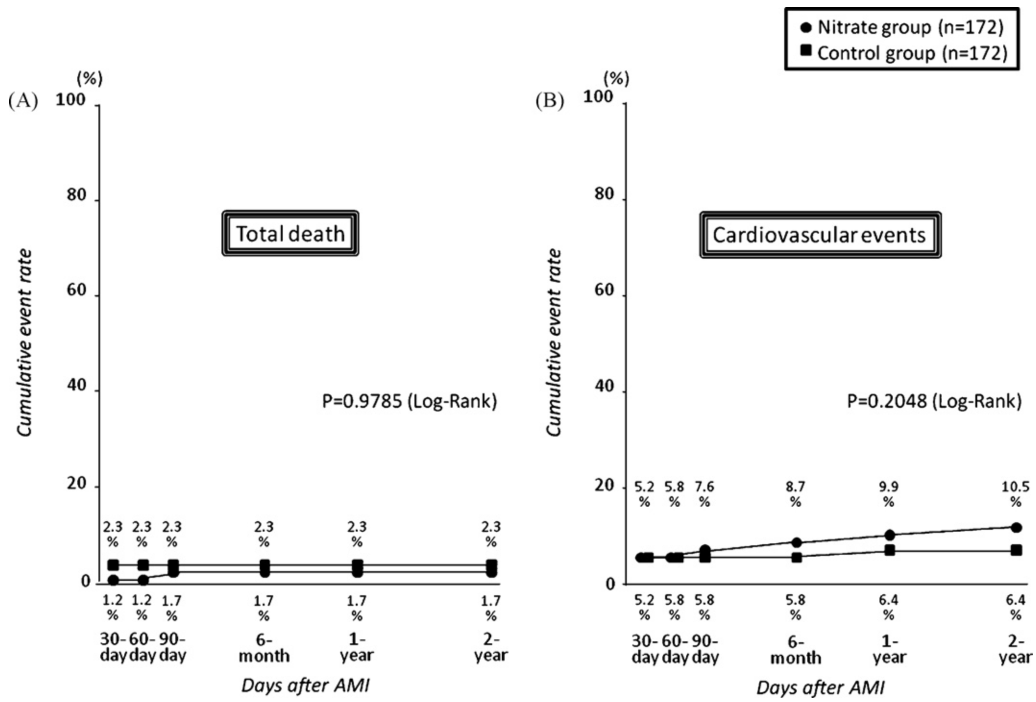

Figure 8 (A) Comparison of cumulative total death rate after propensity score matching in the nitrate group and control group. (B) Comparison of cumulative rate of cardiovascular events (cardiac death, non-fatal reinfarction, unstable angina, heart failure requiring rehospitalization, stroke) after propensity score matching between the nitrate group and control group. AMI, acute myocardial infarction.

in the in-hospital, 30-day, and 1-year mortality rates. Even after various adjustments, there was no difference in the risk of death associated with weekend versus weekday onset of AMI. In conclusion, the results of that study showed similar outcomes for patients who developed acute MI on a weekday or on the weekend. The results express the similar quality of care in Japanese hospitals, regardless of the day of the week.

Is it true that nitrate treatment increases future cardiac events?

In the coronary pre-interventional era, two Japanese studies examined the effects of nitrate treatment in MI patients. However, the overall randomization rate was rather low and data were not adjusted for patient background. There is no clinical evidence for clinical benefits from nitrate treatment in patients undergoing PCI in the acute phase of MI. Another study was designed to determine the effects of long-term nitrate therapy on adverse events in patients with AMI in the coronary interventional era [11]. The results showed that all-cause mortality, cardiac, and cardiovascular events were lower in patients treated with nitrates than untreated controls. However, these crude comparisons included several confounding factors on nitrate prescription. To minimize the effect of selection bias on outcomes, the technique of propensity score matching for clinical characteristics was used and distortion of effective nitrate treatment was excluded. The results of propensity score matching showed that nitrate therapy had no impact on all-cause mortality (Fig. 8A) and cardiovascular events (cardiac death, non-fatal reinfarction, unstable angina, heart failure requiring rehospitalization, and stroke) at 30-day, 60-day, 90-day, 6-month, 1-year, and 2-year follow-up periods (Fig. 8B). The study concluded that long-term nitrate therapy after AMI neither improves nor aggravates prognosis. Prospective randomized clinical trials are warranted to determine the long-term effects of nitrate therapy on secondary prevention of AMI.

Conclusions

There are prospective and retrospective studies in a longitudinal method. The evidence level in prospective studies is higher than that in retrospective studies because prospective studies have less various biases. It takes much time to get the final result in prospective studies while retrospective studies are advantageous to form hasty conclusions. Therefore, retrospective studies show their ability to solve the urgent problems. The JACSS database included more than 5000 consecutive AMI patients and such a large database has not been generally observed in Japanese retrospective studies regarding AMI. The results from JACSS data vividly displayed the modern state of AMI in the interventional era. They may be also helpful to make plans for a novel prospective study. However, there were several problems such as striking missing data in the JACSS database. Therefore, we are now planning to perform a prospective study on AMI (New JACSS) to solve these problems.

Acknowledgments

The authors' work presented in this article was supported in part by grants-in-aid from Cardiovascular Disease (14C-4) from the Ministry of Health, Labour and Welfare, Tokyo. The authors thank Ms. Yuko Kuratsu and Ms. Yukari Hirata for secretarial assistance.

References

[1] TIMI Study Group. The thrombolysis in myocardial infarction (TIMI) trial. Phase I findings. N Engl J Med 1985;312:932—6.
[2] Kosuge M, Kimura K, Kojima S, Sakamoto T, Ishihara M, Asada Y, Tei C, Miyazaki S, Sonoda M, Tsuchihashi K, Yamagishi M, Ikeda Y, Shirai M, Hiraoka H, Inoue T, et al. Effects of preinfarction angina pectoris on infarct size and in-hospital mortality after coronary intervention for acute myocardial infarction. Am J Cardiol 2003;92:840—3.
[3] Kojima S, Sakamoto T, Ishihara M, Kimura K, Miyazaki S, Tei C, Hiraoka H, Sonoda M, Tsuchihashi K, Yamagishi M, Inoue T, Asada Y, Ikeda Y, Shirai M, Ogawa H. The white blood cell count is an independent predictor of no-reflow and mortality following acute myocardial infarction in the coronary interventional era. Ann Med 2004;36:153—60.
[4] Kosuge M, Kimura K, Kojima S, Sakamoto T, Matsui K, Ishihara M, Asada Y, Tei C, Miyazaki S, Sonoda M, Tsuchihashi K, Yamagishi M, Ikeda Y, Shirai M, Hiraoka H, et al. Effects of glucose abnormalities on in-hospital outcome after coronary intervention for acute myocardial infarction. Circ J 2005;69:375—9.
[5] Kojima S, Sakamoto T, Ishihara M, Kimura K, Miyazaki S, Yamagishi M, Tei C, Hiraoka H, Sonoda M, Tsuchihashi K, Shimoyama N, Honda T, Ogata Y, Matsui K, Ogawa H. Prognostic usefulness of serum uric acid after acute myocardial infarction (the Japanese Acute Coronary Syndrome Study). Am J Cardiol 2005;96:489—95.
[6] Kosuge M, Kimura K, Kojima S, Sakamoto T, Ishihara M, Asada Y, Tei C, Miyazaki S, Sonoda M, Tsuchihashi K, Yamagishi M, Ikeda Y, Shirai M, Hiraoka H, Inoue T, et al. Beneficial effect of preinfarction angina on in-hospital outcome is preserved in elderly patients undergoing coronary intervention for anterior acute myocardial infarction. Circ J 2005;69:630—5.
[7] Ishihara M, Kojima S, Sakamoto T, Asada Y, Tei C, Kimura K, Miyazaki S, Sonoda M, Tsuchihashi K, Yamagishi M, Ikeda Y, Shirai M, Hiraoka H, Inoue T, Saito F, et al. Acute hyperglycemia is associated with adverse outcome after acute myocardial infarction in the coronary intervention era. Am Heart J 2005;150:814—20.
[8] Kosuge M, Kimura K, Kojima S, Sakamoto T, Ishihara M, Asada Y, Tei C, Miyazaki S, Sonoda M, Tsuchihashi K, Yamagishi M, Ikeda Y, Shirai M, Hiraoka H, Inoue T, et al. Sex differences in early mortality of patients undergoing primary stenting for acute myocardial infarction. Circ J 2006;70:217—21.
[9] Kawano H, Soejima H, Kojima S, Kitagawa A, Ogawa H. Sex differences of risk factors for acute myocardial infarction in Japanese patients. Circ J 2006;70:513—7.
[10] Ishihara M, Kojima S, Sakamoto T, Asada Y, Kimura K, Miyazaki S, Yamagishi M, Tei C, Hiraoka H, Sonoda M, Tsuchihashi K, Shinoyama N, Honda T, Ogata Y, Ogawa H. Usefulness of combined white blood cell count and plasma glucose for predicting in-hospital outcomes after acute myocardial infarction. Am J Cardiol 2006;97:1558—63.
[11] Kojima S, Matsui K, Sakamoto T, Ishihara M, Kimura K, Miyazaki S, Yamagishi M, Tei C, Hiraoka H, Sonoda M, Tsuchihashi K, Shimoyama N, Honda T, Ogata Y, Ogawa H. Long-term nitrate therapy after acute myocardial infarction does not improve or aggravate prognosis. Circ J 2007;71:301—7.
[12] Matsui K, Kojima S, Sakamoto T, Ishihara M, Kimura K, Miyazaki S, Yamagishi M, Tei C, Hiraoka H, Sonoda M, Tsuchihashi K, Ooie T, Honda T, Ogata Y, Ogawa H. Weekend onset of acute myocardial infarction does not have a negative impact on outcome in Japan. Circ J 2007;71:1841—4.
[13] Kosuge M, Kimura K, Kojima S, Sakamoto T, Ishihara M, Asada Y, Tei C, Miyazaki S, Sonoda M, Tsuchihashi K, Yamagishi M, Shirai M, Hiraoka H, Honda T, Ogata Y, et al. Impact of body mass index on in-hospital outcomes after percutaneous coronary intervention for ST segment elevation acute myocardial infarction. Circ J 2008;72:521—5.
[14] Kosuge M, Kimura K, Morita S, Kojima S, Sakamoto T, Ishihara M, Asada Y, Tei C, Miyazaki S, Sonoda M, Tsuchihashi K, Yamagishi M, Shirai M, Hiraoka H, Honda T, et al. Combined prognostic utility of white blood cell count, plasma glucose, and glomerular filtration rate in patients undergoing primary stent placement for acute myocardial infarction. Am J Cardiol 2009;103:322—7.
[15] Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases. Part I. general considerations, the epidemiologic transition, risk factors, and impact of urbanization. Circulation 2001;104:2746—53.
[16] Pais P, Pogue J, Gerstein H, Zachariah E, Savitha D, Jayprakash S, Nayak PR, Yusuf S. Risk factors for acute myocardial infarction in Indians: a case-control study. Lancet 1996;348:358—63.
[17] Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases. Part II. Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. Circulation 2001;104:2855—64.
[18] Yoshida M, Kita Y, Nakamura Y, Nozaki A, Okayama A, Sugihara H, Kasamatsu T, Hirose K, Kinoshita M, Ueshima H. Incidence of acute myocardial infarction in Takashima, Shiga. Japan Circ J 2005;69:404—8.
[19] Nishigaki K, Yamazaki T, Fukunishi M, Tanihata S, Fujiwara H. Assessment of acute myocardial infarction in Japan by the Japanese Coronary Intervention Study (JCIS) Group. Circ J 2004;68:515—9.

[20] Murry CE, Jennings RB, Reimer KA. Preconditioning with ischemia: a delay of lethal cell injury in ischemic myocardium. Circulation 1986;74:1124—36.
[21] Cohen MV, Liu GS, Downey JM. Preconditioning causes improved wall motion as well as smaller infarcts after transient coronary occlusion in rabbits. Circulation 1991;84: 341—9.
[22] Miura T, Iimura O. Infarct size limitation by preconditioning: its phenomenological features and the key role of adenosine. Cardiovasc Res 1993;27:36—42.
[23] Ottani F, Galvani M, Ferrini D, Sorbello F, Limonetti P, Pantoli D, Rusticali F. Prodromal angina limits infarct size. A role for ischemic preconditioning. Circulation 1995;91: 291—7.
[24] Kloner RA, Shook T, Przyklenk K, Davis VG, Junio L, Matthews RV, Burstein S, Gibson M, Poole WK, Cannon CP, McCabe CH, Braunwald E. Previous angina alters in-hospital outcome in TIMI 4. A clinical correlate to preconditioning? Circulation 1995;91:37—45.
[25] Kloner RA, Shook T, Antman EM, Cannon CP, Przyklenk K, Yoo K, McCabe CH, Braunwald E. Prospective temporal analysis of the onset of preinfarction angina versus outcome: an ancillary study in TIMI-9B. Circulation 1998;97:1042—5.
[26] Ishihara M, Sato H, Tateishi H, Kawagoe T, Shimatani Y, Kurisu S, Sakai K, Ueda K. Implications of prodromal angina pectoris in anterior wall acute myocardial infarction: acute angiographic findings and long-term prognosis. J Am Coll Cardiol 1997;30:970—5.
[27] Anzai T, Yoshikawa T, Asakura Y, Abe S, Akaishi M, Mitamura H, Handa S, Ogawa S. Preinfarction angina as a major predictor of left ventricular function and long-term prognosis after a first Q wave myocardial infarction. J Am Coll Cardiol 1995;26:319—27.
[28] Ross R. Atherosclerosis—an inflammatory disease. N Engl J Med 1999;340:115—26.
[29] Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin, and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997;336: 973—9.
[30] Ridker PM, Buring JE, Shih J, Matias M, Hennekens CH. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. Circulation 1998;98:731—3.
[31] Bradbury J. Renewed interest in leucocyte count as prognostic indicator after AMI. Lancet 2001;358:1787.
[32] Lowe GD, Machado SG, Krol WF, Barton BA, Forbes CD. White blood cell count and haematocrit as predictors of coronary recurrence after myocardial infarction. Thromb Haemost 1985;54:700—3.
[33] Schlant RC, Forman S, Stamler J, Canner PL. The natural history of coronary heart disease: prognostic factors after recovery from myocardial infarction in 2789 men. The 5-year findings of the coronary drug project. Circulation 1982;66:401—14.
[34] Burr ML, Holliday RM, Fehily AM, Whitehead PJ. Haematological prognostic indices after myocardial infarction: evidence from the diet and reinfarction trial (DART). Eur Heart J 1992;13:166—70.
[35] Oswald GA, Corcoran S, Yudkin JS. Prevalence and risks of hyperglycaemia and undiagnosed diabetes in patients with acute myocardial infarction. Lancet 1984;1:1264—7.
[36] Lakhdar A, Stromberg P, McAlpine SG. Prognostic importance of hyperglycaemia induced by stress after acute myocardial infarction. Br Med J (Clin Res Ed) 1984;288:288.
[37] Bellodi G, Manicardi V, Malavasi V, Veneri L, Bernini G, Bossini P, Distefano S, Magnanini G, Muratori L, Rossi G, Zuarini A. Hyperglycemia and prognosis of acute myocardial infarction in patients without diabetes mellitus. Am J Cardiol 1989;64:885—8.
[38] O'Sullivan JJ, Conroy RM, Robinson K, Hickey N, Mulcahy R. In-hospital prognosis of patients with fasting hyperglycemia after first myocardial infarction. Diabetes Care 1991;14:758—60.
[39] Fava S, Aquilina O, Azzopardi J, Agius Muscat H, Fenech FF. The prognostic value of blood glucose in diabetic patients with acute myocardial infarction. Diabet Med 1996;13:80—3.
[40] Capes SE, Hunt D, Malmberg K, Gerstein HC. Stress hyperglycaemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet 2000;355:773—8.
[41] Wahab NN, Cowden EA, Pearce NJ, Gardner MJ, Merry H, Cox JL. Is blood glucose an independent predictor of mortality in acute myocardial infarction in the thrombolytic era? J Am Coll Cardiol 2002;40:1748—54.
[42] Bell CM, Redelmeier DA. Mortality among patients admitted to hospitals on weekends as compared with weekdays. N Engl J Med 2001;345:663—8.
[43] Barnett MJ, Kaboli PJ, Sirio CA, Rosenthal GE. Day of the week of intensive care admission and patient outcomes: a multisite regional evaluation. Med Care 2002;40:530—9.
[44] Bell CM, Redelmeier DA. Waiting for urgent procedures on the weekend among emergently hospitalized patients. Am J Med 2004;117:175—81.
[45] Kostis WJ, Demissie K, Marcella SW, Shao YH, Wilson AC, Moreyra AE. Weekend versus weekday admission and mortality from myocardial infarction. N Engl J Med 2007;356: 1099—109.