The full benefit of scientific progress is often not experienced by patients because of the gap between knowledge and its clinical application. In the United States, the First Scientific Forum on Assessment of Quality of Care and Outcomes Research in Cardiovascular Disease and Stroke was held in 1999, and it created a framework for quantifying the components of care for acute myocardial infarction (AMI) and summarized current methodological considerations in quality assessment. Furthermore, surveys of the disparity in the care of many diseases including AMI have been conducted by many US organizations, such as the Institute of Medicine, compared with the situation in Japan.

Since 1999, we have been registering patients with AMI who were hospitalized in 22 national hospitals in Japan, and we checked their care during hospitalization and the prognosis at 6-month follow-up in order to clarify any disparities in the process and outcome among these hospitals. This study was named the CAMPAIGN Study from its English title “A Study of Cost/benefit and Mortality/Morbidity of Patients with Acute Myocardial Infarction using a System Designed for National Hospitals Network”.

**Methods**

**Subjects**

A total of 2,007 patients with AMI who were admitted to 22 national hospitals in Japan within 7 days of onset were registered between April 1999 and January 2002 for CAMPAIGN Study 1. A further 206 and 238 cases of AMI were registered between October and December 2002 (CAMPAIGN 2) and between October and December 2003 (CAMPAIGN 3), respectively.

The following data were obtained: age, gender, the dates of onset, admission and discharge, infarction site on electrocardiogram, past history of infarction, Forrester classification (when available), and performance of coronary angiography (CAG), thrombolytic therapy, percutaneous transluminal coronary angioplasty (PTCA), coronary artery stenting, and/or emergency coronary artery bypass grafting (CABG) surgery, reperfusion time, final degree of coronary artery stenosis, perfusion classification according to the Thrombolysis in Myocardial Infarction (TIMI) classification system; whether elective CAG prior to discharge (pre-discharge CAG), elective PTCA, elective stenting, and/or elective CABG surgery was performed was also checked. The prognosis at discharge, prescription at discharge, 6-month prognosis, and readmission rate were also investi-
The protocol for this study was approved by the Osaka National Hospital Institutional Review Board.

**Statistical Analysis**

The data are expressed as mean ± SD. The differences between groups were compared by unpaired t-test, analysis of variance (ANOVA) or χ² test where appropriate. Multivariate regression analysis was used to elucidate the factors that determine the length of stay (LOS) in hospital. Differences were considered to be statistically significant when p<0.05.

**Results**

**General Background**

Patient profiles and treatments during the acute phase are summarized in Tables 1 and 2. The mean age of patients in the CAMPAIGN 1, 2 and 3 studies was 66.9±12.2, 67.8±11.4, and 67.2±12.4 years, respectively. There were no significant differences in age, gender ratio, ratio of initial infarction, region of infarction, and peak serum creatine.
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1. In-hospital mortality rates according to Thrombolysis in Myocardial Infarction (TIMI) classification. Patients with TIMI 3 flow had the lowest mortality (p<0.05).

2. In-hospital mortality rates according to the Forrester subset. Patients with Forrester IV had the highest mortality rate.

3. Prescription rate of drugs at discharge. ACE-I, angiotensin-converting enzyme inhibitor.

kinase (CK) level among the 3 studies.

In CAMPAIGN 1, PTCA and the stenting were performed during the acute phase in 80% and 70% of all patients. The PTCA rate by number of registered patients was slightly less at hospitals with more than 100 patients compared with the rate at hospitals with less than 100 patients (78.6% vs 83.1%, p=0.24). Thrombolytic therapy, on the other hand, was performed only in 12% of patients and in those who underwent thrombolytic therapy within 24 h of onset, the mean time to reperfusion from onset was 5.8 h. Aorto-coronary bypass surgery was performed during the acute phase only in 3% of patients. The final degree of stenosis after intervention was 0% in 51% of patients, 25% or less in 31%, and 25–50% in 6%; in 88% of patients, 50% or less stenosis was achieved. A TIMI grading of 3 without delay was achieved in 83% of patients. These findings did not differ in CAMPAIGNS 2 and 3.

Disparities in Process and Outcome During the Acute Phase

In CAMPAIGN 1, anticoagulants were used in 91% of all patients, with heparin used in 98% of cases (Table 1). The usage rate of antiplatelet drugs was 85%; however, aspirin alone was used in 51% of cases, and ticlopidine and/or cilostazol with aspirin were used in other cases.

In CAMPAIGN 1, the in-hospital mortality rate was 12.4%. The mortality rate in patients older than 80 years was higher at 26.0%, compared with 9.1% for patients younger than 80 years. By TIMI classification, the mortality rate of patients with TIMI 3 flow was significantly lower at 6.5%, compared with patients with TIMI 0–2 flow (Fig 1). Right heart catheterization only was performed in 40% of patients (Table 1). By Forrester’s classification, type IV accounted for most (50.0%) of the mortality (Fig 2). Cardiac failure accounted for most (57%) of deaths, followed by arrhythmia (11%), and cardiac rupture (11%). The LOS in hospital of the patients who died of cardiac failure, arrhythmia or cardiac rupture was 7.9±1.1, 10.5±3.3, and 4.5±1.1 days, respectively, without significant differences among them (p=0.23).

The average LOS in hospital was 27.6±23.4 days in CAMPAIGN 1. When patients who died in hospital or whose LOS was 60 days or more are excluded, the mean LOS was 24.8±12.5 days. There were no significant correlations between LOS and severity of infarction. Even in patients with a small infarct (peak CK ≤1,500), the mean LOS was 22.9±11.6 days.

The drugs prescribed at discharge also showed disparities in CAMPAIGN 1 (Fig 3). Antiplatelet drugs were used at a very high rate (95%) compared with the rates of angiotensin converting enzyme (ACE) inhibitors and β-blockers (68% and 25%, respectively). Nitrates, for which there is no evidence for use in the chronic phase of myocardial infarction, were prescribed at 68%.

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The mortality rate in the 947 patients who were followed for 6 months in CAMPAIGN 1 was low at 1.9%. The most frequent causes of death were cardiac failure and re-infarction, with non-cardiac causes accounting for half of the deaths. During the 6-month follow-up period, 566 (55%) of the 1,026 patients followed were readmitted at least once, the most common reason being follow-up CAG (399 patients), followed by PTCA with/without stenting (91 patients), angina pectoris (29 patients), cardiac failure (20 patients), and CABG (13 patients). The 6-month prognosis was the same whether or not pre-discharge CAG was performed. Although there was no difference between the groups in peak CK, the readmission rate during the 6-month follow-up in patients who underwent pre-discharge CAG was significantly higher (Table 3).

Disparities Among Hospitals

In CAMPAIGN 1, the LOS showed a wide variation (SD=12.5 days) and further analysis revealed that it was significantly prolonged by pre-discharge CAG (CAG(–): 21.6±10.3 days; CAG(+): 26.5±10.7 days, p<0.01). Prior to discharge, CAG and PTCA were performed in 58% and 16% of patients, respectively. Furthermore, the LOS in hospitals handling more than 100 AMI patients per year was significantly shorter than in those with fewer AMI patients (>100: 22.8 days; <100: 26.7 days). There were no significant correlations between LOS and infarction site, age, gender, or peak CK. LOS significantly correlated with reperfusion therapy (with: 24.8±0.3 days; without: 22.9±0.7 days, p<0.01), and Forrester’s classification (type I: 26.9±0.5, type II: 29.3±1.1, type III: 26.2±2.3, type IV: 19.3±2.2 days, p<0.001). Multivariate regression analysis revealed that pre-discharge CAG and age are significant factors determining LOS (r=0.32, p<0.001).

The drugs prescribed at discharge also showed large

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Table 3 Mortality and Morbidity 6 Months Post-Discharge in Relation to Elective Pre-Discharge CAG

<table>
<thead>
<tr>
<th></th>
<th>Pre-discharge CAG</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(+)</td>
<td>(–)</td>
</tr>
<tr>
<td>Prognosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Survival</td>
<td>608</td>
<td>301</td>
</tr>
<tr>
<td>Readmission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(+)</td>
<td>247</td>
<td>197</td>
</tr>
<tr>
<td>(–)</td>
<td>401</td>
<td>152</td>
</tr>
</tbody>
</table>

CAG, coronary angiography.

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Fig 4. Disparities in prescriptions at discharge among the hospitals. A–V, the different hospitals. Each bar indicates the total number of patients in each hospital; dark bar indicates the patients prescribed the current drug at discharge.

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Fig 5. Distribution of the mortality rate among the hospitals. Horizontal and vertical bars respectively indicate the mortality rate and its 95% confidence interval of each hospital.
disparities among hospitals (Fig 4). In almost all hospitals, antiplatelet agents were prescribed consistently. In contrast, ACE inhibitors were used at a high rate (70%), but not consistently, indicated by the wide range of the prescription rate (10–90%). The usage of β-blockers was very low (24%), and many hospitals did not include β-blockers in the discharge prescription.

In addition, the mortality rate during the acute phase showed a wide range, from 26.6% to 3.6%, among hospitals (Fig 5). However, the 95% confidence interval of the mortality rate in each hospital embraced the average of all hospitals (12.4%) except for 3 hospitals that were lower.

**Changes in the CAMPAIGN 2 and 3 Studies**

The CAMPAIGN 2 and 3 studies were performed as the follow-up to CAMPAIGN 1 and the changes are summarized in Table 4. The mortality rate during the acute phase decreased and the mean LOS was reduced to 22.2 days in CAMPAIGN 2, and 21.9 days in CAMPAIGN 3. A striking change was observed in the drugs prescribed at discharge. The use of β-blockers increased from 25% to 47%, and that of nitrates decreased from 68% to 21%.

**Discussion**

Systematic surveying of the process and outcome of treatment of AMI is necessary to assess its quality but such nationwide surveys are currently infrequent in Japan. An epidemiological survey of AMI in the Osaka area, as well as an analysis of gene polymorphism, has been conducted mainly by Osaka University since 1998, but our study of the mortality rate, LOS, and treatment of acute phase AMI in national hospitals, is the first systematic survey in Japan.

Even though the mortality rate during the acute phase improved in CAMPAIGNs 2 and 3, there is more room for improvement, particularly in hospitals with a higher-than-average mortality rate, where structural reform with a view to early treatment, and control measures for cardiac failure and arrhythmia may be necessary. Rogers et al maintain that, from the perspective of thrombolytic therapy, patients should opt for treatment at a local hospital in Japan, however, most hospitals perform emergency PTCA and direct PTCA is the mainstream therapy. According to the results of our analysis, the rate of thrombolytic therapy is extremely low and the use of thrombolytic therapy, including use of tissue plasminogen activator, warrants investigation. Casale et al and Vakili et al cited treatment by a cardiovascular specialist, PTCA rate, total number of physicians, and number of patients, as factors involved in mortality. Although the present study did not investigate the total number of physicians, all hospitals had a Department of Cardiovascular Disease and the PTCA rate, which ranged from 70% to 92%, did not differ significantly from one hospital to another. The PTCA rate was slightly less at hospitals with more than 100 patients compared with hospitals with less than 100 patients, but the difference was not significant. In a large-scale study of myocardial infarction in the Osaka area, the in-hospital mortality rate at hospitals with at least 70 registered patients per year was 7.9%, 12.0% at hospitals with 11 to 69 patients per year, and 14.1% at hospitals with no more than 10 patients per year. Therefore, the mortality rate was significantly lower at hospitals with a larger number of patients. However, the emergency PTCA rate in these groups was 90.1, 76.8, and 50.0%, respectively, and this difference may have contributed significantly to the differences in mortality rate. In contrast, no significant association between the volume of AMI patients and mortality was reported in another Japanese study. The mortality rate in our study was similar to that in hospitals with 11–69 patients in the Osaka study and we also found that the mortality rate among elderly patients was significantly high. As society is aging, the treatment strategy for elderly patients should be reviewed in comparison with that for patients aged 70 years or less. The mortality rate among patients with a post-intervention TIMI grading of 3 was lower than that in patients with a TIMI grading of 0–2 (Fig 1) which reconfirms the importance of complete reperfusion. In order to improve the mortality rate, measures such as more aggressive intervention at the site of occlusion or reperfusion, more aggressive use of aortic balloon pumping or bypass surgery for unstable hemodynamics caused by inadequate recanalization, as well as concomitant use of suction thrombectomy and use of drugs to prevent or improve reperfusion injury, should be considered. There was no significant difference in prognosis between a reperfusion time of 6 h or less and 6–24 h (8.6% vs 9.8%, p=0.53). Therefore, we concluded that complete reperfusion is more important than the reperfusion time.

**Table 4 Changes in Mortality Rate, Length of Stay (LOS) and Prescription at Discharge in CAMPAIGN Studies 2 and 3**

<table>
<thead>
<tr>
<th></th>
<th>CAMPAIGN 1</th>
<th>CAMPAIGN 2</th>
<th>CAMPAIGN 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>2,007</td>
<td>266</td>
<td>238</td>
</tr>
<tr>
<td>Peak CK level</td>
<td>2,873±86</td>
<td>2,898±177</td>
<td>2,608±226</td>
</tr>
<tr>
<td>Mortality rate during acute phase (%)</td>
<td>12.0</td>
<td>7.9</td>
<td>8.4</td>
</tr>
<tr>
<td>Age &gt;80 years</td>
<td>26.7</td>
<td>13.0</td>
<td>22.9</td>
</tr>
<tr>
<td>Age &lt;80 years</td>
<td>8.5</td>
<td>6.5</td>
<td>5.9</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>24.6</td>
<td>22.2</td>
<td>21.9</td>
</tr>
<tr>
<td>Peak CK &lt;1,500</td>
<td>22.1±1.0</td>
<td>20.1±1.1</td>
<td>19.8±1.0</td>
</tr>
<tr>
<td>Drugs prescribed at discharge (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti platelet agents</td>
<td>95</td>
<td>98</td>
<td>95</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>68</td>
<td>66</td>
<td>74</td>
</tr>
<tr>
<td>β-blockers</td>
<td>25</td>
<td>36</td>
<td>47</td>
</tr>
<tr>
<td>Nitrates</td>
<td>68</td>
<td>24</td>
<td>21</td>
</tr>
</tbody>
</table>

CK, creatine kinase; ACE, angiotensin-converting enzyme.
ever, the follow-up study needs to be interpreted carefully because of the limited number of patients resulting from the practice of some hospitals that actively discharge improved patients to the referring physician.

Currently, there is still a significant gap in the LOS between Japan, on the one hand, and the USA and Canada where the LOS of AMI is approximately 4 days and 9–11 days, respectively. An extreme reduction in LOS, however, is not embraced by patients because it means a bigger burden in terms of post-discharge care at home. In light of the comprehensive medical care available in Japan, the accumulation of Japanese data will become increasingly more important for policy makers.

The CAMPAIGN 2 and 3 studies were performed as the follow-up study of CAMPAIGN 1. Due to the limitation of the Grant-in-Aid, the registration of patients with AMI was not continuous and was separated into 2 phases, resulting in the small number of registered cases. Even though these factors limited the interpretation of the results, it is clear there were changes during 2 years in the use of β-blockers and nitrates in the discharge prescription. This is considered to have been achieved by feedback of the results of CAMPAIGN 1 to the hospitals, together with educational information about the guideline for AMI treatment.

The current study is based on data from patients hospitalized in national hospitals. Although these hospitals were under the regulation of the Japanese Ministry of Health, Labour and Welfare, there is no reason that the process and outcome of treatment for AMI should be far different from that of other hospitals in Japan. Therefore, the results obtained in this survey represent the current standard in Japan. A larger study in general hospitals will be necessary in the future. A similar study to CAMPAIGN was planned by the National Hospital Organization, and started in January 2005.

Conclusions

Patients with AMI admitted to 22 national hospitals in Japan were registered and their clinical data collected since July 1999 (the CAMPAIGN study). CAMPAIGN 1, which was conducted until December 2001, revealed considerable variations in treatment during the acute phase. LOS, rate of pre-discharge CAG, and prescription at discharge among the hospitals. In mild cases of AMI, in particular, omitting the pre-discharge CAG could reduce the LOS. The use of β-blocker at discharge was low, and nitrates, for which there is no evidence for their use as secondary prevention, were frequently used. CAMPAIGN 2 and 3, the follow-up studies conducted during 2002 and 2003, show the changes in problems revealed by CAMPAIGN 1.

Acknowledgments

We acknowledge the work of all investigators. This study was supported by grants from Ministry of Health, Labor and Welfare in Japan; Health Science Research (to MI, H11-Keiho-016 in 1999-2001), and Clinical Research for Evidenced Based Medicine (to MI, H14-Shinko-002 in 2002, to HK, H15-Shinko-07 in 2003).

References

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Appendix 1

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