Comparison of Outcomes for Patients Undergoing Balloon Angioplasty vs Coronary Stenting for Acute Myocardial Infarction

— Results From Nationwide Japanese Registry —

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Randomized clinical trials have demonstrated that coronary stenting is more successful than balloon angioplasty in improving short- and long-term outcomes. However, it remains unknown whether those results can be generalized to broad-based practice. This study aimed to determine whether the outcome for patients with acute myocardial infarction (AMI) undergoing coronary stent placement would be better than those undergoing balloon angioplasty. The risk-adjusted mortality and subsequent revascularization rates were compared for 2,185 patients from a nationwide Japanese registry during 1997. A total of 1,349 patients were treated with balloon angioplasty alone and 836 had stent placement. There were no statistically significant differences in the prevalence of demographic, clinical, and angiographic variables, except that the angioplasty group had a greater proportion of female patients and those with a left circumflex lesion. Unadjusted in-hospital mortality was comparable (7.6 vs 6.3%; $p=0.28$), despite higher angiographic success rate for the stent group (89.7 vs 97.7%; $p<0.01$). Adjusted odds ratio for in-hospital mortality was 0.75 ($p=0.19$). The same-admission bypass surgery rate was also similar. The 1.9-year post-discharge mortality rate was similar. The need for subsequent revascularization procedures was also similar, but restenosis was significantly lower in the stent group (34 vs 45%; $p<0.01$). The superiority of clinical outcome for stenting rather than balloon angioplasty could not be demonstrated in broad-based registry patients, despite technically successful results. (Circ J 2003; 67: 369–374)

Key Words: Acute myocardial infarction; Coronary intervention; In-hospital mortality; Long-term mortality

The efficacy of percutaneous coronary intervention (PCI) has been established for the treatment of patients with acute myocardial infarction (AMI)^{1,2} and there is now increasing evidence from randomized trials that coronary stent placement yields significantly better results than balloon angioplasty.^{3–8} However, there is scant information available from routine clinical practice to determine the effects of stents on short- and long-term outcome. As in many randomized controlled studies, these trials included only a small proportion of selected patients, and the hospitals participating in the trials are particularly experienced and large-volume centers. In fact, previous subgroup analyses using the registry data from New York⁹ and Germany¹⁰ and a retrospective analysis of a single institution's data¹¹ could not observe a significant improvement in clinical outcomes in AMI patients receiving coronary stents. In contrast, a recent report from Veterans Affairs'

medical centers indicated that stent placement was associated with better short- and long-term outcomes.¹² Therefore, it has not been explicitly clarified whether the results of randomized trials apply to the 'real world' of broad-based practice. To justify the use of coronary stents, one must quantify the effects of coronary stenting in actual clinical practice.

Therefore, the purpose of this study was to compare the early (in-hospital) and long-term (1.9 year) follow-up data from patients with AMI who had undergone PCI with either balloon angioplasty or stent placement. The Japanese Coronary Intervention Study (JCIS) is an extensive nation-wide survey of practice in Japan,^{13–15} designed to accumulate information on contemporary broad-based clinical practice. We analyzed not only mortality, but also the incidence of revascularization procedures, including repeat PCI and coronary artery bypass grafting (CABG), during follow-up.

Methods

Patient Population

Patient selection and data collection have been described previously.^{13,15} Briefly, the JCIS survey demonstrated that 109,788 PCI procedures were performed at 1,023 hospitals during 1997 in Japan. The patients' characteristics and outcomes were evaluated in a total of randomly selected 10,642 PCIs, which represented approximately 10% of all PCIs registered in the JCIS. All patients with AMI ($n=2,540$) who had undergone PCI were identified. Inclusion

(Received December 2, 2002; revised manuscript received February 21, 2003; accepted February 27, 2003)

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criteria were patients with AMI who presented within 6 h of symptom onset, or between 6 and 24 h if they had persistent symptoms with evidence of ongoing ischemia, including chest pain and ST-segment elevation in the infarct region. Patients in whom PCI was interrupted during the procedure (n=20) and those with an incomplete data set regarding the infarct-related artery (n=306) and in-hospital complications (n=3) were excluded. Further exclusions were patients who underwent other PCIs such as atherectomy or laser angioplasty in addition to balloon angioplasty or stent placement (n=12). Patients who had more than one lesion attempted were also excluded (n=14) because it was impossible to determine whether balloon angioplasty or stent placement was the only intervention attempted on all lesions. This approach led to the identification of 2,185 patients, 1,349 of whom underwent balloon angioplasty and 836 of whom underwent stent placement. For each patient, baseline demographic information, clinical factors, angiographic findings, procedural data, in-hospital and long-term outcomes were collected by the investigators in each institution.

Data Collection

The patients' demographic information, cardiovascular

history, their risk factors (ie, hypercholesterolemia, smoking, hypertension, and diabetes mellitus) were recorded. Hypercholesterolemia was defined as total cholesterol ≥ 220 mg/dl; hypertension was defined as systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg; diabetes mellitus was defined as fasting blood sugar ≥ 140 mg/dl or blood sugar during a 75 g oral glucose tolerance test ≥ 200 mg/dl; renal failure was defined as serum creatinine ≥ 2.5 mg/dl. Single-vessel disease was defined as $\geq 51\%$ stenosis in any of the major coronary arteries or their major branches, and multivessel disease was defined as $\geq 51\%$ stenosis in either 2 or all 3 major epicardial coronary arteries. Further, the left ventricular ejection fraction (LVEF) was assessed by any method including left ventricular (LV) angiography, echocardiography, and radio-nuclide angiography, and categorized as (1) $\geq 50\%$ and (2) $<50\%$ or unknown.

Outcome

Follow-up data were obtained by reviewing the medical records and/or mail or telephone contact with the patients.¹⁵ We assessed death and the use of revascularization procedures including repeat PCI and CABG during and after the

Table 1 Characteristics for the Patients Treated With Balloon Angioplasty vs Those With Stent Placement

	Angioplasty (n=1,349)	Stent (n=836)	p value
Age (mean $\pm$ SD, years)	65.1 $\pm$ 11.5	64.8 $\pm$ 11.1	0.29
≥ 75 year (%)	22.2	19.9	0.19
Male (%)	73.1	77.3	0.03
Prior myocardial infarction (%)	2.0	2.0	0.96
Hypercholesterolemia (%)	36.5	37.1	0.81
Smoking (%)	51.8	54.0	0.14
Hypertension (%)	50.8	49.9	0.66
Diabetes mellitus (%)	28.8	27.4	0.41
Renal failure (%)	2.0	1.7	0.58
Cerebrovascular disease (%)	8.4	8.0	0.68
Prior PCI (%)	5.4	5.5	0.94
Prior CABG (%)	0.6	0.7	0.73
Affected coronary artery (%)			
Left anterior descending	50.3	52.0	0.42
Right	34.8	37.7	0.18
Left circumflex	13.9	8.9	<0.01
Left main	1.0	1.4	0.31
No of diseased vessels (%)			
Single vessel	60.6	60.5	0.97
Multivessel	37.5	37.0	0.88
Left main	1.9	2.5	0.37
Ejection fraction (mean $\pm$ SD, %)	55.0 $\pm$ 14.0	54.4 $\pm$ 14.0	0.92
$\geq 50\%$ (%)	48.9	45.7	0.14

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Table 2 Unadjusted and Adjusted Odds Ratio (OR) of In-Hospital Outcomes for Patients Treated With Balloon Angioplasty vs Those With Stent Placement

Outcome	Number (%)		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	Angioplasty (n=1,349)	Stent (n=836)		
In-hospital mortality	102 (7.6%)	53 (6.3%)	0.83 (0.59–1.17) p=0.28	0.75 (0.49–1.16) p=0.19
Repeat PCI	42 (3.1%)	34 (4.1%)	1.32 (0.83–2.10) p=0.24	1.29 (0.81–2.06) p=0.28
CABG	13 (1.0%)	8 (1.0%)	0.99 (0.41–2.41) p=0.99	0.91 (0.35–2.34) p=0.84
Angiographic success	1210 (89.7%)	817 (97.7%)	0.20 (0.12–0.33) p<0.0001	0.23 (0.12–0.45) p<0.0001

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CI, confidence interval.

hospitalization.

Angiographic success was defined as successful dilation to $\leq 50\%$ residual stenosis or Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow of the attempted lesions. Restenosis was defined as a final stenosis $>50\%$ at follow-up or a loss of at least 50% of the gain in luminal diameter achieved by PCI.

In-hospital follow-up data were collected for all patients. Long-term follow-up data were obtained in 1,914 of 2,030 discharged patients (94.3 %). The mean follow-up interval was approximately 1.9 years in both groups (697 ± 174 days for the angioplasty group and 699 ± 179 days for the stent group; $p=0.808$).

Statistical Analysis

Patient characteristics and outcomes were compared between the angioplasty and stent groups; chi-square statistic was used for categorical variables and unpaired t test for continuous variables. As for in-hospital outcomes, odds ratios (OR) for patients treated with balloon angioplasty as compared with stenting were calculated by logistic regression analysis. Long-term outcomes in the 2 groups were examined by Kaplan-Meier curves, and Cox's proportional-hazards models were used to calculate relative risk. Adjustment was made for variables potentially associated with treatment selection including age, gender, previous MI, hypercholesterolemia, smoking, hypertension, diabetes mellitus, renal failure, cerebrovascular disease, prior PCI, prior CABG, attempted lesion, number of diseased vessels, and LVEF. Both short- and long-term outcomes were also compared for angioplasty vs stenting within subgroups classified by the baseline characteristics: number of diseased vessels, proximal left anterior descending (LAD) disease, diabetes mellitus, and normal/abnormal LVEF. Statistical analyses were performed by using the SAS (version 8.1), and a two-sided p value less than 0.05 was regarded as statistically significant.

Results

Patient characteristics including demographic data, medical history, risk factors, and angiographic data are shown in Table 1. As noted, patients treated by balloon angioplasty were less often males and were more likely to have had a left circumflex coronary artery lesion than patients treated by stents. There were no significant differences in other variables between the 2 groups of patients.

Fig 1. Odds ratios for in-hospital mortality with confidence intervals (CI) for balloon angioplasty versus stents were obtained from logistic regression analysis models comparing balloon angioplasty and stents with adjustment for all variables for the entire group and within each of the specified subgroups. LAD, left anterior descending coronary artery. LV, left ventricle.

Even though the rate of angiographic success was higher in the stent group (89.7 vs 97.7 %, $p<0.0001$), the in-hospital mortality rate was comparable (7.6 vs 6.3%) between the balloon angioplasty and stent groups (Table 2). Even after adjustment for all potentially confounding factors, the risk of in-hospital mortality was similar (OR 0.75). The adjusted rates of need for repeat PCI or CABG during the hospitalization were also comparable between the 2 groups. Fig 1 shows the adjusted OR for in-hospital mortality for 8 subgroups of patients: single and multivessel disease, proximal LAD and non-LAD disease, diabetes and nondiabetes, and normal and abnormal or missing LV function data. In-hospital mortality was comparable in all subgroups that were examined. Even though the in-hospital mortality in the stent group tended to be lower in the subgroup of proximal LAD disease (10.2 vs 7.0 %), this difference did not reach statistical significance ($p=0.053$).

Despite the benefits of stents in reducing restenosis (44.5 vs 34.2 %, $p<0.0001$), they were not associated with a statistically significant reduction in long-term outcomes including all cause mortality, cardiac mortality, or the need for revascularization procedures (Table 3). All results were essentially unchanged even after adjustment for all potentially confounding variables. Fig 2 represents the 1.9-year adjusted mortality curves for the angioplasty and stent groups. As indicated, the cumulative adjusted mortality

Table 3 Unadjusted and Adjusted Relative Risk (RR) of Long-Term Outcomes for Patients Treated With Balloon Angioplasty vs Those With Stent Placement

Outcome	Number (%)		Unadjusted RR (95% CI)	Adjusted RR (95% CI)
	Angioplasty (n=1,171)	Stent (n=836)		
All-cause mortality	69 (5.9%)	47 (6.3%)	1.09 (0.75–1.58) $p=0.65$	1.07 (0.73–1.58) $p=0.71$
Cardiac mortality	25 (2.1%)	26 (3.5%)	1.63 (0.94–2.83) $p=0.08$	1.57 (0.88–2.80) $p=0.12$
Repeat PCI	417 (35.6%)	267 (35.9%)	1.00 (0.86–1.17) $p=1.00$	0.99 (0.85–1.16) $p=0.96$
CABG	77 (6.6%)	51 (6.9%)	1.04 (0.73–1.49) $p=0.81$	1.01 (0.70–1.47) $p=0.93$
Restenosis	427 (44.5%)	220 (34.2%)	0.65 (0.53–0.80) $p<0.0001$	0.63 (0.52–0.78) $p<0.0001$

PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; CI, confidence interval.

Fig2. Kaplan-Meier analysis of 1.9-year post-discharge mortality for patients having balloon angioplasty (solid line) or stent placement (dashed line).

Fig3. Kaplan-Meier analysis of the need for repeat PCI and CABG for patients having balloon angioplasty (solid line) or stent placement (dashed line).

rates were similar. In addition to mortality rates, the requirement for repeat PCI or CABG was also similar (Fig3). Fig4 shows the adjusted mortality relative risks for long-term mortality for balloon angioplasty and stent placement for 8 subgroups of patients as shown in Fig1. Again, adjusted post-discharge mortality rates were comparable in all subgroups analyzed.

Discussion

The present study demonstrated that stent placement did not significantly reduce the risk of in-hospital mortality and the need for subsequent revascularization compared with balloon angioplasty in patients with AMI despite a significantly higher angiographic success. Further, stents reduced the incidence of restenosis of the infarcted coronary artery, but did not affect the long-term mortality and the need for revascularization procedures including repeat PCI or CABG after discharge.

Previous randomized clinical trials comparing balloon angioplasty with stent placement in the treatment of patients with AMI have demonstrated improved short- and long-term outcomes in the stent-treated patients.³⁻⁸ In contrast, the present study analyzing broad-based registry patients with AMI could not demonstrate any benefits in coronary stenting compared with balloon angioplasty.

There are several explanations for the lack of a beneficial relationship between stents and clinical outcomes. First, this is not a randomized clinical trial. Consequently, the choice of treatment was influenced by the attending physician's decision. It is possible that patients receiving stents were at higher risk of cardiac events, therefore making a

Fig4. Relative risks for long-term mortality with confidence intervals (CI) for balloon angioplasty versus stents were obtained from multivariate Cox's proportional-hazards models comparing balloon angioplasty and stents with adjustment for all variables for the entire group and within each of the specified subgroups. LAD, left anterior descending coronary artery. LV, left ventricle.

truly beneficial effect of stenting. In fact, there was a small, although statistically insignificant, excess of patients with left main disease (1.0 vs 1.4 %, $p=0.31$) in the stent group (Table 1). In addition, more patients with a left circumflex lesion were treated with balloon angioplasty (13.9 vs 8.9 %, $p<0.01$) and this group of patients might have had a reasonably good prognosis.¹¹ However, the 2 patient groups were quite similar with respect to preprocedural risk factors. Furthermore, we attempted to minimize the treatment selection bias by adjusting the differences among patients in the prevalence of potentially confounding demographic, clinical, and angiographic variables. Therefore, uncontrolled confounding is unlikely to explain the results. Despite this, it cannot be excluded that patients undergoing stent placements might have had clinical signs of severity that escaped the usual clinical description taken into account in the present study. Second, stents used as bailout therapy for abrupt closure (not discernible from the data set in this study) might increase the risk of adverse outcomes in the stent group.¹⁶ Third, the design of the present study could result in a failure to detect a reduction in risk from stents because of chance. However, the consistency of the lack of benefit in the different subgroups suggests that these findings were not from chance. Fourth, an even higher risk for in-hospital adverse outcomes with coronary stenting compared with balloon angioplasty has been shown,¹⁷ and might be related to slower antegrade flow after stenting,¹⁸ which is at least partly attributable to thrombus formation at the site of stent implantation followed by distal embolization.¹⁹ Therefore, stenting might have reduced epicardial flow, which would have adversely affected the in-hospital outcomes in the present study. Whatever the reason, the present findings are consistent with those obtained from the New York⁹ and German registries,¹⁰ which both found that there was not a short- or long-term outcome benefit for stent placement in patients with AMI. The similarities between those 2 registries and ours are striking, and are also supported by a recent retrospective analysis of patients with AMI treated with PCI.¹¹ Given the larger sample sizes, registry data can be an important supplement to randomized clinical trial data.

The present study demonstrated that stents reduced the incidence of restenosis, but not the need for revascularization (Table 3). Even though the angiographic findings, such

as reference coronary artery diameter and minimal luminal diameter, were not available for the present study, there are several potential explanations for this finding. First, more of the patients treated with balloon angioplasty might not have undergone revascularization despite the occurrence of angiographic restenosis. Second, the diameter of stents might have been too small and the inflation pressure might have been too low, which would increase the rate of restenosis in the stent-treated patients.

In considering the findings between randomized trials and observational studies, one has to keep in mind that the patient population in randomized multicenter clinical trials may be a selected group of patients with a low risk profile compared with the large-scale observational studies from a more diverse range of hospitals and patients. Recently, it has been postulated that the same selection bias contributes to the differences in the results between randomized controlled studies^{20,21} and nonrandomized, observational studies comparing thrombolysis with primary angioplasty.²² Registries can document the relationship between therapeutic modalities used in the real world and clinical outcomes, despite their methodological biases; in particular the comparability of different groups of patients receiving different treatments. Therefore, further evaluation is needed before we can definitively recommend routine stent placement as the standard care for patients with AMI.

Study Limitations

First, important angiographic variables, such as target lesion morphology, as well as clinical variables, such as cardiogenic shock, heart failure and antecedent thrombolytic therapy, were not included in the present study. In addition, the lack of information on medications, such as β -blockers, angiotensin-converting enzyme inhibitors and statins, is also a potential limitation. These variables should be included in the future registry. Second, the present study was performed before platelet glycoprotein IIb/IIIa inhibitors were available in Japan. Previous studies reported more cardiac events with stent placement and argued that stenting might actually increase risk in the absence of glycoprotein IIb/IIIa inhibitors.^{23,24} The introduction of glycoprotein IIb/IIIa receptor inhibitors into PCI practice may improve immediate clinical outcome as well as reduce the requirement for repeat PCI. However, the limitation of the inclusion of patients in the era before glycoprotein IIb/IIIa inhibitors does have the advantage of permitting the present study to examine the effects of stenting independent of the effects of these drugs. Third, the practice of interventional cardiology continues to change with improvements in stent design, increasing experience of cardiologists with the techniques, and more appropriate use of adjunct pharmacotherapy. Therefore, continual assessment of progress in the evolution of PCI is essential.

Conclusions

Stent placement in the present broad-based cohort of patients with AMI did not show superior short- or long-term clinical outcomes compared with balloon angioplasty.

Acknowledgments

This survey could not have been carried out without the help, cooperation and support of the cardiologists and cardiac surgeons in the survey institutions. We thank the participating cardiologists for allowing us to obtain the data. This work was supported by Health Sciences Research

Grants (Research on Health Services) from the Japanese Ministry of Health, Labour and Welfare (#10150305) and Japan Arteriosclerosis Prevention Fund.

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Appendix 1

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