J Jpn Coron Assoc 2006; **12**: 1–8

In-hospital charge for primary coronary intervention in patients with diabetes mellitus

Susumu Ui, Susumu Nakagawa

There is no published report regarding the difference of in-hospital charge for primary percutaneous coronary intervention (PCI) between diabetic (DM) and non-diabetic (NDM). To reveal the difference of in-hospital charge for primary PCI between two groups, we analyzed the PCI database of our hospital and clarified the clinical variables that influenced on the in-hospital charge. The cases presenting cardiogenic shock on admission were excluded. One-hundred and twenty-six (55 cases of DM and 71 cases of NDM) for 2 years from 2001 to 2002 were included with a follow-up period of average 19.6 months. In comparison between these two groups, DM was older and more in number of female with greater incidences of prior coronary artery bypass grafting, multivessel disease (MVD) and congestive heart failure (CHF) on admission. Moreover, longer hospital stay (median, 17 vs. 13 days, p=0.0042) and higher in-hospital charge (250±122 vs. 206±84×10^4 yen, p=0.0016) were statistically significant in DM. However, no clinical difference was shown among these groups regarding the PCI outcomes and major adverse cardiac events. It is concluded that higher in-hospital charge of DM was due to longer hospital stay. This result was probably derived from some clinical characteristics of DM itself, like the trend toward more frequent MVD and CHF.

KEY WORDS: primary percutaneous coronary intervention, acute myocardial infarction, diabetes mellitus, hospital stay, in-hospital charge

I. Introduction

It is known that diabetic patient with acute myocardial infarction (AMI) has a poor prognosis compared to non-diabetic patient, even though treating with reperfusion therapy of thrombolysis or percutaneous coronary intervention (PCI).[1] With the development of PCI, it has been noticed that primary PCI is more effective than thrombolytic therapy among diabetic patients with AMI.[2] In Japan, most patients with AMI undergo primary PCI and favorable outcomes were obtained compared to those in other countries.[3] This tendency probably results in treating many diabetic patients with AMI by primary PCI in Japan. Although a procedure of PCI needs more resources compared to thrombolysis or other conservative therapies, such invasive treatment is expected to improve the prognosis and advocated to be attempted for diabetic patients with AMI. Nowadays there is a great question if such invasive care for diabetic patients needs more resources than for non-diabetic patients or not.

II. Purpose

There is no published report addressing the difference of in-hospital charge of the primary PCI between diabetic and non-diabetic patients. We retrospectively investigated our PCI database to clarify the difference of in-hospital charge of the primary PCI between diabetic (DM) and non-diabetic (NDM).

III. Methods

We retrospectively analyzed the PCI database of consecutive AMI patients treated with primary PCI from January 2001 to December 2002 on our PCI database. These cases were clinically followed until December 2004. Firstly, we compared the clinical characteristics between DM and NDM. Secondly, significant factors influencing on the in-hospital charge were investigated.

1. Inclusion criteria for primary PCI

In our institution, the patients with ST elevation in myocardial infarction are generally treated with primary PCI and included in the PCI database.

Department of Cardiology, Tokyo Saiseikai Central Hospital, 1–4–17 Mita, Minato-ku, Tokyo 108–0073, Japan

Summary of this article was presented at The 18th Annual Meeting of the Japanese Coronary Association, December 2004, Kumamoto.
Received August 24, 2005; Accepted September 26, 2005

AMI is defined according to the presence of two or more of the following criteria: persistent chest pain for ≧30 minutes, ST elevation in at least two contiguous leads of ≧1 mm in limb leads or ≧2 mm in precordial leads, respectively, and a more than twofold increase of serum creatinine phosphokinase (CPK) level.[4]

It is required to get written informed consents from the patient before performing coronary angiography (CAG) and PCI. The usual contraindications to thrombolytic therapy, for example recent ischemic stroke or recent internal bleeding, are included.

2. Exclusion criteria

If the patient is considered to be contraindicated to CAG and PCI or informed consent for PCI is not obtained, these patients are excluded. Angiographical findings as the diameter stenosis of infarct-related artery <70% with thrombolysis in myocardial infarction (TIMI) grade 3 flow and inability to identify the infarct-related artery are also excluded for primary PCI.

AMI patients in cardiogenic shock with marked and persistent hypotension with systolic arterial pressure less than 80 mmHg were not eligible for this study.

3. PCI database

Our PCI database includes demographic, clinical, angiographic and procedural variables with a length of hospital stay and in-hospital charge. In-hospital and out-of-hospital events are also recorded.

a. Clinical variables are coronary risk factors (smoking, hypertension, hypercholesterolemia and diabetes mellitus), hemo- or peritoneal dialysis, history of PCI or coronary artery bypass graft surgery (CABG), history of old myocardial infarction and the presence of congestive heart failure (CHF) on admission. Positive risk factor of smoking includes previous smoker quitting less than three years ago and current smoker. The diagnosis of hypertension in our database is defined as systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg. If the patient has been informed of this diagnosis or is on antihypertensive drugs, the presence of hypertension is defined. The diagnosis of hypercholesterolemia is defined as total cholesterol ≧220 mg/dl and/or low-density lipoprotein cholesterol ≧140 mg/dl. If the patient has been informed of this diagnosis or is on lipid-lowering drugs, the presence of hypercholesterolemia is defined. Diabetes mellitus is diagnosed if the patient has been informed of this diagnosis or is on prescribed anti-diabetic treatment (diet, tablets and/or insulins). The patient with the blood glucose on admission ≧200 mg/dl is also defined as having diabetes mellitus.

CHF is considered present on admission if the patient has pulmonary congestion ≧class II with a clinical classification proposed by Killip et al.

b. Angiographic variables are the number of diseased vessels, target vessel, infarct-related artery, the angiographical morphology by American College of Cardiology/American Heart Association (ACC/AHA) classification, quantitative coronary analysis and ejection fraction measured by left ventriculography (LVG). LVG is routinely performed just after completion of PCI. Extent of coronary artery disease (CAD) are expressed as one vessel disease (1VD), two vessel disease (2VD), three vessel disease (3VD) by the number of major epicardial artery with significant stenosis of ≧75% angiographically. In left main trunk (LMT) disease, stenosis of ≧50% is considered significant. Target vessel means infarct-related artery with the TIMI grade flow <2. In case of TIMI 0 or 1, the angiographical morphology by ACC/AHA classification was diagnosed after the lesion morphology became clear, being crossed with guidewire.

c. Procedural variables are PCI procedures including plain old balloon angioplasty (POBA), cutting balloon angioplasty (CB), intracoronary stent implantation (STENT), directional coronary atherectomy (DCA), rotational coronary atherectomy (RA) and intravascular ultrasound (IVUS). POBA means that the culprit lesion is treated only with one or more balloons. CB means PCI is performed only with one or more cutting balloons. PCI including STENT is carried out with one or more bare metal stents after conventional balloon or CB. Direct stenting is also included in the procedure of STENT. DCA means PCI is completed with one atherectomy catheter. RA means PCI is completed with one or more balloons after ablation with one or more burrs. Angiographic success is defined as a residual stenosis of <50% and TIMI grade 3 flow. Procedural success is defined as angiographic success without in-hospital event. In-hospital events include reinfarction, target lesion revascularization (TLR) during same hospitalization, inguinal bleeding or hematoma which surgical repair or blood transfusion is needed and death from any cause. Staged PCI is defined as elective PCI for the non-culprit lesion some other day after primary PCI.

4. PCI procedures

In our institute, the patients with suspected acute coronary syndrome are initially admitted either to emergency room or directly to coronary care unit (CCU). As soon as the diagnosis of AMI is established, aspirin 330 mg is chewed, followed by drip infusions of nitrate and heparin sodium. Heparin infusion is begun at a bolus of 3,000 IU and titrated to keep an activated partial thromboplastin time of 60 to 85 seconds. After informed consents for CAG and PCI are obtained, the patient is transferred to cardiac catheterization room. PCIs are mostly performed through transfemoral approach using 7.2 or 8.2 French sized sheath by at least two cardiologists. If multivessel disease (MVD) or multiple lesions are disclosed by CAG, the target lesion for primary angioplasty is only the culprit lesion.

Concerning medication, glycoprotein IIb/IIIa receptor antagonist (abciximab) had not been approved in Japan as yet.

5. Patient's care following primary PCI

All the patients treated with primary PCI are admitted to CCU. In the CCU, the serum levels of CPK are measured every 4 hours until CPK reaches to maximum level. The patient is routinely prescribed aspirin 100 to 200 mg per day orally, and in case of STENT, ticlopidine 100 to 200 mg per day is added. After confirming the downward trend of the serum CPK level, the drip infusion of heparin is withdrawn and indwelled sheath is removed. And then, the patient who underwent primary PCI receives cardiac rehabilitation according to the program proposed by the Japanese Association of Cardiac Rehabilitation.[5] This guideline recommends two types of cardiac rehabilitation for reperfused AMI patient during acute phase; one is a 2-week program and the other is a 3-week one. Discharge from CCU is determined by the decline of serum CPK level to the near-normal level and by the patient's general medical condition. This cardiac rehabilitation is continued in the general ward of the Cardiology Department until hospital discharge.

6. Treatment of DM

If the patient's blood glucose on admission is over than 200 mg/dl, the glucose level of capillary blood is tested every 6 hours by Blood Glucose Test Meter, Glutestace R™ (Arkray Factory Co., Ltd., Japan). Regular insulin is administered to control the glucose level in the range from 100 to 200 mg/dl. This regimen of insulin therapy is succeeded after admittance to the general ward. An intensified therapy for DM as the DIGAMI (Diabetes mellitus, Insulin Glucose infusion in Acute Myocardial Infarction)[6] study and the Munich registry[7] is not applied in our cases.

7. Major adverse cardiac event (MACE)

After hospital discharge, cardiac death, readmission due to reinfarction, recurrent angina, CHF or TLR are diagnosed as MACEs. Inguinal complication such as hematoma which surgical repair or blood transfusion is needed is also included. These follow-up data were recorded in PCI database by reviewing the medical records or telephone contact with the patients.

8. In-hospital charge and cost of device

The hospital charges were calculated from medical insurance payment. In Japan, doctors' fees are included in hospital charges. Care costs for PCI are fully covered by the medical insurance and paid on a fee-for-services basis.

Device cost was roughly estimated by the summation of the costs for major particular therapeutic materials used (conventional balloon, cutting balloon, bare metal stent, DCA, rotablator and IVUS catheters), as follows. Device cost is presented as the sum of 200,000 yen×the number of balloons and IVUS used, 300,000 yen×the number of stent and rotablator used and 400,000 yen×the number of DCA catheter used.

One US dollar is equivalent to 110 Japanese yen.

IV. Statistical Analysis

The categorical data are expressed as percent. Continuous variables are generally recorded as mean±standard deviation (SD). Only the length of hospitalization is presented as median. A chi-square analysis was used to compare dependence of categorical variables. Student's t test was used to compare the continuous variables between two groups. Analysis of variance was used to compare the means of continuous variables.

The process of statistical analysis was as follows. Comparing the demographic, clinical, angiographic and procedural variables between DM and NDM, the characteristics of DM were analyzed. Then the univariate analysis determined the significant factors influencing on in-hospital charge. Significant variables by the univariate analysis were included in the multivariate models. Significant variables that influenced on in-hospital charge were identified by multivariate stepwise regression test.

Data were analyzed using JMP Version 5.0 (SAS Campus Drive). A p value of <0.05 was considered statistically significant.

V. Results

The number of the patients treated with primary PCI was 143 for 2 years from January 1st 2001 in our institute (63 cases in DM and 80 cases in NDM). The number of cases with cardiogenic shock on admission was 8 in DM and 9 in NDM. These 17 cases were excluded and 126 cases were included in our analysis. These 126 patients were divided into two groups. The number of cases belonging to DM group was 55 (44%) and the other was 71. All the patients were followed up for the average 31.7 months.

Table 1 Characteristics of diabetic (DM) and non-diabetic (NDM) treated with primary percutaneous coronary intervention from 2001 to 2002

	DM (n=55)	NDM (n=71)	p value
Age (years)	66±10	63±12	0.0045
Male gender (%)	78	87	0.01
Coronary risk factors			
Smoking (%)	57	64	ns
Hypertension (%)	56	53	ns
Hypercholesterolemia (%)	48	58	ns
Hemo- or peritoneal dialysis (%)	4	6	ns
History of PCI (%)	24	13	ns
History of CABG (%)	11	1	0.011
History of OMI (%)	13	23	ns
Lesion morphology by ACC/AHA			ns
A (%)	3	3	
B1 (%)	11	18	
B2 (%)	60	54	
C (%)	25	26	
Extent of coronary artery disease			0.0017
1VD (%)	38	61	
2VD (%)	25	26	
3VD (%)	32	8	
LMT (%)	5	5	
Ejection fraction (%)	45±12	45±8	ns
Infarct-related artery			ns
Left anterior descending (%)	49	44	
Left circumflex (%)	22	20	
Right coronary (%)	22	34	
Left main trunk (%)	0	1	
Others (%)	7	1	
Congestive heart failure (%)	33	8	0.0005

Continuous variables are expressed as means±SD
PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; OMI, old myocardial infarction; ACC/AHS, American College of Cardiology/American Heart Association; VD, vessel disease; LMT, left main trunk; DM, diabetic; NDM, non-diabetic; ns, not significant.

Table 2 Procedural data, outcomes and in-hospital charges of diabetic and non-diabetic treated with primary percutaneous coronary intervention from 2001 to 2002

	DM (n=55)	NDM (n=71)	p value
PCI			ns
POBA (%)	22	34	
CB (%)	11	5	
STENT (%)	60	45	
DCA (%)	0	6	
RA (%)	5	5	
IVUS (%)	25	38	ns
Procedural success (%)	96	92	ns
MACE (%)	25	21	ns
Volume of contrast media used (ml)	213±72	212±55	ns
Fluoroscopy time (min)	25±16	28±18	ns
Follow-up days (day)	583±311	590±313	ns
Length of hospitalization (median, day)	17	13	0.0042
Cost of device ($\times 10^4$ yen)	47±23	45±31	ns
(US dollar)	4273±2091	4091±2818	
In-hospital charge ($\times 10^4$ yen)	250±122	206±84	0.0016
($\times 10^3$ US dollar)	23±11	19±8	

Cost expressed with US dollar was calculated by estimating one dollar equivalent to 110 yen. POBA, plain old balloon angioplasty; CB, cutting balloon angioplasty; STENT, intracoronary stent implantation; DCA, directional coronary atherectomy; RA, rotational coronary atherectomy (rotablator); IVUS, intravascular ultarasound; MACE, major adverse cardiac event; DM, diabetic; NDM, non-diabetic; ns, not significant.

1. Clinical characteristics (Table 1)

Among these two groups, diabetic patients were older and more often female with a greater incidence of prior CABG. Diabetics had more frequent MVD and pulmonary congestion on admission. There was no significant difference between two groups regarding coronary risk factors, an incidence of hemo- or peritoneal dialysis, prior PCI, prior myocardial infarction, lesion morphology class by ACC/AHA, the distribution of infarct-related artery and ejection fraction by LVG.

2. Procedural data, outcomes and in-hospital charges (Table 2)

As in Table 2, there was no significant difference among these groups in the modality of PCI, procedural success rate, in-hospital event and MACE. The most cause of MACE was TLR. Ten TLRs (71%) of 14 MACEs were observed in DM group and 13 TLRs (87%) of 15 MACEs were in NDM group.

Diabetic patient had statistically significant trend toward longer hospitalization and more expensive in-hospital charge compared to those in nondiabetic.

No staged PCI or TLR was undertaken during the same hospitalization.

3. Univariate analysis

The univariate analysis was performed among the variables listed in Table 1 and 2 to determine the significant factors influencing on in-hospital charge. This analysis of in-hospital charge selected 10 significant factors including hospital stay ($p<0.0001$), hemo- or peritoneal dialysis ($p=0.0009$), ACC/AHA lesion class ($p=0.0016$), CHF ($p=0.0035$),

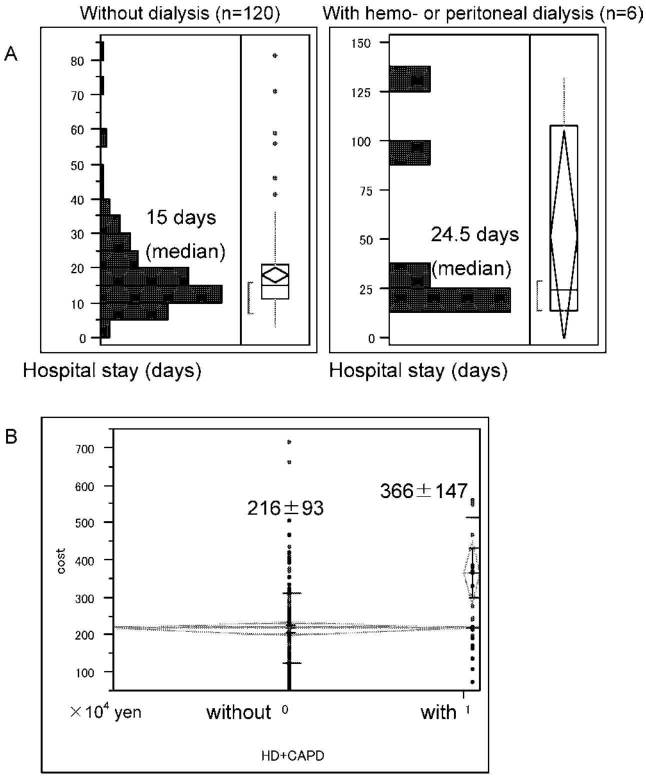

Fig. 1 Influences of hemo- or peritoneal dialysis on hospital stay and in-hospital charge.
A. The length of hospitalization with or without hemo- or peritoneal dialysis (p<0.0001).
B. In-hospital charge with or without hemo- or peritoneal dialysis (p=0.0009).

Table 3 Multivariate stepwise regression test among the variables selected by univariate analysis regarding in-hospital charge, after excluding the variables of hospital stay and hemo- or peritoneal dialysis from analysis

Variables	R^2	F value	p value
Extent of coronary artery disease	0.21	8.896	0.0035
Lesion morphology by ACC/AHA	0.12	7.584	0.0069
Congestive heart failure	0.25	5.903	0.0168
Diabetes mellitus	0.28	1.742	ns
Fluoroscopy time	0.27	1.734	ns
Cost of device	0.29	1.364	ns
History of PCI	—	0.601	ns
Age	—	0.550	ns

ACC/AHS, American College of Cardiology/American Heart Association; PCI, percutaneous coronary intervention; ns, not significant.

extent of CAD (p=0.0091), age (p=0.03), cost of device (p=0.033), fluoroscopy time (p=0.034), prior PCI (p=0.037) and DM (p=0.04).

4. Multivariate stepwise regression test

Multivariate stepwise regression test was performed among the 9 variables selected by the univariate analysis regarding in-hospital charge, after excluding the variable of hospital stay. Five variables were selected as the significant factor influencing on in-hospital charge; extent of CAD (F=9.677, p=0.0024), hemo- or peritoneal dialysis (F=6.148, p=0.0147), CHF (F=5.874, p=0.017), cost of device (F=4.585, p=0.033) and ACC/AHA lesion class (F=4.524, p=0.0016). The parameters of age, fluoroscopy time, prior PCI and DM were excluded.

The most significant factor that influenced on in-hospital charge was identified to be the length of hospital stay.

5. Influences of hemo- or peritoneal dialysis on hospital stay and in-hospital charge

The influences of hemo- or peritoneal dialysis on the length of hospitalization and in-hospital charge were shown in Fig. 1. As we expected, the patients undergoing hemo- or peritoneal dialysis have primarily a trend toward of longer hospitalization and more expensive in-hospital charge. Because this result was considered to be due to hemo- or peritoneal dialysis itself, we excluded this factor from the analysis. And multivariate stepwise regression test was performed again, among the 8 variables after excluding the variable of hemo- or peritoneal dialysis from the last 9 factors.

6. Finally as in Table 3, three variables were selected as more significant factor influencing on in-hospital charge; extent of CAD (F=8.896, p=0.0035), ACC/AHA lesion class (F=7.584, p=0.0069) and CHF (F=5.903, p=0.0168). Figure 2 made it clear that these three variables were independent predictors of in-hospital charge.

VI. Discussion

1. Review of the trials and registries reported, regarding diabetic and non-diabetic AMI patients treated with reperfusion therapies

In the history of the treatments for AMI, many trials and registries have proved that both thrombolysis and primary PCI are effective strategies to reperfuse the infarct-related artery as soon as possible after symptom onset.[8, 9] Such reperfusion of the occluded coronary artery contributes to reduce postinfarction morbidity and mortality during both early and late stage of AMI.[10–12] It has been recognized that diabetes mellitus is undoubtedly independent predictor of in-hospital and out-of-hospital cardiac events.[13–19] As diabetes mellitus is one of the high-risks to worsen the prognosis of the patients with AMI, high-risk patients with DM are more likely than low-risk patients to benefit from primary PCI.[20] Immediate success rates after PCI are similar for patients with and without diabetes.

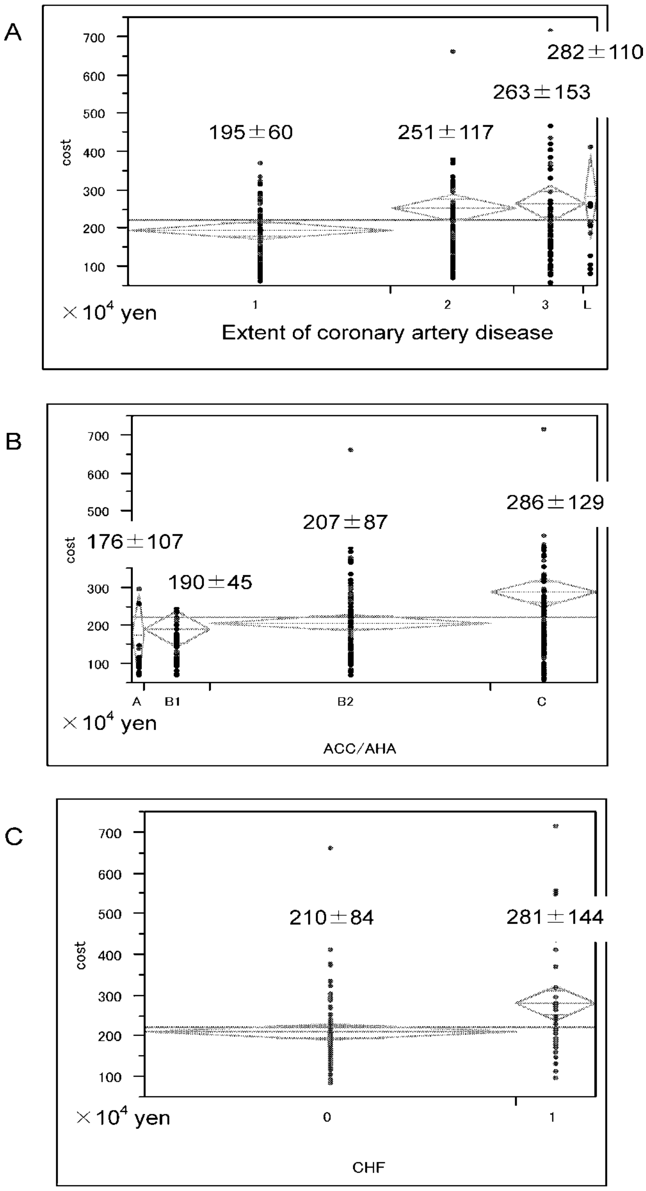

Fig. 2 Three independent predictors of in-hospital charge selected by multivariate stepwise regression analysis, after excluding the variables of hospital stay and hemo- or peritoneal dialysis from analysis.
A. The relation between extent of coronary artery disease and in-hospital charge (p=0.0035).
B. The relation between lesion morphology by American College of Cardiology/American Heart Association (ACC/AHA) lesion class and in-hospital charge (p=0.0069).
C. The relation between congestive heart failure on admission and in-hospital charge (p=0.0168). CHF, congestive heart failure.

However, the incidence of MACEs generally is higher among patients with diabetes. Moreover, long-term mortality is much higher for patients with diabetes.

The etiology of poor prognosis of diabetes with AMI has been discussed throughout the world and has been attributed to several factors. Diffuse coronary atherosclerosis, endothelial dysfunction,[21] disease of the coronary artery microvasculature,[22] autonomic dysfunction and platelet and coagulation abnormalities are contributing to left ventricular dysfunction[23] and poor prognosis of diabetes.

2. Our results

a. Longer hospitalization of diabetes: In our cases, although there was no significant difference regarding the left ventricular ejection fraction between DM and NDM, higher incidence of CHF was observed in DM. This result may imply that our diabetic patients tended to have not systolic but diastolic failure. Diffuse atherosclerotic lesion of the coronary artery also contributed to diastolic dysfunction of the left ventricle along with microvasculature abnormality. These several factors might decrease cardiac reserve after AMI, resulting in delayed convalescence and longer hospitalization. As there was no significant difference between two groups regarding PCI related variables such as entire fluoloscopy time, volume of contrast media used and cost of devices used, we can imagine that longer hospital stay of diabetes was due not to the process of PCI procedure but to other factors including CHF as mentioned above.

b. More resources for diabetes treated with primary PCI: It is also clarified in our study that more expensive in-hospital charge of diabetes was due to longer hospitalization. In the Munich registry, hospital stay were comparable between DM and NDM (14.1±9.5 vs. 14.5±9.0 days, respectively).[7] The cause of such difference from our result is suspected to be due to multifactorial, for example, the difference of rehabilitation program compared to that in Germany.

Moreover, in order to shorten the hospital stay of diabetes with AMI, meticulous medical treatment for diabetic status along with the therapy of CHF is mandatory.

c. Prognosis after primary PCI: MACEs were also comparable between our two groups. In our cases, some patients had already been prescribed with lipid-lowering drugs like HMG-CoA reductase inhibitor before primary PCI. Therefore, the characteristic of atherosclerotic plaque might be modified by such medications and substantially different from that of untreated diabetic patients.

In the present new-device era, for example, drug eluting stent (DES) is expected to improve the poor prognosis of diabetes.[24] However, DES is at present approved not for AMI patient but for elective case. We hope that the indication of DES for AMI will be studied in near future.

d. Finally, primary PCI for diabetes contributed to reduce both the early and late cardiac events. Although longer hospital stay and more expensive in-hospital charge were observed in the diabetic patients treated with primary PCI, it may be no exaggeration to say that the improvement of the prognosis compensates more resources used for acute phase of AMI.

VII. Study Limitation

1. Patients selection

The patients enrolled in our study were limited to the AMI patients treated with primary PCI. The cases treated without primary PCI were excluded. The fact is that higher-risk patients had more severe CHF and were not candidate for primary PCI. These more severe AMI patients were mostly treated with conservative therapy or deferred PCI. Such selection bias toward including the patients with less severe complications probably favored better prognosis after AMI.

2. Treatment before primary PCI and patients' medical conditions

Incidence of DM accounted for 44% of all the patients who underwent primary PCI. This high incidence of DM maybe means that more patients were already on anti-diabetic treatment, demonstrating the characteristics of our institute. In our PCI database, the modality of treatment and medical condition of diabetes mellitus were not included. For example, the blood glucose level after AMI is an independent predictor of long-term mortality in patients with and without known diabetes mellitus.[25] Blood glucose level with the level of HbA1c should be monitored.

3. The length of stay in CCU

Referring to in-hospital charge, we can imagine that longer the patient stays in CCU, more expensive in-hospital charge is. The length of stay in CCU must be longer for the patients with complications and it is expected that diabetes with AMI and CHF stays longer with a delayed rehabilitation. It was not clear in our record how long the patients stayed in CCU.

4. Cost-effectiveness of primary PCI for diabetes

Cost-effectiveness should be evaluated in the long-term clinical course. To prove the favor of primary PCI for diabetes, it is necessary to compare the diabetes treated without primary PCI to those treated with it in longer clinical course.

VIII. Conclusion

Higher in-hospital charge of DM was due to its longer hospital stay. The clinical characteristics of DM itself, for example, higher incidence of MVD and CHF, were contributing to using more resources in the invasive treatment. However, short-term and long-term outcomes of primary PCI were comparable between DM and NDM. It is expected for the primary PCI that such intensive care for acute phase results in cost-effective treatment for long-term prognosis.

References

1) Mak KH, Topol EJ: Emerging concepts in the management of acute myocardial infarction in patients with diabetes mellitus. J Am Coll Cardiol 2000; **35**: 563–568
2) Hasdai D, Granger CB, Srivatsa SS, Criger DA, Ellis SG, Califf RM, Topol EJ, Holmes DR Jr: Diabetes mellitus and outcome after primary coronary angioplasty for acute myocardial infarction: lessons from the GUSTO-IIb Angioplasty Substudy. J Am Coll Cardiol 2000; **35**: 1502–1512
3) Ui S, Chino M, Isshiki T: Rates of primary percutaneous coronary intervention worldwide. Circ J 2005; **69**: 95–100
4) Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction—executive summary. Circulation 2004; **110**: 588–636
5) Saito M: Guidelines for rehabilitation in patients with heart disease. The Cardiovascular Research Division of the Health, Labor and Welfare Ministry 1997 (in Japanese)
6) Malmberg K: Prospective randomized study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. BMJ 1997; **314**: 1512–1515
7) Schnell O, Schafer O, Kleybrink S, Doering W, Standl E, Otter W: Intensification of therapeutic approaches reduces mortality in diabetic patients with acute myocardial infarction. Diabetes Care 2004; **27**: 455–460
8) Weaver WD, Simes RJ, Betriu A, Grines CL, Zijlstra F, Garcia E, Grinfeld L, Gibbons RJ, Ribeiro EE, DeWood MA, Ribichini F: Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction. JAMA 1997; **278**: 2093–2098
9) Buiatti E, Barchielli A, Marchionni N, Balzi D, Carrabba N, Valente S, Olivotto I, Landini C, Filice M, Torri M, Regoli G, Santoro GM: Determinants of treatment strategies and survival in acute myocardial infarction: a population-based study in the Florence district, Italy: results of the acute myocardial infarction Florence registry (AMI-Florence). Eur Heart J 2003; **24**: 1195–1203
10) Boersma E, Mercado N, Poldermans D, Gardien M, Vos J, Simoons ML: Acute myocardial infarction. Lancet 2003; **361**: 847–858
11) De Luca G, Suryapranata H, Zijlstra F, van't Hof AWJ, Hoorntje JCA, Gosselink ATM, Dambrink JH, de Boer MJ, ZWOLLE Myocardial Infarction Study Group: Symptom-onset-to balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. J Am Coll Cardiol 2003; **42**: 991–997
12) De Luca G, Suryapranata H, Ottervanger JP, Antman EM: Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction, every minute of

delay counts. Circulation 2004; **109**: 1223–1225
13) Lee KL, Woodlief LH, Topol EJ, Weaver WD, Betriu A, Col J, Simoons M, Aylward P, van de Werf F, Califf RM, for the GUSTO-I Investigators: Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction, results from an international trial of 41021 patients. Circulation 1995; **91**: 1659–1668
14) Lowel H, Koenig W, Engel S, Hormann A, Keil U: The impact of diabetes mellitus on survival after myocardial infarction: can it be modified by drug treatment? Results of a population-based myocardial infarction register follow-up study. Diabetologia 2000; **43**: 218–226
15) Laskey WK, Selzer F, Vlachos HA, Johnston J, Jacobs A, King SB III, Holmes DR, Douglas J, Block P, Wilensky R, Williams DO, Detre K, Dynamic Registry Investigators: Comparison of in-hospital and one-year outcomes in patients with and without diabetes mellitus undergoing percutaneous catheter intervention. Am J Cardiol 2002; **90**: 1062–1067
16) Shihara M, Tsutsui H, Tsuchihashi M, Tada H, Kono S, Takeshita A, for the Japanese Coronary Intervention Study (JCIS) Group: In-hospital and one-year outcomes for patients undergoing percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2002; **90**: 932–936
17) Bolognese L, Carrabba N, Santoro GM, Valenti R, Buonamici P, Antoniucci D: Angiographic findings, time course of regional and global left ventricular function, and clinical outcome in diabetic patients with acute myocardial infarction treated with primary percutaneous transluminal coronary angioplasty. Am J Cardiol 2003; **91**: 544–549
18) Bovenzi F, De Luca L, De Luca I: Which is the best reperfusion strategy for patients with high-risk myocardial infarction? Ital Heart J 2004; **5** (Suppl 6): 83S–91S
19) Mathew V, Gersh BJ, Williams BA, Laskey WK, Willerson JT, Tilbury RT, Davis BR, Holmes DR Jr: Outcomes in patients with diabetes mellitus undergoing percutaneous coronary intervention in the current era: a report from the Prevention of REStenosis with Tranilast and its Outcomes (PRESTO) trial. Circulation 2004; **109**: 476–480
20) Kent DM, Schmid CH, Lau J, Selker HP: Is primary angioplasty for some as good as primary angioplasty for all? J Gen Intern Med 2002; **17**: 887–894.
21) Yanagisawa H, Chikamori T, Tanaka N, Usui Y, Takazawa K, Yamashina A: Application of pressure-derived myocardial fractional flow reserve in assessing the functional severity of coronary artery stenosis in patients with diabetes mellitus. Circ J 2004; **68**: 993–998
22) Iwakura K, Ito H, Ikushima M, Kawano S, Okamura A, Asano K, Kuroda T, Tanaka K, Masuyama T, Hori M, Fujii K: Association between hyperglycemia and the no-reflow phenomenon in patients with acute myocardial infarction. J Am Coll Cardiol 2003; **41**: 1–7
23) Grundy SM, Howard B, Smith S Jr, Eckel R, Redberg R, Bonow RO: Prevention Conference IV: Diabetes and Cardiovascular Disease: executive summary. Conference proceeding for healthcare professionals from a special writing group of the American Heart Association. Circulation 2002; **105**: 2231–2239
24) Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, Caputo RP, Kereiakes DJ, Williams DO, Teirstein PS, Jaeger JL, Kuntz RE, for the SIRIUS Investigators: Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med 2003; **349**: 1315–1323
25) Stranders I, Diamant M, van Gelder RE, Spruijt HJ, Twisk JWR, Heine RJ, Visser FC: Admission blood glucose level as risk indicator of death after myocardial infarction in patients with and without diabetes mellitus. Arch Intern Med 2004; **164**: 982–988