Influence of Diabetes Mellitus on Outcome in the Era of Primary Stenting for Acute Myocardial Infarction

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The purpose of the present study was to examine the influence of diabetes mellitus (DM) on the clinical and angiographic outcomes in 62 diabetic and 152 nondiabetic patients with acute myocardial infarction (AMI) treated with primary coronary stenting within 12 h of the onset of symptoms. The diabetic patients had a greater incidence of hyperlipidemia, prior myocardial infarction (MI) and multivessel disease. There were no statistically significant differences in other variables. Procedural success was similar in the 2 groups. At a mean follow-up of 2.1±0.6 years, 13% of diabetic and 11% of nondiabetic patients had died (p=0.70). The percentage of target vessel revascularization (TVR) was 37% of diabetic and 20% of nondiabetic patients (p=0.003). Rates of major adverse cardiac events (MACE: death, non-fatal MI, TVR) were 50% of diabetic and 32% of nondiabetic patients (p=0.007). On multivariate analysis, DM was not a predictor of death. Independent predictors of death were age, multivessel disease, TIMI ≤2 and cardiogenic shock. However, DM and age were independent predictors of MACE. In conclusion, DM is not an independent predictor of death in patients with AMI after stenting, but diabetic patients had a higher incidence of TVR, making DM an independent predictor of MACE. (Circ J 2002; 66: 800–804)

Key Words: Acute myocardial infarction; Diabetes mellitus; Primary coronary stenting

Diabetes mellitus (DM) has been regarded as an independent predictor of mortality in patients with acute myocardial infarction (AMI). Although thrombolytic therapy has improved the mortality rate of AMI patients, the prognosis of diabetic patients has remained poor. Recent studies have demonstrated that reperfusion therapy using balloon angioplasty and stenting has a better prognosis for AMI patients with and without DM than thrombolytic therapy. Therefore, we evaluated the influence of DM on the clinical outcome and angiographic findings of AMI patients who underwent primary stenting.

Methods

Patient Population

Between January 1998 and June 2000, 323 consecutive patients with AMI admitted to hospital underwent primary balloon angioplasty and of these, 214 patients (62 diabetics, 152 non-diabetics) underwent stenting within 12 h of symptom onset. Informed consent for primary coronary angioplasty was obtained from all patients and/or their families before the procedure. We retrospectively examined these patients in this study.

Procedure

All patients were administered a bolus dose of intravenous heparin (10,000 U) just before the procedure. Balloon angioplasty, followed by immediate stenting, was performed using the standard femoral approach. After the procedure, heparin was infused intravenously at 500 U/h. The mean duration of postprocedural heparin therapy was 21.8 h. Patients were routinely treated with oral aspirin (162 mg/day) and ticlopidine (200 mg/day) for 1 month after the procedure, and then aspirin alone (81 mg/day).

Follow-up Care

Follow-up visits were scheduled every 2 months and follow-up angiography was performed 6 months after the procedure. Subsequently, long-term follow-up by review of medical records (n=124) or by telephone interview (n=89) was completed in 213 patients (99%).

Definitions

Diabetes mellitus was confirmed if one or more of the following criteria were met: (1) treatment with insulin or an oral hypoglycemic agent or both; (2) fasting blood glucose levels ≥126 mg/dl and casual blood glucose levels of 200 mg/dl or over; and (3) either fasting or casual blood sugar levels higher than the above values and hemoglobin A1c levels of 6.5% or higher. Hyperlipidemia was confirmed if one or more of the following criteria were met: (1) treatment with lipid-lowering agents; (2) cholesterol level ≥220 mg/dl; and (3) triglyceride concentration ≥150 mg/dl.

Procedural success was defined as the achievement of Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow in the culprit coronary artery and a reduction in the diameter of the stenosis to less than 50%. Restenosis was...
defined as 50% or more diameter stenosis at 6-month follow-up angiography. The indication for repeat target vessel revascularization (TVR) was confirmed by symptoms, electrocardiogram or by scintigraphic evidence of ischemia at rest or during exercise.

**Angiographic Analysis**

Quantitative coronary angiography (QCA) was performed using Cardio 500 (Contron Co, Ltd) and CDM 3500 (Philips Co, Ltd). The measurements were taken before procedure, immediately after stenting, and at the 6-month follow-up. We measured the reference vessel diameter, minimal lumen diameter (MLD), percent diameter stenosis, and lesion length.

**End-Points**

Major adverse cardiac events (MACE) were the primary end-points of this study and were a composite of overall death, nonfatal myocardial infarction (MI) and repeat TVR at long-term follow-up. Overall event-free survival, including MACE and revascularization for non-culprit coronary arteries, was also evaluated. In addition, restenosis was assessed among patients who underwent follow-up angiography.

**Statistical Analysis**

Continuous variables were expressed as mean±SD and analyzed with Student’s t test. Categorical variables were compared by the chi-square test. Unadjusted plots of the estimated cumulative event-free survival rate (MACE: death, nonfatal MI and TVR) were produced by the Kaplan-Meier method. The groups were compared by the log-rank test to retrieve the statistical significance. At late follow-up, Cox regression analysis was used to assess the relative risk (RR) of DM on death and MACE. A p<0.05 was considered statistically significant.

**Results**

**Clinical and Angiographic Characteristics**

The diabetic patients had a greater prevalence of hyperlipidemia and prior MI (Table 1). There were no statistical differences in other clinical variables. The angiographic characteristics and procedural data are summarized in Table 2. Diabetic patients had multivessel disease more frequently than nondiabetic patients (68% vs 51%, p=0.03)
and the culprit coronary artery was more frequently the left circumflex artery (18% vs 7%) and less frequently the right coronary artery (37% vs 46%) in comparison with the nondiabetic patients. However, these differences did not reach statistical difference. Procedural success was accomplished in 92% of the diabetic and in 91% of the nondiabetic patients and the number of stents was similar in the 2 groups. The stents tended to be longer in diabetic patients, but the difference was not statistically significant (20.4±10.9 mm vs 18.5±8.6 mm, p=0.16). Cardiac medications at discharge and at the follow-up were similar in the 2 groups.

**In-Hospital Outcome**

The frequency of major in-hospital adverse outcomes was similar in both diabetic and nondiabetic patients, except for TVR, which was more common among diabetics (12% vs 4%, p=0.04). One diabetic (2%) and 2 nondiabetic patients (1%) had recurrent MI as a result of stent thrombosis, but all were successfully treated with balloon angioplasty. One diabetic patient (2%) with multivessel disease underwent elective coronary bypass surgery 4 weeks after the procedure (Table 3).

**Results of 6-month Follow-up Angiography**

Follow-up angiography at 6 months was performed in 156 patients (78%), representing 163 lesions (Table 4). Reference diameter, lesion length and MLD before and after the procedure were similar in the 2 groups. The MLD at follow-up was significantly less in diabetic patients (1.60±0.85 mm vs 1.96±0.78 mm, p=0.02). The incidence of restenosis (39% vs 27%) and TVR (16% vs 19%) tended to be higher in diabetics than in nondiabetics, but the difference was not statistically significant. The incidence of MACE at 6 months also tended to be higher in diabetics (40%) than in nondiabetics (29%). The ejection fraction also tended to be lower in diabetic patients, but there was no significant difference between the 2 groups (56.9±12.9% vs 61.9±12.7%, p=0.06).

**Late Follow-up**

The long-term outcomes using survival analysis are shown in Fig 1. Mean follow-up of 2.1±0.6 years was available for 213 patients (99%). During this follow-up, there was no significant difference in the number of deaths or nonfatal MI between the 2 groups, but the rate of freedom from TVR was significantly lower in diabetic than nonfatal MI.
nondiabetic patients (63% vs 80%, p=0.003). Therefore, freedom from MACE was significantly decreased in diabetic patients (50% vs 68%, p=0.007). In addition, the rate of revascularization for non-culprit coronary arteries, including coronary artery bypass surgery, was more prevalent in diabetic patients (50% vs 34%, p=0.02). Thus, overall event-free survival was significantly worse in diabetic patients (32% vs 55%, p=0.003).

On multivariate analysis, the independent predictors of all-cause death were age, multivessel disease, TIMI ≤2, and cardiogenic shock (Table 5); that is, DM did not have an independent influence on all-cause death. However, DM was independently associated with MACE (RR 1.96, 95% confidence interval 1.21–3.18).

**Discussion**

Diabetes mellitus has long been regarded as an independent risk factor for predicting short and long-term prognosis of AMI patients, even in the era of thrombolytic therapy.15–19 Later, balloon angioplasty was accepted as a more effective reperfusion therapy in terms of prompt and secure restoration of coronary blood flow.21–26 The GUSTO II-b substudy20 evaluating the influence of DM on AMI patients who underwent primary angioplasty, showed that similar procedural success was achieved in both diabetic and nondiabetic patients. In addition, the 1-year survival was not significantly different between diabetic and nondiabetic patients. However, that study did not assess the rates of restenosis and TVR at late follow-up. In recent times, reperfusion of the culprit coronary artery with stenting is carried out more frequently, with excellent angiographic and clinical results than with balloon angioplasty alone.27–30 In the present study, TIMI grade 3 flow was achieved in 92% of diabetic patients and in 91% of nondiabetic patients and furthermore, there was no significant difference in the frequency of death and nonfatal MI between the 2 groups during the follow-up period. Multivariate analysis also demonstrated that DM was not an independent predictor for all-cause death at late follow-up.

The effect of stenting on the prevention of restenosis and TVR in diabetic AMI patients at the chronic stage has not been sufficiently evaluated.30–31 We found the rate of angiographic restenosis was slightly higher in diabetic than in nondiabetic patients at 6-month follow-up, but there was no significant difference. However, the rates of TVR and revascularization for non-culprit coronary arteries were significantly higher in diabetic than in nondiabetic patients during a mean follow-up of 2.1 years. Therefore, overall event-free survival was significantly decreased in diabetic patients. In addition, multivariate analysis indicated that DM was an independent predictor for MACE. Taking into consideration the quality of life and the adjunctive costs of a repeat revascularization procedure, TVR is obviously an important endpoint for AMI patients who have survived after discharge. In diabetic AMI patients with multivessel disease or restenosis, revascularization by bypass surgery should also be contemplated in order to avoid frequent TVR.

It has recently been reported that drug-eluting stents can dramatically decrease the rate of restenosis.32,33 In the near future, these new stents may overcome the TVR issue in patients with diabetic AMI.

The rate of TVR was higher in our study than in other randomized studies,28–31 but the follow-up period was shorter in those studies. In addition, patients with cardiogenic shock, severe multivessel disease, and small reference diameter of infarct vessel were excluded, whereas we included all AMI patients who underwent primary stenting within 12 h of symptom onset between January 1998 and June 2000. All these factors may have contributed to the higher rate of TVR. Setsuda et al studied the impact of primary stenting in diabetic patients with AMI in a similar type of retrospective study and found that the rates of restenosis and TLR at 6-month follow-up were higher in diabetic patients than in nondiabetic patients (53% and 41% vs 21% and 14%)34 which are similar results to ours.

**Study Limitations**

(1) This was a retrospective study; (2) the number of patients was small and differed between the 2 groups; (3) follow-up angiography was not performed in all patients; and (4) the degree of control of DM and the influence of diabetic treatment were not evaluated.

**Conclusions**

In the era of primary stenting for AMI patients, DM does not appear to be an independent predictor for death at late follow-up. However, the present diabetic patients had more frequent TVR and so DM remains an independent predictor for MACE.
References


