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Influence of diabetes on >10-year outcomes after percutaneous coronary intervention

Abstract There are few reports showing the relationship between diabetes and the long-term outcome following percutaneous coronary intervention (PCI) in Asians. As well, the association between glycosylated hemoglobin (HbA1c) level and outcome remains controversial. In this analysis, 748 Japanese patients including 298 with diabetes (DM) and 450 without diabetes (non-DM) who underwent PCI from 1984 to 1992 were evaluated over the long term. The mean follow-up was 12.0 ± 3.6 years. There were 47 (15.8%) total deaths in DM and 41 (9.1%) in non-DM [hazard ratio (HR) 1.71, 95% confidence interval (CI) 1.11–2.65, \( P = 0.013 \)] and 28 (9.4%) cardiovascular deaths in DM and 19 (4.2%) in non-DM (HR 2.09, 95% CI 1.14–3.81, \( P = 0.016 \)). Among DM, increased HbA1c was associated with both total (HR 1.25, 95% CI 1.03–1.53, \( P = 0.024 \)) and cardiovascular (HR 1.30, 95% CI 1.00–1.69, \( P = 0.048 \)) mortality. Even in Asians, DM showed an increased mortality following PCI. Among DM, increased HbA1c level was also associated with mortality.

Key words Type 2 diabetes mellitus · Percutaneous coronary intervention · Long-term outcome · Glycosylated hemoglobin · Asian

Introduction

There is a large evidence base linking diabetes and the development and progression of coronary artery disease (CAD).\(^1\)–\(^5\) Diabetes, one of the important risk factors for progression of CAD, is also associated with a worse outcome after revascularization.\(^6\)–\(^8\) Several clinical studies have shown that patients with diabetes have a greater incidence of cardiovascular events following percutaneous coronary intervention (PCI), and that this might increase long-term mortality.\(^9\)–\(^10\) In fact, many studies have shown that the presence of diabetes at the time of PCI increased long-term mortality.\(^11\)–\(^15\) However, in most of these studies follow-up was limited to less than 10 years; in only a few studies was follow-up over 10 years. In addition, most studies were done in Western countries, while no long-term studies have been done in Asian populations to determine whether the presence of type 2 diabetes at the time of PCI affects long-term (>10 years) mortality.

Asians tend to have a lower body mass index than non-Asians and have remarkably different obesity-related characteristics. Actually, the prevalence and incidence of type 2 diabetes varies among ethnic groups, such as higher rates in Asians than in Western populations even under the condition of similar body mass index (BMI).\(^16\) Studies in Asian countries showed that the risk of having type 2 diabetes is high at leaner body mass.\(^17\) Therefore, it is of interest to determine whether Asian diabetic patients who reveal a leaner body mass have a similar risk to the Western patient population for long-term mortality after PCI.

Furthermore, although the increasing prevalence of type 2 diabetes among patients with CAD is a concern, it is controversial whether the degree of glycemic control at the time of PCI is associated with long-term outcome.\(^18\)–\(^22\) On the other hand, it has been shown that strict glycemic control is associated with a decreased incidence of microvascular complications.\(^9\)–\(^23\) However, the association between the degree of glycemic control and the incidence of macrovascular complications has not yet been established. Recently, several studies have shown that strict glycemic control improves outcome after acute myocardial infarction.\(^24\) Given these results, the association between the degree of glycemic control and the incidence of macrovascular complications has been questioned. Furthermore, though one study showed that periprocedural glucose levels affect relatively long-term outcome following PCI, no studies have shown an association between the degree of glycemic control and long-term (>10 years) outcome.
Therefore, we investigated the long-term (>10 years) mortality after PCI among type 2 diabetic patients with leaner body mass and analyzed whether the degree of glycemic control, as reflected by the glycosylated hemoglobin (HbA1c) level, which mirrors glycemic control levels more accurately than the glucose level, was important.

**Subjects and methods**

**Subjects and data collection**

We retrospectively analyzed 748 consecutive Japanese patients who had undergone a PCI at Juntendo University Hospital from January 1984 to December 1992. In all cases, the indications for PCI were either objective evidence of myocardial ischemia (positive stress test) or ischemic symptoms associated with significant angiographic stenosis. Demographic data, coronary risk factors, medication use, and intervention procedures were prospectively recorded in our institution’s database. As well, in the diabetic cases, the HbA1c level at the time of PCI was noted. Blood samples were obtained in the early morning after an overnight fast. Blood pressures were measured at the time of admission for elective cases or a few days after admission for emergency cases. Patients were classified based on the presence or absence of diabetes at baseline using the following definitions: fasting plasma glucose level ≥126 mg/dl during hospitalization, or treatment with oral hypoglycemic drugs or insulin injection. Each patient was further categorized based on the presence of coronary risk factors using the following criteria. Hypertension was defined as a systolic blood pressure ≥140 mmHg, or a diastolic blood pressure ≥90 mmHg, or treatment with antihypertensive medications. A current smoker was defined as one who smoked at the time of PCI or had quit smoking within 1 year prior to the procedure. A patient with kidney failure was defined as one under dialysis or whose estimated creatinine clearance was <15 ml/min. Mortality data were collected until September 2002. The medical records of patients who died in our hospital were examined. For patients who were admitted to or followed by other hospitals or clinics during the follow-up period, the institutions were asked to provide the details and cause of death. Informed consent was obtained from all patients or their families. Mortality data were categorized according to the cause of death, such as death from all causes or composite cardiovascular death. Cardiovascular death included death from coronary artery disease, cardiogenic shock, stroke, and sudden death.

**Statistical analysis**

Continuous variables are expressed as mean ± standard deviation and were compared using Student’s t-test or the Mann–Whitney U-test. Categorical data are tabulated as frequencies and percentages, and they were compared using the χ² test or Fisher’s exact test. Kaplan–Meier estimation with the log-rank test was used for the unadjusted survival analysis. Multivariate Cox proportional-hazards regression was also done to examine the adjusted risks for total death and cardiovascular death in the diabetic patients compared to nondiabetic patients. In the adjusted analysis, several covariates, which included age, gender, BMI, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol level, triglyceride level, presence or absence of hypertension, smoking history, presence or absence of kidney failure, prior history of myocardial infarction, undergoing prior coronary artery bypass graft, presentation of acute coronary syndrome, left ventricular ejection fraction measured by echocardiogram, vessel disease, and procedural success (defined as a residual stenosis <50% after PCI) were used and entered into the analysis along with the presence or absence of diabetes. Further analysis of the diabetic patients was done using multivariate Cox proportional hazards regression to determine the independent predictors for long-term prognosis following PCI among diabetic patients with CAD. In this analysis, instead of the presence or absence of diabetes, the HbA1c level was entered along with the other covariates. A P value of less than 0.05 was considered statistically significant. All data were analyzed with Dr. SPSS II for Windows (SPSS, Chicago, IL, USA).

**Results**

**Baseline characteristics**

The baseline and clinical event data were fully documented during the follow-up period (mean follow-up, 12.0 ± 3.6 years) for all patients. Hence, all 748 patients were enrolled. Of these, 298 patients (39.8%) had diabetes at the time of PCI (diabetic group) and 450 patients (60.2%) did not have diabetes (nondiabetic group). There were no patients with type 1 diabetes. The baseline characteristics of the two groups are shown in Table 1. Most patients in both groups were middle-aged, nonobese males with single vessel disease and normal left ventricular contraction. However, the diabetic patients were significantly older and had more severely impaired left ventricular contraction than non-diabetic patients. There were no significant differences between the two groups with respect to other characteristics. As well, all patients underwent PCI using only balloon angioplasty; no stent implants were performed.

Among the diabetic group, 6.4% of patients were treated with insulin injection, 23.2% of patients were treated with sulfonylurea and others were diet treated. The mean HbA1c level of diabetic group was 7.4% ± 1.3%.

Unadjusted and adjusted analysis for total and cardiovascular mortality

Overall, 88 patients died from all causes (including 47 patients with cardiovascular death) during follow-up. Using Kaplan–Meier estimation, the presence of diabetes at the time of PCI was associated with increased long-term total