Outcomes in Patients with Diabetes Mellitus According to Insulin Treatment After Percutaneous Coronary Intervention in the Second-Generation Drug-Eluting Stent Era

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Limited data exist regarding the clinical outcomes of patients with diabetes mellitus (DM) after percutaneous coronary intervention (PCI) using second-generation drug-eluting stents (DES), especially according to DM treatment. The purpose of this study was to compare clinical outcomes among patients without DM, with non-insulin-treated DM (non-ITDM), and with ITDM after PCI using second-generation DES. We analyzed 4,812 consecutive patients who underwent PCI using second-generation DES. Primary outcomes were patient-oriented composite outcome (a composite of all-cause mortality, any myocardial infarction, and any revascularization) at 3 years. Among the total population, 3,026 patients have no DM, 1,169 have non-ITDM, and 617 have ITDM. Patients with DM, regardless of non-ITDM and ITDM, showed significantly higher risk of patient-oriented composite outcome (21.0% vs 14.5%; adjusted hazard ratio [HR_{adj}]1.41, 95% confidence interval [CI] 1.19 to 1.66, p <0.001), mainly driven by significantly higher risk of cardiac death and any revascularization compared with non-DM. Among DM population, ITDM showed significantly higher risk of cardiac death (7.7% vs 3.7%; HR_{adj} 1.97, 95% CI 1.19 to 3.27, p = 0.009), any revascularization (17.0% vs 11.4%; HR_{adj} 1.40, 95% CI 1.01 to 1.93, p = 0.041), and definite/probable stent thrombosis (1.7% vs 0.7%; HR_{adj} 2.80, 95% CI 1.04 to 7.56, p = 0.042) compared with non-ITDM. In conclusion, even in the era of second-generation DES, patients with DM are at significantly higher risk of patient-oriented adverse events. Among these, patients with ITDM showed the highest risk of adverse events, mainly driven by higher risk of mortality, any revascularization, and definite/probable stent thrombosis. **(Am J Cardiol 2018;■■:■■–■■)**

Diabetes mellitus (DM) is the third most common co-morbidity in patients with cardiovascular disease observed in 20% to 30% of patients who undergo percutaneous coronary intervention (PCI) for ischemic heart disease.[1] Patients with DM treated with bare-metal stents (BMS) or first generation drug-eluting stents (DES) have shown worse prognosis compared with patients without DM.[2,3] Although outcomes after PCI have been improved by second-generation DES with the biocompatible polymer and thinner struts, DM is still an independent predictor of major adverse events.[4] Insulin-treated DM (ITDM), which accounts for 1/4 of all patients with DM,[5] generally has a prolonged duration of disease, a high incidence of co-morbidities, and poor glycemic control.[6] Previous studies presented significantly worse clinical outcomes after PCI in patients with ITDM compared with non-ITDM;[1,7–9] yet, the results were not consistent.[10,11] However, in contemporary second-generation DES era, only a few studies have reported a differential prognosis in patients with DM according to insulin treatment status,[6,12,13] and evidence is limited due to relatively small sample size of ITDM. Therefore, we sought to compare clinical outcomes of patients with DM according to their insulin treatment status after PCI using second-generation DES.

Methods

For the present analysis, we analyzed patients from an administrative pooled registry of 2 tertiary university hospitals,

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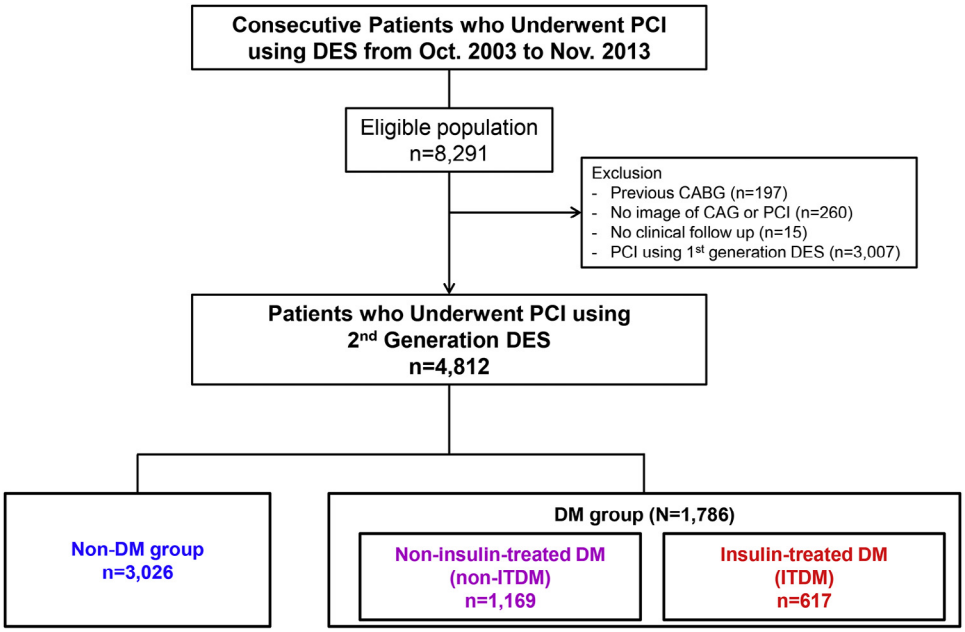

Figure 1. Patient flow. CAG = coronary angiography.

who underwent PCI at Samsung Medical Center or Kangbuk Samsung Hospital. During the period from October 2003 through November 2013, 8,291 consecutive patients underwent PCI with DES for coronary artery disease and were prospectively enrolled into the institutional registries. For the present analysis, patients with a previous history of coronary artery bypass graft surgery, who were treated with first-generation DES, were excluded. As a result, 4,812 patients who underwent PCI using second-generation-biocompatible- or biodegradable-polymer-coated DES were analyzed (Figure 1). Among the total population, 1,786 patients with DM (37.1%) were classified according to their insulin treatment status. The study protocol was approved by the ethics committee at each participating center and was conducted according to the principles of the Declaration of Helsinki. All patients provided written informed consent.

DM was defined as under treatment for known diabetes, or newly diagnosed with DM according to the diagnostic criteria suggested in the most recent American Diabetes Association guideline.[14] Patients were classified as ITDM if they were administered any kind of insulin, and non-ITDM if they were prescribed oral hypoglycemic agents or lifestyle modification.

Baseline characteristics, angiographic and procedural findings, and clinical outcome data were collected prospectively by research coordinators. Patients were routinely followed up at 1, 6, and 12 months after the index procedure, and annually thereafter. Further information was collected by telephone contact or medical records, if necessary. In addition, using the unique identification numbers of the Korean nationwide healthcare system, the vital status of 100% of patients was crosschecked, and the mortality events were confirmed, even in patients lost to follow-up. The median follow-up duration was 1,125 days (Q1 to Q3: 888 to 1,682).

Coronary interventions were performed according to the current standard techniques. The choice of stent, poststenting adjunctive balloon inflation, and the use of intravascular ultrasound or glycoprotein IIb/IIIa inhibitors were left to the operators' discretion. All patients received a loading dose of aspirin or were on chronic therapy before the procedure. A loading dose of P2Y12 inhibitors was administered to all patients who were not on a P2Y12 inhibitor before the procedure. The choice of P2Y12 inhibitor was left to the operators' discretion. Unless there was an undisputed reason for discontinuing dual antiplatelet therapy, all patients were recommended to take aspirin (at least 100 mg/day) indefinitely and a P2Y12 inhibitor for at least 6 months after their index procedure.

The primary outcome was patient-oriented composite outcome (POCO), a composite of all-cause death, any myocardial infarction (MI, including nontarget vessel territory), and any revascularization. The secondary outcomes were individual components of POCO and definite/probable stent thrombosis (ST). Cardiac death was defined by the Academic Research Consortium (ARC), and all deaths were considered cardiac unless an unequivocal noncardiac cause could be established. MI was defined according to the ARC and extended historical protocol definition, and periprocedural MI was not considered.[15] The definite or probable ST was defined according to the ARC criteria.[15] All events were adjudicated by an independent event adjudication committee.

Categorical variables were presented as numbers and relative frequencies (percentages), and continuous variables as means and standard deviations or median with interquartile range (Q1 to Q3) according to their distribution, which was checked by the Kolmogorov-Smirnov test. Categorical variables were compared using chi-square tests, and continuous variables were compared using Student *t* test or analysis of variance. Cumulative events rates were calculated based on Kaplan-Meier censoring estimates, and the log-rank test was used to compare survival curves between groups. To evaluate the independent effect of DM and insulin treatment on clinical outcomes, multivariable-adjusted Cox proportional