Risk of Major Cardiovascular or Cerebrovascular Events After PCI or CABG Increased in Diabetes Mellitus Patients Receiving Insulin

Written by Emma Hitt Nichols, PhD

The risk of developing major cardiovascular or cerebrovascular events (MACCE) following percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) is greater in insulin-treated diabetes mellitus (ITDM) patients compared with diabetes mellitus patients not treated with insulin (non-ITDM). George D. Dangas, MD, PhD, Mount Sinai Hospital, New York, New York, USA, presented data from a subgroup analysis of the Comparison of Two Treatments for Multivessel Artery Disease in Individuals With Diabetes trial [FREEDOM; Farkouh ME et al. *N Engl J Med* 2012].

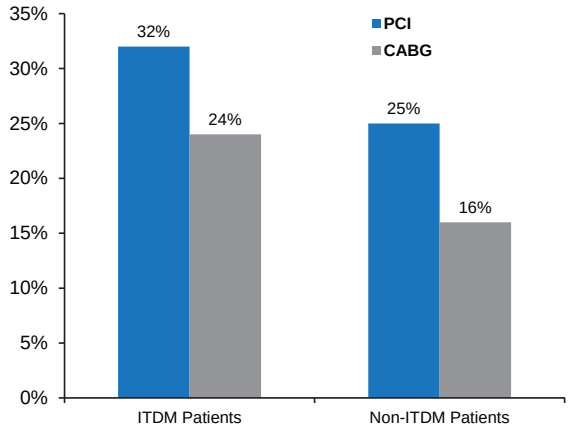
Diabetes mellitus is currently estimated to affect 6.4% of the worldwide population and is expected to increase in prevalence to 7.7% by 2030. In the United States, ~26% of patients have ITDM and these patients are at a greater risk of experiencing a cardiovascular (CV) event after PCI, as well as developing wound infections and death following CABG. The purpose of the FREEDOM trial was to evaluate the best method of revascularization (PCI vs CABG) for patients with diabetes who have multivessel coronary artery disease.

Out of 1900 subjects with diabetes enrolled in the FREEDOM trial, 1850 underwent revascularization. The majority of patients were not receiving insulin (non-ITDM, n=1248) and the remainder were receiving insulin (ITDM, n=602) [Farkouh ME et al. *N Engl J Med* 2012]. Of the non-ITDM patients, 631 underwent PCI with a drug-eluting stent (DES) and 617 underwent CABG. In the ITDM patients, 325 underwent PCI with a DES and 277 underwent CABG. Many baseline characteristics differed significantly between the non-ITDM and ITDM patients ($p \leq 0.02$), with body mass index, duration of diabetes, HbA1C, blood glucose levels on the day of the procedure, blood urea nitrogen, history of hypertension, peripheral neuropathy, congestive heart failure, and acute coronary syndrome greater in the ITDM patients. Non-ITDM patients were older and more likely to have NYHA Class I heart failure when compared with ITDM patients.

In the FREEDOM trial, the composite endpoint of death, stroke, or myocardial infarction (MI) occurred in 29% of patients with ITDM and 19% of patients with non-ITDM (HR, 1.63; 95% CI, 1.32 to 2.02; $p<0.001$). In addition, ITDM patients were at a greater risk of experiencing 30-day MACCE (HR, 1.54; 95% CI, 1.02 to 2.33; $p=0.04$) and 1-year MACCE (HR, 1.51; 95% CI, 1.18 to 1.92; $p=0.001$) when compared with non-ITDM patients.

The risk of developing death, stroke, or MI in patients with ITDM was greater following PCI (32%; 95% CI, 26 to 39%) compared with CABG (24%; 95% CI, 19 to 30) at 5 years. A similar trend occurred in patients with non-ITDM, with 25% (95% CI, 19 to 28; Figure 1) of patients experiencing the composite endpoint following PCI compared with 16% (95% CI, 12 to 19) following CABG at 5 years. Risk of death, stroke, or MI was greater in patients with ITDM than in patients with non-ITDM.

Figure 1. Death, Stroke, or MI Following PCI or CABG



CABG=coronary artery bypass grafting; ITDM=insulin-treated diabetes mellitus ; PCI=percutaneous coronary intervention.

Dr. Dangas concluded that data from this subanalysis of the FREEDOM trial suggest that ITDM patients experience more MACCE events than non-ITDM patients. However, there was a greater risk of MACCE in patients following PCI compared with CABG regardless of insulin treatment. In addition, Dr. Dangas pointed out that limitations of the study included the lack of randomization of ITDM versus non-ITDM patients, and that the differences in outcomes between patients with ITDM and non-ITDM could be attributed to residual confounding, insulin resistance, or side effects of insulin therapy.

Thrombectomy Does Not Prevent Microvascular Obstruction in Patients Undergoing PCI for NSTEMI

Written by Emma Hitt Nichols, PhD

Aspiration thrombectomy does not improve the extent of microvascular obstruction compared with standard percutaneous coronary intervention (PCI) in patients with non-ST-elevation myocardial infarction (NSTEMI). Holger Thiele, MD, University of Leipzig, Leipzig, Germany, presented data from the Thrombus Aspiration

in Thrombus containing culprit lesions in Non-ST-Elevation Myocardial Infarction study [TATORT-NSTEMI; NCT01612312]. The trial protocol has been described in detail by de Waha and colleagues [*Trials* 2013].

Although the European Society of Cardiology and the American College of Cardiology/American Heart Association guidelines suggest that thrombectomy may be indicated in patients with NSTEMI, [Steg G et al. *Eur Heart J* 2012; O'Gara PT et al. *Circulation* 2013] there is currently little data to support its use. The hypothesis of the TATORT-NSTEMI trial is that thrombectomy in patients that have experienced NSTEMI will improve myocardial perfusion and thrombus burden [de Waha S et al. *Trials* 2013].

In the prospective, randomized, controlled, multicenter, open-label TATORT-NSTEMI trial, 440 NSTEMI patients were randomized in 1:1 fashion to PCI or PCI with adjunctive thrombectomy [de Waha S et al. *Trials* 2013]. To be eligible for the trial, patients had to have an NSTEMI with >20 minutes of ischemic symptoms that occurred within 72 hours prior to randomization, and identifiable culprit lesions with relevant thrombus (TIMI thrombus Grade 2 to 5). Exclusion criteria included cardiogenic shock, STEMI, unsuitable coronary morphology for thrombectomy, need for coronary artery bypass grafting (CABG), life expectancy <6 months, contraindication to heparin, acetylsalicylic acid, or thienopyridine.

The primary endpoint of the TATORT-NSTEMI trial was microvascular obstruction from Days 1 through 4 as measured by cardiac magnetic resonance imaging [de Waha S et al. *Trials* 2013]. The secondary endpoints included infarct size, myocardial salvage, the composite of mortality, reinfarction, target vessel revascularization (TVR), and congestive heart failure at 6 months, TIMI-flow post PCI, myocardial blush grade post PCI, and enzymatic infarct size as measured by Troponin T at 24 and 48 hours.

The median age of the participants was 69 years and 68 years in the thrombectomy and standard PCI arms, respectively. Prior MI occurred in 7% and 12% of the patients in the thrombectomy and PCI arms, respectively, and the rates of prior PCI (13%) and CABG (3% vs 5%) were similar among the arms. Most patients had a TIMI thrombus grade of 3 to 5, and the median GRACE score was 145 in the thrombectomy arm and 137 in the PCI arm.

Results of the TATORT-NSTEMI trial demonstrated no significant difference in microvascular obstruction between the thrombectomy and standard PCI arms (p=0.74). In addition, there was no significant difference in the extent of the microvascular obstruction between the treatment arms (p=0.17). Furthermore, there was no significant difference in any of the secondary endpoints, including clinical outcome at 6 months.

Prof. Thiele stated that the data from the TATORT-NSTEMI trial indicate that aspiration thrombectomy did not decrease the extent of microvascular obstruction as measured by cardiac MRI when compared with standard PCI.

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