Long-Term Prognosis in Patients With Type 1 and 2 Diabetes Mellitus After Coronary Artery Bypass Grafting

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ABSTRACT

BACKGROUND Patients with diabetes mellitus (DM) have an increased risk of adverse outcomes after coronary artery bypass grafting (CABG). Previous studies have reported prognosis in relation to treatment with or without insulin, and not to the type of diabetes.

OBJECTIVES This study investigated long-term survival in patients with type 1 DM (T1DM) and type 2 DM (T2DM) following CABG.

METHODS We included all patients from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) register who underwent primary isolated CABG in Sweden during 2003 through 2013. We identified patients with T1DM or T2DM in the Swedish National Diabetes Register. We calculated hazard ratios (HRs) with 95% confidence intervals (CIs) for all-cause mortality in patients with T1DM or T2DM.

RESULTS In total, 39,235 patients were included, of whom 725 (1.8%) had T1DM and 8,208 (21%) had T2DM. Patients with TDM1 were younger (59 vs. 67 years), had reduced kidney function (31% vs. 24%), and had peripheral vascular disease (21% vs. 11%) more often than patients with TDM2 or no diabetes. During a mean follow-up of 5.9 ± 3.2 years (230,085 person-years), 6,765 (17%) patients died. Among patients with T1DM, 152 (21%) died, and among patients with T2DM, 1,549 (19%) died. Adjusted hazard ratio (95% confidence interval) for death in patients with T1DM and T2DM, compared with patients without diabetes, were 2.04 (1.72 to 2.42), and 1.11 (1.05 to 1.18), respectively.

CONCLUSIONS Patients with T1DM had more than double the long-term risk of death after CABG compared with patients without diabetes. The long-term risk of death in patients with T2DM was only slightly increased. (J Am Coll Cardiol 2015;65:1644–52) © 2015 by the American College of Cardiology Foundation.

The prevalence of diabetes mellitus (DM) is increasing worldwide, with an estimated doubling of cases within the next 20 years (1). Patients with DM have an increased risk of cardiovascular disease and death compared with those without DM. In the general population of patients with type 1 diabetes mellitus (T1DM), the excess risk of death is 4-fold in men and 8-fold in women relative to those without DM (2,3). In the general population of patients with type 2 diabetes mellitus (T2DM),

there is a doubling of the age-adjusted prevalence of coronary heart disease, and the risk of death is between 2 and 4 times higher than in those without DM (4,5). Approximately 25% of all U.S. patients who undergo multivessel coronary revascularization have DM (6).

T1DM and T2DM have different underlying pathophysiology. T1DM is usually characterized by onset at an early age, in which the underlying cause is autoimmunity and destruction of the insulin-producing β cells, leading to insulin deficiency. By contrast, T2DM is characterized by an adult onset of hyperinsulinemia that is due to insulin resistance and, as a consequence, a slow progression of hyperglycemia. T2DM is associated with obesity, and its incidence increases with age (7,8).

A number of studies have investigated the impact of DM on prognosis after coronary artery bypass grafting (CABG) (9–12). The categorization of DM in these studies has varied from dividing patients according to only the presence or absence of DM (10–12) to, more specifically, insulin-treated or not insulin-treated diabetes (9). Results from these studies have been conflicting: some demonstrating an association with adverse outcome (11), and others finding no independent association with outcome (10,12). In another study, it was reported that compared with non-insulin-treated diabetes, those with insulin-treated diabetes had an increased long-term risk of death (9). To the best of our knowledge, there is only 1 study that has categorized CABG patients into T1DM and T2DM (13). In that study, the authors found an association with death and myocardial infarction (MI) for both T1DM and T2DM.

On the basis of recent findings, the quality of care has improved in patients with T1DM, and consequently, there is a paucity of evidence regarding prognosis in contemporary patients with T1DM and coronary artery disease. Recently, the American Heart Association and the American Diabetes Association published a scientific statement calling for more studies in patients with T1DM and cardiovascular disease (14). Consequently, we performed a nationwide population-based cohort study in patients who underwent CABG in Sweden over a period of 11 years to investigate the importance of T1DM and T2DM regarding the long-term risk of death.

METHODS

This observational, nationwide population-based cohort study database was created by cross-linking several national Swedish health data registers. The unique personal identity number assigned to every Swedish citizen was used as the identifier in the records linkage procedure at the Swedish National Board of Health and Welfare. The database was then anonymized according to regulations. The personal identity number and national registers are described in the Online Appendix.

In brief, all patients who underwent primary isolated nonemergency CABG in Sweden between 2003 and 2013 were included. The study population and baseline characteristics were obtained from the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) register, and further expanded with information from the National Patient Register, the Swedish Renal Register, and socioeconomic data from Statistics Sweden (a government agency) (15). Data sources are described in detail in the Online Appendix. The regional Human Research Ethics Committee, Stockholm, Sweden, approved the study.

DEFINITIONS OF DM. The type of DM (1 or 2) was obtained from the Swedish National Diabetes Register (Online Appendix). All patients who were not included in the Swedish National Diabetes Register were considered as being nondiabetic. The epidemiological definition of T1DM was onset of DM at age <30 years and treatment with insulin only (16). T2DM was defined as DM treated with diet or oral hypoglycemic agents alone, or age >40 years at onset and treated with insulin alone or in combination with oral hypoglycemic agents (17).

OUTCOMES. We obtained the date and cause of death from the national Cause of Death Register. Causes of death were categorized as cardiovascular or noncardiovascular. Rehospitalization for MI, heart failure, stroke, or repeat revascularization (percutaneous coronary intervention [PCI] or CABG) data were obtained from the National Patient Register. A major adverse coronary event (MACE) was defined as hospital stay for MI, stroke, heart failure, or revascularization. International Classification of Diseases codes for the outcome measures are shown in the Online Appendix.

MISSING DATA. Missing data (renal function [4.5%], ejection fraction [2.6%], body mass index [7.6%], education [2.5%], number of bypass grafts [14%]) were managed by multiple imputation (Online Appendix).

STATISTICAL METHODS. Patient characteristics were described using frequencies and percents for

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CI = confidence interval

DM = diabetes mellitus

HbA$_{1c}$ = glycosylated hemoglobin

HR = hazard ratio

MI = myocardial infarction

PCI = percutaneous coronary intervention

T1DM = type 1 diabetes mellitus

T2DM = type 2 diabetes mellitus