JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER INC.

VOL. 66, NO. 5, 2015
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2015.05.054

Glycemic Control in Type 1 Diabetes and Long-Term Risk of Cardiovascular Events or Death After Coronary Artery Bypass Grafting

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ABSTRACT

BACKGROUND Patients with type 1 diabetes mellitus (T1DM) have a high risk of cardiovascular events.

OBJECTIVES The aim of this study was to investigate whether preoperative hemoglobin A_{1c} (HbA_{1c}) levels could predict cardiovascular events or death after coronary artery bypass grafting (CABG).

METHODS This was a nationwide population-based observational cohort study that included all patients with T1DM who underwent primary isolated nonemergency CABG in Sweden between 1997 and 2012, according to the Swedish National Diabetes Register and the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) register. We calculated the crude incidence rates and 95% confidence intervals (CIs) and used Cox regression and multivariable hazard ratios (HRs) to estimate the risk of both all-cause mortality and major adverse cardiovascular events (MACE), defined as myocardial infarction, stroke, heart failure, or repeat revascularization, in relation to HbA_{1c} levels.

RESULTS In total, 764 patients with T1DM were included. During a median follow-up of 4.7 years, 334 (44%) patients died or had MACE (incidence rate: 82 events/1,000 person-years). After multivariable adjustment, the HR (95% CI) for death or MACE in patients with HbA_{1c} levels of 7.1% to 8.0%, 8.1% to 9.0%, 9.1% to 10.0%, and >10.0% were 1.34 (0.82 to 2.21), 1.59 (1.00 to 2.54), 1.73 (1.03 to 2.90), and 2.25 (1.29 to 3.94), respectively, compared with the reference category. When HbA_{1c} was used as a continuous variable, the HR for a 1% increase in HbA_{1c} level was 1.18, and the 95% CI was 1.06 to 1.32.

CONCLUSIONS In patients with T1DM, poor glycemic control before CABG was associated with increased long-term risk of death or MACE. (HeAlth-data Register sTudies of Risk and Outcomes in Cardiac Surgery [HARTROCS]; NCT02276950) (J Am Coll Cardiol 2015;66:535–43) © 2015 by the American College of Cardiology Foundation.

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Manuscript received January 15, 2015; revised manuscript received May 11, 2015, accepted May 19, 2015.

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CHD = coronary heart disease

CVD = cardiovascular disease

HbA_{1c} = hemoglobin A_{1c}

MACE = major adverse cardiovascular event(s)

T1DM = type 1 diabetes mellitus

Advances in treatment for type 1 diabetes mellitus (T1DM) have improved life expectancy and decreased mortality rates over time (1). Despite declining rates of diabetes-associated complications in the past 2 decades (2), the disease persists in large numbers, and the prevalence of cardiovascular disease (CVD), the most common complication among patients with diabetes, remains very high (3). Abnormal vascular findings associated with atherosclerosis are much more common in patients with T1DM compared with nondiabetic patients (4). The risk of CVD events is high and occurs earlier in patients with T1DM; incidence rates of deaths, even in patients with T1DM who have good glycemic control, are reached at a much younger age compared with the general population (5,6).

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Revascularization surgery for patients with multivessel coronary heart disease (CHD) is a common procedure; approximately 25% of these patients have diabetes. Patients with diabetes and established CHD often have more complicated atherosclerosis and are at higher risk of developing major adverse CVD events and death than are patients without diabetes (7–10). Revascularization studies have evaluated patients on the basis of various categorizations, including the presence or absence of diabetes (8,9) and the presence of insulin-dependent or not insulin-dependent diabetes (7). In patients with T1DM and CHD, the association between glycemic control and cardiovascular outcomes after revascularization remains unclear (11). Because patients with T1DM have a high risk of CVD events and death (5), we wanted to investigate whether different levels of glycemic control could predict CVD events after coronary artery bypass graft (CABG) procedures in these patients.

The aim of this study was to analyze the association between preoperative hemoglobin A_{1c} (HbA_{1c}) levels and combined all-cause mortality and myocardial infarction, heart failure, stroke, or repeat revascularization in patients with T1DM who were undergoing primary isolated nonemergency CABG.

METHODS

STUDY DESIGN. This was an observational nationwide population-based cohort study. The study was approved by the regional Human Research Ethics Committee, Stockholm, Sweden.

STUDY POPULATION. The study population was obtained by cross-referencing patient-level data from the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) register (12) and the National Diabetes Register (13). All patients with T1DM (according to the Swedish National Diabetes Register) who underwent primary isolated nonemergency CABG in Sweden between 1997 and 2012 were included. Further information regarding baseline characteristics was extracted from the National Patient Register. Cross-referencing was possible through the unique personal identity number assigned to every Swedish citizen (14). The epidemiological definition of T1DM in the Swedish National Diabetes Register is onset of diabetes before the age of 30 years and treatment with insulin only (13).

HEMOGLOBIN A_{1c}. Analyses of HbA_{1c} were carried out at local laboratories with the high-performance liquid chromatography Mono-S method and were quality assured nationwide by regular calibration. We converted all HbA_{1c} values to standard values according to the National Glycohemoglobin Standardization Program (15). We calculated the mean of all available HbA_{1c} values before the date of CABG for each patient (16). On the basis of their preoperative mean HbA_{1c} values, patients were assigned to 1 of the following HbA_{1c} categories: ≤7.0%, 7.1% to 8.0%, 8.1% to 9.0%, 9.1% to 10.0%, and >10.0%.

OUTCOMES. The primary outcome measure was a combination of all-cause mortality and major adverse cardiovascular event (MACE), defined as rehospitalization for a primary diagnosis of myocardial infarction (International Classification of Diseases-Tenth Revision [ICD-10] codes: I21 to I21.9), heart failure (ICD-10 codes: I50 to I50.9), stroke (ICD-10 codes: I60 to I69.9), or repeat revascularization (ICD-10 codes: FNG, FNA, FNC). The date and cause of death were obtained from the national Cause of Death Register; the date and cause of rehospitalization were obtained from the National Patient Register. The validity of the diagnoses of myocardial infarction, heart failure, and stroke has been evaluated in the National Patient Register and found to be 95% for a primary diagnosis of heart failure; the positive predictive value is 98% to 100% for myocardial infarction and 98.6% for stroke (17,18). We also assessed death from cardiovascular and noncardiovascular causes separately. Finally, the following ICD-10 codes were used to analyze hospitalizations for hypoglycemia: E10.0, E10.6, and E16 to E16.2.

MISSING DATA. We excluded patients with missing information regarding preoperative HbA_{1c}. For the following variables that were used as covariates in the