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 cardio-vascular 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),

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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

HbA₁c = glycosylated hemoglobin

HR = hazard ratio

MI = myocardial infarction

PCI = percutaneous coronary intervention

T1DM = type 1 diabetes mellitus

T2DM = type 2 diabetes mellitus

categorical variables, and means and standard deviations for continuous variables. The primary outcome measure was death from any cause. Patients contributed person-time in days from the date of surgery until the date of death from any cause or the end of follow-up (March 24, 2014). Secondary outcome measures included cardiovascular death, and a combination of hospital stay for MI, heart failure, stroke, or repeat revascularization. Information regarding cause of death and hospital stay was available until December 31, 2012; therefore, the follow-up period for the secondary outcome measures ended on December 31, 2012. As a result, patients who underwent surgery during 2013 (n = 2,473) were excluded from the secondary outcome analyses.

We used Cox regression to estimate the risk of all-cause mortality or a combined endpoint (all-cause mortality or hospital stay for MI, heart failure, stroke, or repeat revascularization) in patients with T1DM or T2DM in a comparison with reference patients without diabetes. We calculated crude and multivariable adjusted hazard ratios (HRs) and 95% confidence intervals (CIs). We included all the variables listed in **Table 1** as covariates in the final multivariable model.

We investigated differences in each cause of mortality (cardiovascular death or other causes) by competing risk regression based on the Fine-Gray proportional subhazards model (18), and calculated subdistribution HR and 95% CI.

Data management and statistical analyses were performed using Stata 13.1 (Stata Corp, College Station, Texas) and R version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patient characteristics are presented in **Table 1**. A total of 39,235 patients with a mean age of 67 years were included, of whom 21% (8,170 of 39,235) were women. In total, there were 23% (8,933 of 39,235) patients with DM, of whom 1.8% (725 of 39,235) had T1DM and 21% (8,208 of 39,235) had T2DM. Patients with T1DM were more likely to be younger, female, and have chronic kidney disease, peripheral vascular disease, and heart failure in comparison with patients with no DM or T2DM.

During a mean follow-up time of 5.9 ± 3.2 years (230,085 person-years), in total, 17% (6,765 of 39,235) patients died: 17% (5,064 of 30,302) with no DM, 21% (152 of 725) with T1DM, and 19% (1,549 of 8,208) with T2DM. The unadjusted Kaplan-Meier estimated

survival curve is shown in **Figure 1**, and the age-adjusted survival curve is shown in **Figure 2**. The crude incidence rate of death in patients with no DM, T1DM, and T2DM was 28 (95% CI: 27 to 29), 39 (95% CI: 33 to 45), and 33 (95% CI: 31 to 35) per 1,000 person-years, respectively. After 1 year of surgery, survival was 97%, 96%, and 97% in patients with no DM, T1DM, and T2DM, respectively. The corresponding figures after 5 years were 89%, 85%, and 89%, respectively. After multivariable adjustment, the HR (95% CI) for death was 2.04 (1.72 to 2.42) in patients with T1DM and 1.11 (1.05 to 1.18) in patients with T2DM, compared with no DM. Furthermore, we categorized causes of death into cardiovascular death or noncardiovascular death. The point estimates indicated a stronger association between T1DM and noncardiovascular death than with cardiovascular death. The association between T2DM and cardiovascular death was not significant (HR: 1.08, 95% CI: 0.95 to 1.19).

When we analyzed death and MACE as a composite outcome, the associations found were similar to those for death alone, with nearly a doubling of risk in patients with T1DM and only a small increase in risk in patients with T2DM (**Central Illustration**).

In a subset of patients with T1DM and T2DM (n = 8,933), we found that there was a significantly higher risk for all-cause mortality in T1DM compared with T2DM (adjusted HR: 1.70 [95% CI: 1.40 to 2.06]). In 99.6% (8,899 of 8,933) of these patients, information regarding preoperative glycosylated hemoglobin (HbA$_{1c}$) and diabetes duration was available. When HbA$_{1c}$ and duration of disease were added to the multivariable model, the risk for all-cause mortality in T1DM compared with T2DM was slightly attenuated (adjusted HR: 1.44 [95% CI: 1.14 to 1.80]).

RELATIONSHIP BETWEEN TYPE OF DM, DURATION OF DISEASE, AND GLYCEMIC CONTROL. Patients with T1DM had a longer duration of disease than patients with T2DM (mean 40.8 vs. 9.6 years) (**Table 2**). In patients with T1DM, 94% had a longer duration of disease than 20 years, compared with 10% in patients with T2DM. Furthermore, patients with T1DM had, in general, higher HbA$_{1c}$ levels than patients with T2DM.

RELATIONSHIP BETWEEN T1DM, T2DM, AND DEATH ACCORDING TO SEX. In men with T1DM, 19% (79 of 420) died during follow-up compared with 24% (73 of 305) among women with T1DM. The adjusted risk of death was similar among men and women with T1DM: HR: 1.83 (95% CI: 1.45 to 2.30) and HR: 2.17 (95% CI: 1.66 to 2.84), respectively (**Table 3**). The absolute risk
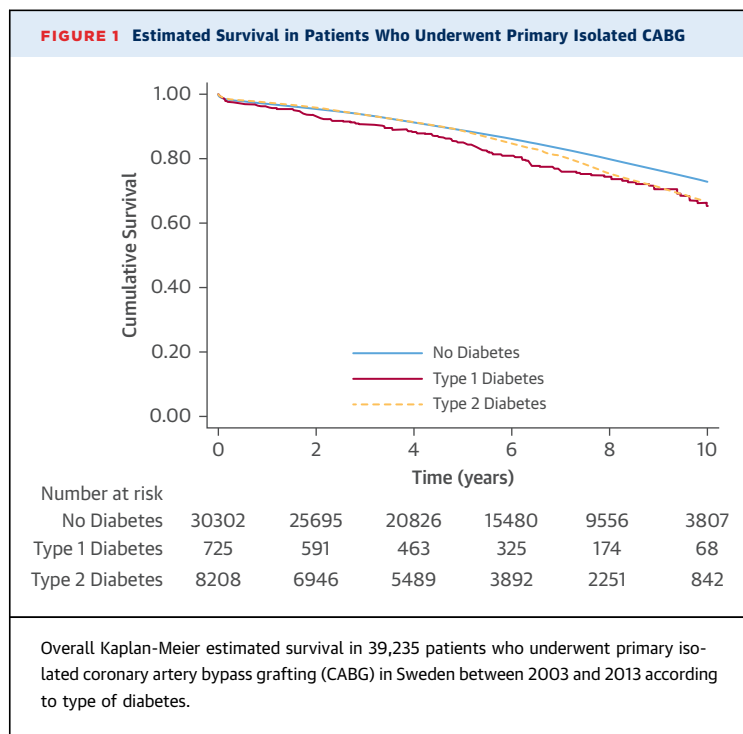
TABLE 1 Baseline Characteristics

	All Patients	No Diabetes	T1DM	T2DM
Number of patients	39,235 (100)	30,302 (77)	725 (1.8)	8,208 (21)
Age, yrs	67.3 ± 9.2	67.5 ± 9.3	58.8 ± 9.2	67.4 ± 8.4
Female	8,170 (20.8)	5,973 (19.7)	305 (42.1)	1,892 (23.1)
Body mass index, kg/m²	27.3 ± 4.1	26.9 ± 3.9	26.3 ± 4.3	28.8 ± 4.3
eGFR				
>60 ml/min/1.73 m²	29,502 (78.7)	23,167 (80.0)	441 (62.8)	5,894 (75.1)
45-60 ml/min/1.73 m²	5,287 (14.1)	3,986 (13.8)	94 (13.4)	1,207 (15.4)
30-44 ml/min/1.73 m²	1,852 (4.9)	1,248 (4.3)	63 (9.0)	541 (6.9)
15-29 ml/min/1.73 m²	369 (1.0)	236 (0.8)	26 (3.7)	107 (1.4)
End-stage renal disease	488 (1.3)	311 (1.1)	78 (11.1)	99 (1.3)
Hypertension	15,749 (40.1)	11,097 (36.6)	358 (49.4)	4,294 (52.3)
Hyperlipidemia	9,626 (24.5)	6,951 (22.9)	201 (27.7)	2,474 (30.1)
Peripheral vascular disease	4,077 (10.4)	2,846 (9.4)	172 (23.7)	1,059 (12.9)
Prior PCI	4,654 (11.9)	3,433 (11.3)	102 (14.1)	1,119 (13.6)
Chronic pulmonary disease	3,090 (7.9)	2,299 (7.6)	41 (5.7)	750 (9.1)
Prior myocardial infarction	21,676 (55.2)	16,527 (54.5)	408 (56.3)	4,741 (57.8)
Heart failure	3,860 (9.8)	2,676 (8.8)	119 (16.4)	1,065 (13.0)
Stroke	3,425 (8.7)	2,449 (8.1)	90 (12.4)	886 (10.8)
Atrial fibrillation	2,555 (6.5)	1,942 (6.4)	24 (3.3)	589 (7.2)
Left ventricular ejection fraction				
>50%	26,497 (69.3)	20,840 (70.7)	472 (66.3)	5,185 (64.7)
30%-50%	10,120 (26.5)	7,495 (25.4)	206 (28.9)	2,419 (30.2)
<30%	1,604 (4.2)	1,160 (3.9)	34 (4.8)	410 (5.1)
EuroSCORE	4.1 ± 2.7	4.1 ± 2.7	3.5 ± 2.5	4.2 ± 2.6
Alcohol dependency	902 (2.3)	691 (2.3)	9 (1.2)	202 (2.5)
Birth region				
Nordic countries	35,351 (90.1)	27,497 (90.7)	696 (96.0)	7,158 (87.2)
Other	3,883 (9.9)	2,804 (9.3)	29 (4.0)	1,050 (12.8)
Education				
<10 yrs	16,668 (43.6)	12,663 (42.9)	239 (33.1)	3,766 (46.9)
10-12 yrs	14,869 (38.9)	11,410 (38.6)	339 (46.9)	3,120 (38.9)
>12 yrs	6,734 (17.6)	5,452 (18.5)	145 (20.1)	1,137 (14.2)
Marital status				
Married	25,896 (66.0)	20,127 (66.4)	432 (59.6)	5,337 (65.0)
Other	13,338 (34.0)	10,174 (33.6)	293 (40.4)	2,871 (35.0)
Off-pump CABG	1,309 (3.3)	1,078 (3.6)	17 (2.3)	214 (2.6)
Number of grafts				
1-2	6,444 (19.1)	5,167 (19.8)	118 (19.2)	1,159 (16.7)
3-4	23,622 (70.1)	18,207 (69.6)	438 (71.1)	4,977 (71.6)
>4	3,641 (10.8)	2,770 (10.6)	60 (9.7)	811 (11.7)
Type of graft				
Internal mammary artery	36,909 (94.1)	28,551 (94.2)	689 (95.0)	7,669 (93.4)
Bilateral internal mammary arteries	468 (1.2)	399 (1.3)	11 (1.5)	58 (0.7)
Radial artery	1,313 (3.3)	1,033 (3.4)	22 (3.0)	258 (3.1)
More than 1 arterial graft	1,718 (4.4)	1,381 (4.6)	31 (4.3)	306 (3.7)

Values are n (%) or mean ± SD. End-stage renal disease was defined as eGFR <15 ml/min/1.73 m² or on dialysis/renal transplant.

CABG = coronary artery bypass grafting; eGFR = estimated glomerular filtration rate; PCI = percutaneous coronary intervention; T1DM = diabetes mellitus type 1; T2DM = diabetes mellitus type 2.

of death in women with T2DM was higher than that in men with T2DM (22% vs. 18%). However, after adjustment for confounders, the relative risks were similar for both men and women with T2DM (**Table 3**). Similar sex-specific associations between types of diabetes were also found for death and MACE combined as outcome (**Table 3**).
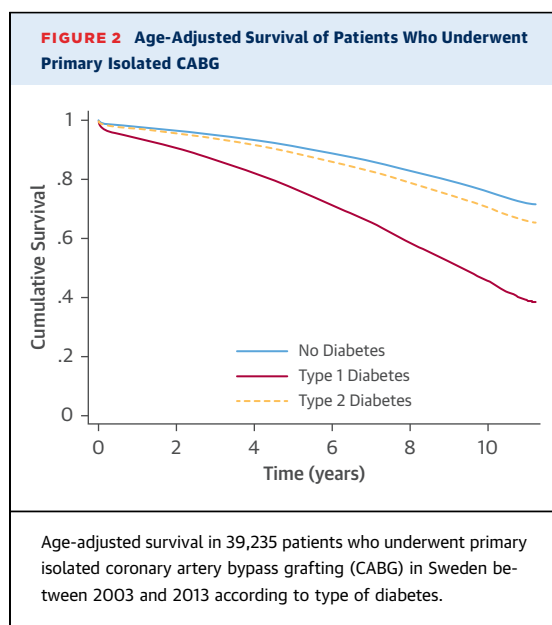
DISCUSSION

In a large nationwide cohort of patients who underwent a first isolated CABG during an 11-year period in Sweden, we found that patients with T1DM had a risk of death after CABG double that of patients without DM. There was a small, but statistically significant,
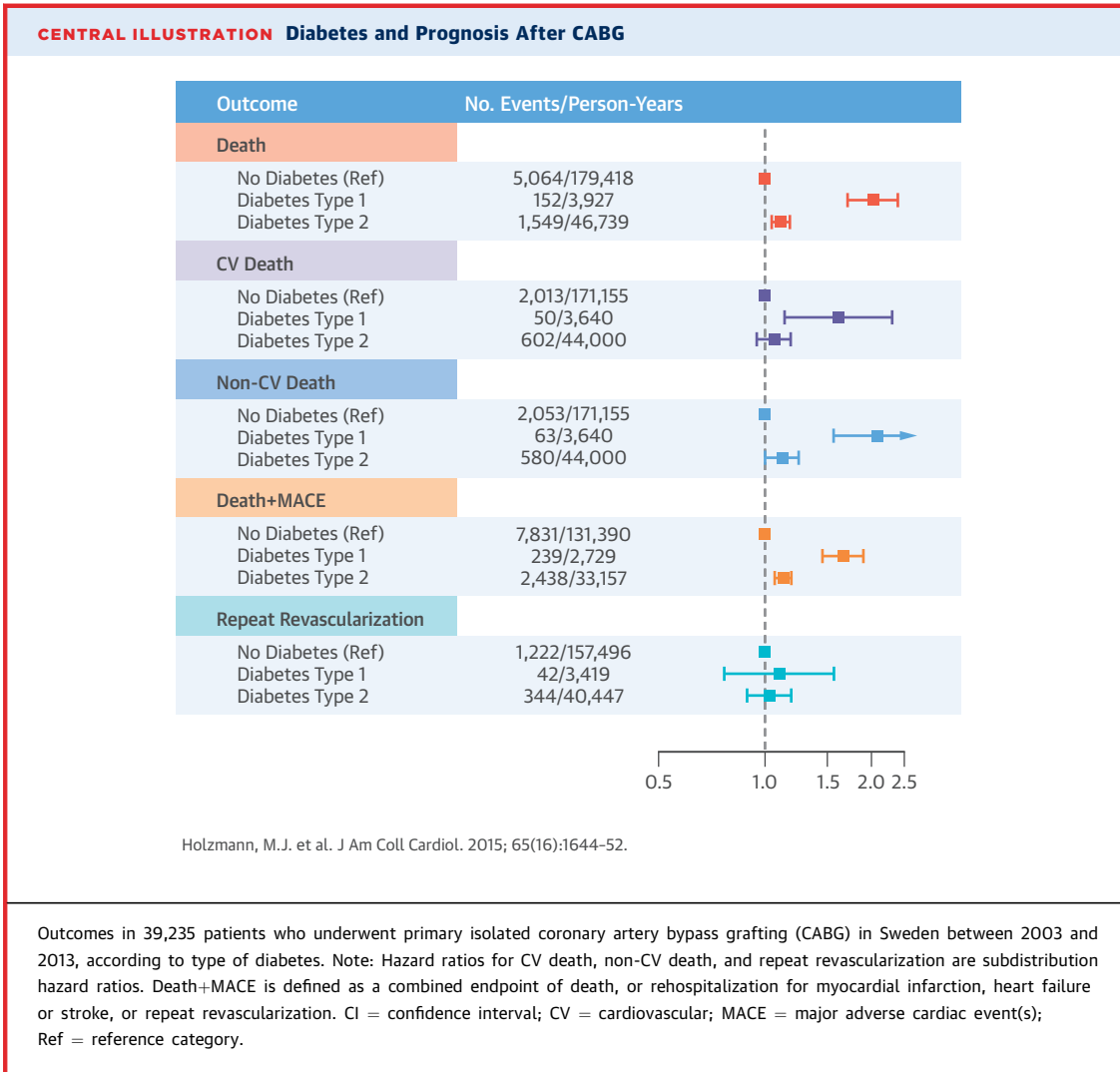
FIGURE 1 Estimated Survival in Patients Who Underwent Primary Isolated CABG

Number at risk						
No Diabetes	30302	25695	20826	15480	9556	3807
Type 1 Diabetes	725	591	463	325	174	68
Type 2 Diabetes	8208	6946	5489	3892	2251	842

Overall Kaplan-Meier estimated survival in 39,235 patients who underwent primary isolated coronary artery bypass grafting (CABG) in Sweden between 2003 and 2013 according to type of diabetes.

increase in the risk of death in patients with T2DM when compared with those without DM (**Central Illustration**). In addition, there was no difference in relative risks for death or cardiovascular events between women and men, neither in those with T1DM or T2DM.

A number of either population-based or randomized trials have reported on the association between

FIGURE 2 Age-Adjusted Survival of Patients Who Underwent Primary Isolated CABG

Age-adjusted survival in 39,235 patients who underwent primary isolated coronary artery bypass grafting (CABG) in Sweden between 2003 and 2013 according to type of diabetes.

DM and the risk of cardiovascular disease (14). However, most of these studies have either only included patients with T2DM or have not made any distinction between T1DM and T2DM, and thus have analyzed patients as being merely diabetic or nondiabetic. This also holds true for previous studies on the importance of DM for prognosis after CABG, which may explain the conflicting results found in previous studies (7-11). To the best of our knowledge, only 1 previous study has investigated the association between T1DM and T2DM and outcomes after CABG (11), wherein both subtypes of DM were associated with the combined outcome of death or MI. That study included only 50 patients with T1DM, and the inclusion period was 1980 to 1995. Thus, considering the recent rather steep decline in cardiovascular events and death associated with DM (19-22), and the small number of events reported in that study, we believe that the findings may not be applicable to contemporary cohorts of CABG patients.

The 2 main findings in our study were that T1DM was associated with a doubling of mortality, but also that patients with T2DM had only a minimally increased risk of death in comparison with nondiabetic patients (**Central Illustration**). Furthermore, patients with T1DM were more likely than patients with T2DM or without diabetes to have comorbidities, such as chronic kidney disease, end-stage renal disease, peripheral vascular disease, or heart failure, which all have been associated with a worse prognosis in diabetic patients who undergo CABG (9,10). However, even after adjustment for these risk factors, the association between T1DM and adverse outcome was significant. One of the main differences between the 2 subtypes of diabetes is the duration of the disease. In the present study, the difference in mean duration of disease between patients with T1DM and T2DM was >30 years. This fact may help explain the differences seen in prognosis between the 2 subtypes of diabetes, because the duration of exposure to risk factors and comorbidities was considerably longer in patients with T1DM than in those with T2DM. In addition, HbA$_{1c}$ levels were higher in patients with T1DM than in those with T2DM, revealing poorer glycemic control in patients with T1DM. The association between glycemic control and micro- and macro-angiopathy seems to be more significant in T1DM than in T2DM (16,22). Although we do not have any data on microvascular complications, the increase in HbA$_{1c}$ levels together with the longer duration of diabetes seen in T1DM might explain our findings. Interestingly, in a recently published study, HbA$_{1c}$ levels in patients with insulin-treated DM who underwent PCI were not related to mortality (23). In the

CENTRAL ILLUSTRATION Diabetes and Prognosis After CABG

Outcome	No. Events/Person-Years
Death	
No Diabetes (Ref)	5,064/179,418
Diabetes Type 1	152/3,927
Diabetes Type 2	1,549/46,739
CV Death	
No Diabetes (Ref)	2,013/171,155
Diabetes Type 1	50/3,640
Diabetes Type 2	602/44,000
Non-CV Death	
No Diabetes (Ref)	2,053/171,155
Diabetes Type 1	63/3,640
Diabetes Type 2	580/44,000
Death+MACE	
No Diabetes (Ref)	7,831/131,390
Diabetes Type 1	239/2,729
Diabetes Type 2	2,438/33,157
Repeat Revascularization	
No Diabetes (Ref)	1,222/157,496
Diabetes Type 1	42/3,419
Diabetes Type 2	344/40,447

Holzmann, M.J. et al. J Am Coll Cardiol. 2015; 65(16):1644–52.

Outcomes in 39,235 patients who underwent primary isolated coronary artery bypass grafting (CABG) in Sweden between 2003 and 2013, according to type of diabetes. Note: Hazard ratios for CV death, non-CV death, and repeat revascularization are subdistribution hazard ratios. Death+MACE is defined as a combined endpoint of death, or rehospitalization for myocardial infarction, heart failure or stroke, or repeat revascularization. CI = confidence interval; CV = cardiovascular; MACE = major adverse cardiac event(s); Ref = reference category.

same study, patients with DM without insulin treatment were more likely to benefit from better glycemic control. However, the investigators were unable to subtype their patients into T1DM or T2DM, but only into treatment groups with or without insulin. Furthermore, in a recently published study from the same register where our T1DM patients were retrieved, even those T1DM patients who had a HbA$_{1c}$ level below 7.0% had a more than doubled risk of death as compared with the general population (24). This indicates that even with optimal glycemic control T1DM patients are at high risk of premature death.

We found only a small increase in the risk of death in patients with T2DM when compared with those without DM. This finding may have several explanations. First, previous studies have suggested that a large proportion of patients with MI have either glucose intolerance or established T2DM, which has gone undetected until they are admitted for an acute coronary syndrome (24). Thus, if a large proportion of patients were categorized as non-DM patients and truly had either glucose intolerance or established T2DM, and this was related to outcome, this may have diluted the associations seen between both T2DM and T1DM and the outcome measures. However, studies that have investigated the prognostic importance of glucose intolerance in patients with MI have failed to show any convincing associations with adverse outcomes (25). Second, because all patients with T2DM already had established coronary artery disease, and as a consequence a very high risk of recurrent cardiovascular events, they may have been treated with optimal medications and measures to reduce their risk of future cardiovascular events (26). Their treatment may even have been better

TABLE 2 HbA$_{1c}$ and DM Duration in Patients With T1DM and T2DM

			T1DM n = 725	T2DM n = 8,208
Diabetes duration			40.8 ± 12.3	9.6 ± 8.1
≤20 yrs			44 (6.1)	7,351 (89.6)
>20 yrs			681 (93.9)	857 (10.4)
HbA$_{1c}$	IFCC (mmol/mol)	NGSP (%)		
IFCC, mmol/mol			67.8 ± 10.7	57.9 ± 12.0
NGSP, %			8.4 ± 1.0	7.4 ± 1.1
	<53	<7.0	52 (7.2)	3,053 (37.3)
	53–73	7.0–8.8	460 (63.5)	4,264 (52.2)
	>73	>8.8	212 (29.3)	858 (10.5)

Values are mean ± SD or n (%), unless otherwise noted. All p values <0.001.

DM = diabetes mellitus; HbA$_{1c}$ = glycosylated hemoglobin; IFCC = International Federation of Clinical Chemistry; NGSP = National Glycohemoglobin Standardization Program; other abbreviations as in **Table 1**.

than that for patients without DM, thus diluting the differences in risk between those with T2DM and those without DM.

It is generally thought that women with DM have a higher relative risk of cardiovascular events than men with DM (12,27,28). However, recent studies have challenged this statement and have found similar

TABLE 3 Absolute and Relative Risks of Death or MACE+Death After Primary Isolated CABG in Patients With T1DM or T2DM Compared With Patients Without DM Stratified by Sex

	No DM	T1DM	T2DM
Death			
Men	3,918/24,329 (16.1)	79/420 (18.8)	1,134/6,316 (17.9)
Crude rate per 1,000 person-yrs	27.3 (26.5–28.2)	34.1 (27.3–42.5)	31.7 (29.9–33.6)
Crude HR	1.00	1.28 (1.02–1.60)	1.18 (1.10–1.26)
Adjusted HR	1.00	1.83 (1.45–2.30)	1.09 (1.02–1.17)
Women	1,146/5,973 (19.2)	73/305 (23.9)	415/1,892 (21.9)
Crude rate per 1,000 person-yrs	31.8 (30.0–33.7)	45.4 (36.1–57.1)	37.8 (34.4–41.7)
Crude HR	1.00	1.46 (1.15–1.85)	1.21 (1.08–1.35)
Adjusted HR	1.00	2.17 (1.66–2.84)	1.18 (1.04–1.32)
MACE+death*			
Men	6,070/22,777 (26.7)	123/391 (31.5)	1,821/5,887 (30.9)
Crude rate per 1,000 person-yrs	57.6 (56.2–59.1)	75.4 (63.2–90.0)	71.9 (68.7–75.3)
Crude HR	1.00	1.30 (1.08–1.55)	1.24 (1.17–1.30)
Adjusted HR	1.00	1.51 (1.26–1.82)	1.14 (1.08–1.21)
Women	1,761/5,635 (31.2)	116/282 (41.1)	617/1,790 (34.5)
Crude rate per 1,000 person-years	67.6 (64.6–70.9)	106 (88.1–127)	78.7 (72.7–85.2)
Crude HR	1.00	1.51 (1.25–1.82)	1.15 (1.05–1.26)
Adjusted HR	1.00	1.75 (1.42–2.16)	1.10 (1.00–1.21)

Values are n events/n patients (%) or HR (95% CI). All variables listed in **Table 1** were included as covariates in the final multivariable model. *MACE+death is defined as a combined endpoint of death, or rehospitalization for myocardial infarction, heart failure, or stroke, or repeat revascularization.

CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiac event(s); other abbreviations as in **Table 1**.

risks in men and women (19). In the present study, we found no sex differences in relative risks between outcomes and both T1DM and T2DM cohorts.

By using the National Diabetes Register, we were able to classify all patients according to the type of DM, and thus investigate the importance of the 2 subtypes for prognosis. The information used for categorization into T1DM and T2DM has been shown to have high validity (16). To the best of our knowledge, this was the first study of a contemporary cohort of patients undergoing CABG where the association between subtypes of DM and prognosis were investigated. Moreover, we also had information on the characteristics that distinguish T1DM from T2DM in general, that is, duration of diabetes and glycemic control, which allowed us to speculate to some extent on potential mechanisms responsible for the differences seen in prognosis among patients with T1DM and T2DM. The nationwide population-based design allowed for a large study population, and the rather long follow-up led to a large number of events, which gave us the opportunity to analyze additional clinically relevant outcomes, such as cause-specific mortality and need for repeat revascularization. The high-quality Swedish national registers from which we derived the study population and retrieved patient characteristics and outcomes have been found to have high validity in previous studies (15,29,30). Furthermore, as the coverage of these registers is virtually complete and countrywide, the risk of misclassification of disease or outcome was small, and there was no loss to follow-up. In addition, considering the nationwide design of our study and the recent study period, reflecting current standard of care, we believe that our results have a high external validity and are applicable to other patients with DM undergoing CABG in countries with a similar level of healthcare.

STUDY LIMITATIONS. We did not have any information on patients with DM who underwent PCI instead of CABG for multivessel disease. Therefore, our results cannot be generalized to this group of patients. However, a number of early and recent studies have investigated which method of revascularization (PCI or CABG) is preferred in patients with DM (31). There is a general consensus that CABG is superior to PCI in patients with DM and multivessel disease, particularly in patients with more complex coronary artery disease, provided that they are candidates for cardiac surgery (32). Thus, we believe that our findings are of great importance for patients with DM who may need to undergo multivessel revascularization.

There may have been misclassification of glycemic control among patients without DM. This was

a potential limitation because it has been shown that a large proportion of patients with acute coronary syndromes have undetected T2DM or glucose intolerance (24).

CONCLUSIONS

We found that patients with T1DM had a doubling of the risk of death, whereas patients with T2DM had almost a similar risk of death as patients without diabetes in a nationwide cohort of 39,235 patients who underwent CABG. Our data indicate that patients with T1DM are at high risk for adverse outcome after CABG and should be closely followed up, and that all possible measures to mitigate their risk of death or recurrent cardiovascular events should be instituted.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Patients with type 1 diabetes mellitus have a greater risk of death and cardiovascular events after CABG surgery than patients without diabetes, but these risks are only marginally increased among patients with type 2 diabetes.

TRANSLATIONAL OUTLOOK: Future studies should attempt to define the specific types and timing of secondary prevention measures that best mitigate the risk of adverse outcomes for patients with diabetes undergoing CABG surgery.

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KEY WORDS isolated CABG, major adverse coronary event, prognosis, revascularization

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APPENDIX For supplemental tables and an expanded Methods section, please see the online version of this article.