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PCI Versus CABG in Patients With Type 1 Diabetes and Multivessel Disease

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ABSTRACT

BACKGROUND It is unknown if coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) may offer a survival benefit in patients with type 1 diabetes (T1D) in need of multivessel revascularization.

OBJECTIVES This study sought to determine if patients with T1D and multivessel disease may benefit from CABG compared with PCI.

METHODS In an observational cohort study, the authors included all patients with T1D who underwent a first multivessel revascularization in Sweden from 1995 to 2013. The authors used the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) register, the Swedish National Diabetes Register, and the Swedish National Patient Register to retrieve information about patient characteristics and outcomes. They estimated hazard ratios (HRs) adjusted for confounders with 95% confidence intervals (CIs) for all-cause and coronary heart disease mortality, myocardial infarction, repeat revascularization, stroke, and heart failure using inverse probability of treatment weighting based on propensity scores.

RESULTS In total, 683 patients who underwent CABG and 1,863 patients who underwent PCI were included. During a mean follow-up of 10.6 years, 53% of patients in the CABG group and 45% in the PCI group died. PCI, compared with CABG, was associated with a similar risk of all-cause mortality (HR: 1.14; 95% CI: 0.99 to 1.32), but higher risks of death from coronary heart disease (HR: 1.45; 95% CI: 1.21 to 1.74), myocardial infarction (HR: 1.47; 95% CI: 1.23 to 1.78), and repeat revascularization (HR: 5.64; 95% CI: 4.67 to 6.82). No differences in risks of stroke or heart failure were found.

CONCLUSIONS Notwithstanding the inclusion of patients with T1D who might not have been able to undergo CABG in the PCI group we found that PCI, compared with CABG, was associated with higher rates and risks of coronary heart disease mortality, myocardial infarction, and repeat revascularizations. Our findings indicate that CABG may be the preferred strategy in patients with T1D in need of multivessel revascularization. (J Am Coll Cardiol 2017;■:■–■)

Among patients who undergo multivessel revascularization with coronary artery bypass grafting (CABG), or percutaneous coronary intervention (PCI), 25% have diabetes. A mortality benefit favoring CABG over PCI has been proven for patients with diabetes. In the BARI (Bypass Angioplasty Revascularization Investigation) study, patients with diabetes who underwent PCI had almost double the 5-year mortality of those who underwent CABG (1). Later, the FREEDOM

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CI = confidence interval

HR = hazard ratio

PCI = percutaneous coronary intervention

T1D = type 1 diabetes

T2D = type 2 diabetes

(Future REvascularization Evaluation in patients with Diabetes Mellitus) study, where 1,900 patients with diabetes and multivessel disease were randomized to undergo either PCI or CABG, demonstrated a reduction in the composite outcome of death from any cause, nonfatal myocardial infarction, or nonfatal stroke in favor of CABG over PCI (2). Similarly, in a subgroup analysis of 452 patients with diabetes who were randomized to either PCI or CABG in the SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) trial, a survival benefit was found for patients treated with CABG (3). For this reason, current guidelines support CABG over PCI as the preferred treatment of multivessel disease in patients with diabetes (4,5).

None of the abovementioned studies reported the proportion of patients with type 1 diabetes (T1D) included. However, type of diabetes may also be of great importance because the long-term prognosis after CABG is dire in patients with T1D (6), compared with patients with type 2 diabetes (T2D) whose long-term prognosis is similar to that of patients without diabetes (3,6). The reason for the poor prognosis in patients with T1D after CABG is not fully understood; however, factors such as diabetes duration and glycemic control may be of great importance (7). Therefore, the recommendation that all diabetes patients in need of multivessel revascularization should undergo CABG cannot easily be translated to patients with T1D.

Thus, it is unknown whether patients with T1D have the same benefit as patients with T2D from CABG compared with PCI. Therefore, we performed a nationwide, population-based cohort study in all patients with T1D who underwent a first multivessel revascularization with either CABG or PCI over a period of 19 years in Sweden.

METHODS

DATA SOURCES AND STUDY POPULATION. The study database was created by using the unique personal identity number assigned to every Swedish resident as the identifier to crosslink a number of Swedish national health care registries. The records linkage procedure was performed at the Swedish National Board of Health and Welfare, which anonymized the database before it was returned to the research group.

All patients with T1D who underwent a first isolated multivessel (defined as involving at least 2 significantly stenosed coronary arteries) cardiac revascularization with PCI or isolated CABG from 1995 to 2013 in Sweden were included. Exclusion criteria were prior cardiothoracic surgery; prior or current left main coronary artery revascularization; emergency procedure; valvular heart surgery or vascular surgery concurrently with CABG, or PCI for ST-segment elevation myocardial infarction; prior single-vessel PCI in the PCI group; and T1D diagnosed after the index date. The study population was identified and baseline characteristics obtained from the SWEDEHEART (Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies) register (8) and the NDR (Swedish National Diabetes Register) register (9), and further expanded with information about comorbidities and outcomes from the National Patient Register (10), date and cause of death from the Cause-of-Death register, and socioeconomic data from Statistics Sweden. Data sources are described in detail in the Online Appendix. How data from different sources was retrieved is described in Online Figure 1.

DEFINITION OF T1D. Data from all patients with T1D, according to either an epidemiological or clinical definition, were obtained from the NDR register (Online Appendix). The epidemiological definition of T1D was onset of diabetes before the age of 30 years and treatment with insulin only (9). The clinical definition of T1D in the NDR register was decided at an outpatient visit, normally to an endocrinologist, and registered in the NDR register. The coverage of T1D patients in the NDR register is virtually complete for the whole country of Sweden (9).

FOLLOW-UP AND OUTCOMES. The primary outcome was all-cause mortality, and secondary outcomes were death from coronary heart disease, myocardial infarction, stroke, and repeat revascularization. Follow-up started when the first multivessel PCI or CABG was performed for all-cause mortality, and stroke. For repeat revascularization follow-up started at 8 days after revascularization, and for myocardial infarction, and heart failure 31 days after revascularization. Follow-up ended for all outcomes when the patient died, was hospitalized for each outcome, or on December 31, 2014. Data on rehospitalizations for myocardial infarction, heart failure, stroke, or repeat revascularization was obtained from the National Patient Register or the SWEDEHEART register. International Classification of Diseases codes for the outcome measures and comorbidities are shown in Online Table 1.

STATISTICAL ANALYSIS. Missing baseline values were imputed using multiple chained equations imputation, as implemented in the MICE package in R, version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria), creating 10 imputed datasets. The percentage

TABLE 1 Characteristics of 2,546 Patients With Type 1 Diabetes Who Underwent Multivessel Revascularization From 1995–2013 in Sweden

	CABG	PCI	Standardized Difference
Patients	683 (27)	1,863 (73)	N/A
Time period of revascularization			
1995–2000	441 (58)	324 (42)	N/A
2001–2006	197 (21)	741 (79)	N/A
2007–2013	45 (5)	798 (95)	N/A
Age, yrs	57.2 ± 10.0	61.1 ± 10.5	0.378
Female	36.6	41.1	0.093
HbA_{1c}, mmol/mol	68.8 ± 14.6	67.3 ± 13.4	0.111
Diabetes duration, yrs	29.6 ± 16.0	31.6 ± 16.8	0.122
Macroalbuminuria	24.1	22.4	0.040
Microalbuminuria	25.6	28.5	0.065
GFR, ml/min/1.73 m^2	70 ± 23	67 ± 29	0.094
Current smoker	15.0	14.5	0.016
BMI, kg/m^2	26.0 ± 3.9	26.4 ± 4.3	0.087
Systolic BP, mm Hg	142 ± 19	139 ± 18	0.141
Diastolic BP, mm Hg	75 ± 9	73 ± 10	0.152
Triglycerides, mg/dl	133 ± 80	133 ± 97	0.033
HDL cholesterol mg/dl	58 ± 23	58 ± 19	0.038
LDL cholesterol, mg/dl	104 ± 39	108 ± 39	0.163
MI			0.602
Acute MI, within 14 days	13.6	36.7	
Previous MI	54.3	47.6	
Comorbidities			
Previous stroke	6.6	9.6	0.111
Previous HF	16.3	19.5	0.086
Atrial fibrillation	7.0	6.0	0.043
COPD	2.9	3.3	0.023
Peripheral arterial disease	4.4	4.5	0.003
End-stage renal disease	3.2	7.0	0.179
Active cancer	1.5	3.9	0.149
Psychiatric disease	1.3	2.7	0.101
Education			0.126
<10 yrs	37.2	33.1	
10–12 yrs	42.5	44.8	
>12 yrs	17.0	16.7	
Income (Swedish krona)			0.289
Quartile 1	31	23	
Quartile 2	29	24	
Quartile 3	23	26	
Quartile 4	17	28	
Marital status			0.162
Married	63.4	55.8	
Other	36.6	44.2	
Birth region			0.076
Nordic countries	90.8	88.5	
Other	9.2	11.5	
Region			0.404
North	10.5	10.0	
Stockholm	13.3	20.3	
Southeast	7.2	11.1	
South	15.4	17.9	
Uppsala-Örebro	20.6	23.8	
West	32.9	17.0	

Continued in the next column

Values are n (%), mean ± SD, or %. Glomerular filtration rate (GFR) was estimated using the Chronic Kidney Disease Epidemiology Collaboration formula. Macroalbuminuria was defined as >200 mg/l and microalbuminuria was defined as 20–200 ng/l. End-stage renal disease was defined as dialysis-dependent kidney disease, or need of kidney transplantation. Previous myocardial infarction (MI) means MI that occurred any time before the index date. Income is defined as yearly household disposable income. Region shows the proportion of all revascularizations during the whole study period that were performed in hospitals belonging to different regions of Sweden.

BMI = body mass index; BP = blood pressure; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; HbA_{1c} = glycated hemoglobin A1c; HDL = high-density lipoprotein; HF = heart failure; LDL = low-density lipoprotein; N/A = not applicable; PCI = percutaneous coronary intervention.

of missing values ranged from 61.1% for low-density lipoprotein to 0% for age, sex, and comorbidities (Online Table 2). The imputation worked well according to the convergence and distribution of the imputed variables. Observed and imputed values of missing data are shown in Online Figure 2.

Descriptive statistics are presented in terms of averages and percentages, together with the standardized difference before weighting. Comparisons between CABG and PCI with respect to health outcomes were made using weighted Cox regressions where the weights were derived as the average weights from propensity scores estimated using gradient boosting. The balance before and after weighting for patient characteristics is shown in Online Figure 3. The assumption of proportional hazards was evaluated by plotting the log(log[S(t)]), where S(t) is the estimated survival function. Although the assumption of proportional hazards was not exactly met, as it rarely is in practice, the hazard ratio (HR) was judged a reasonably fair summary of the effect of treatment as an average over time. To account for residual confounding, the models contained age, prior coronary heart disease, and index year.

Statistical hypothesis tests were evaluated using the 5% significance level without any adjustment for multiple comparisons. The analysis was implemented using R and SAS statistical analysis software, version 9.4 (SAS Institute Inc., Cary, North Carolina).

RESULTS

STUDY GROUP. During the study period, 2,546 patients with T1D underwent a first multivessel revascularization, of which 73% underwent PCI. The selection of the study group is described in **Figure 1**. Patients treated with PCI were older, more often women, had a longer duration of diabetes, and were

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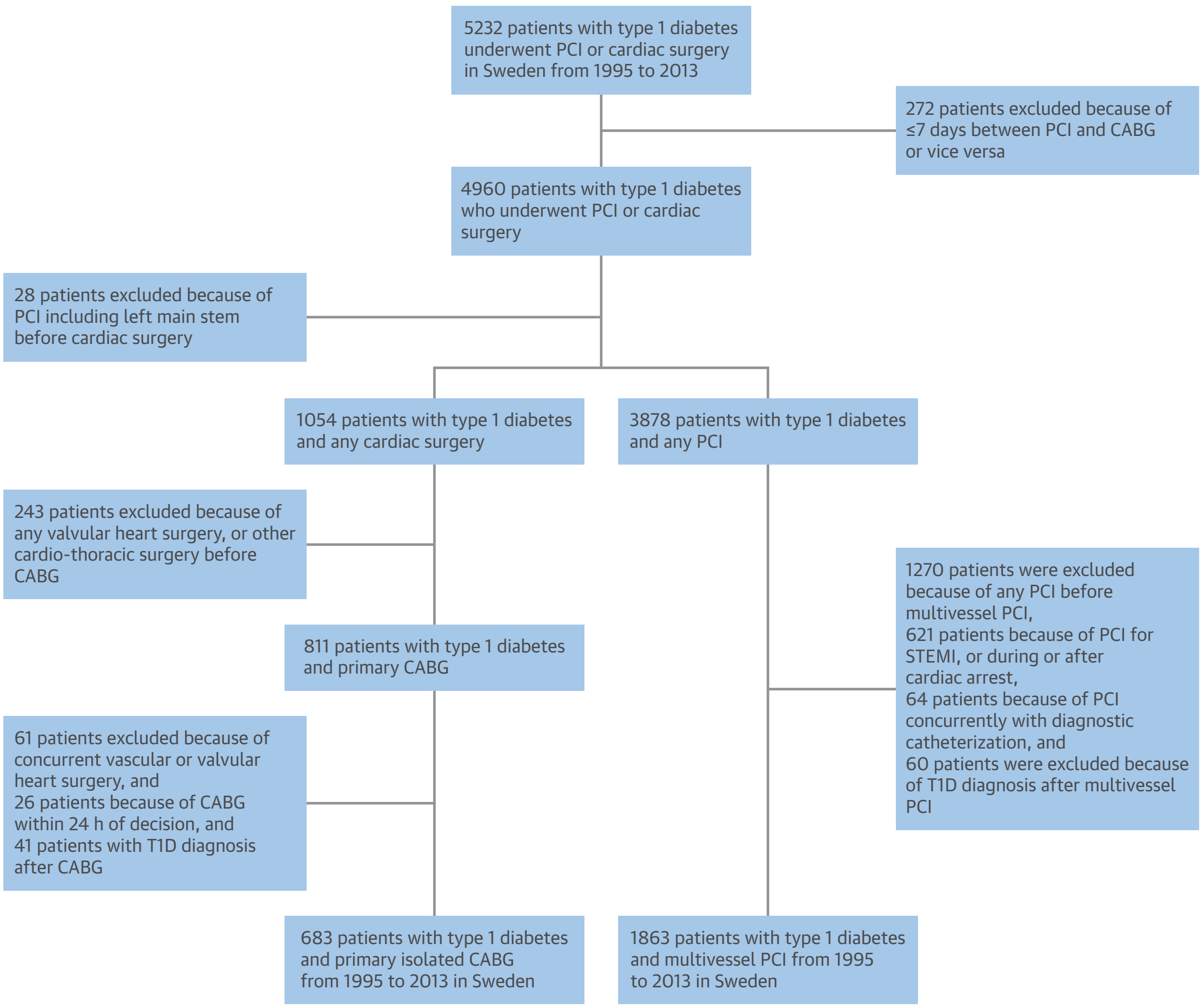
FIGURE 1 Selection of the Study Population



This figure shows how the study population, which included patients with type 1 diabetes (T1D) and multivessel disease who underwent either percutaneous coronary intervention (PCI) (n = 1,863), or coronary artery bypass grafting (CABG) (n = 683) in Sweden from 1995 to 2013, was selected, and how many patients were excluded and for what reason at each step. STEMI = ST-segment elevation myocardial infarction.

more likely to have had previous myocardial infarctions and strokes (**Table 1**). Three-vessel disease was more common in the CABG group compared with the PCI group (84% vs. 58%). From 1995 to 1999, the predominant strategy for multivessel revascularization was CABG (62% vs. 38%). Thereafter, there was a steady decline in the proportion of CABG compared with PCI, with 2% CABG versus 98% PCI from 2010 to 2013 (**Table 1,** Online Table 3).

MORTALITY. During a mean 10.6 ± 5.1 years (22,386 person-years) of follow-up, 44.6% patients in the PCI group and 53.3% in the CABG group died (**Table 2**). The absolute risk of death was higher at 1 year (5.0% vs. 0.7%), 2 years (8.3% vs. 1.2%), and 5 years (18.6% vs. 6.4%) after revascularization in patients who underwent PCI compared with CABG (**Table 3, Central Illustration**). The rate of death per 100 person-years was higher in the PCI group than in the CABG group (6.0/100 person-years vs. 4.3/100 person-years). The risk of death after adjustment for differences between groups was similar in the PCI group compared to the CABG group (HR: 1.14; 95% CI: 0.99 to 1.32). Cause-specific mortality showed that patients who

TABLE 2 Risk of Death, MI, HF, Stroke, and Repeat Revascularization in Patient With T1D Who Underwent Multivessel PCI or CABG in Sweden From 1995-2013

Outcome	Number of Events (%)	Person-Years of Follow-Up	Event Rate/ 100 Person-Years	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Death					
CABG	364 of 683 (53.3)	8,564	4.3	Referent	Referent
PCI	831 of 1,863 (44.6)	13,823	6.0	1.86 (1.64-2.11)	1.14 (0.99-1.32)
MI					
CABG	224 of 683 (34.1)	8,315	2.7	Referent	Referent
PCI	502 of 1,863 (33.5)	11,006	4.6	1.67 (1.42-1.96)	1.47 (1.23-1.78)
HF					
CABG	251 of 683 (39.1)	7,765	3.2	Referent	Referent
PCI	561 of 1,863 (33.0)	12,257	4.6	1.41 (1.21-1.64)	1.10 (0.91-1.32)
Stroke					
CABG	127 of 683 (18.6)	9,072	1.4	Referent	Referent
PCI	237 of 1,863 (12.7)	15,489	1.5	1.00 (0.80-1.25)	1.00 (0.76-1.31)
Repeat revascularization					
CABG	166 of 683 (24.3)	8,821	1.9	Referent	Referent
PCI	1,222 of 1,863 (65.6)	6,089	20.1	5.65 (4.78-6.68)	5.64 (4.67-6.82)
Death from CHD					
CABG	190 of 683 (27.8)	9,203	2.1	Referent	Referent
PCI	430 of 1,863 (23.1)	15,020	2.9	1.63 (1.37-1.94)	1.45 (1.21-1.74)

Follow-up started at the time of revascularization for death, stroke, and death from coronary heart disease. For MI and heart failure (HF), follow-up started 31 days after revascularization, and follow-up for repeat revascularization started 8 days after revascularization.

CHD = coronary heart disease; CI = confidence interval; HR = hazard ratio; T1D = type 1 diabetes; other abbreviations as in Table 1.

underwent PCI were more likely to die from coronary heart disease than were patients who underwent CABG (HR: 1.45; 95% CI: 1.21 to 1.74) (Table 2, Figure 2A).

MYOCARDIAL INFARCTION, HEART FAILURE, STROKE, AND REPEAT REVASCULARIZATION. The absolute risks at 1 year, 2 years, and 5 years after revascularization for myocardial infarction, heart failure, stroke, and repeat revascularizations were consistently higher in patients who underwent PCI compared with those who underwent CABG, with the largest difference found for repeat revascularizations (Table 3, Figures 2B to 2E). The rate and adjusted risk of myocardial infarction in the PCI group was higher than in the CABG group (4.6/100 person-years vs. 2.7/100 person-years; adjusted HR: 1.47; 95% CI: 1.21 to 1.77) (Table 2). Similarly, the adjusted risk for and the frequency of repeat revascularization was higher in the PCI group than in the CABG group (20.1/100 person-years vs. 1.9/100 person-years; adjusted HR: 5.64; 95% CI: 4.67 to 6.82). Repeat revascularization was performed using CABG in 64% of the cases in the PCI group, compared with 1% in the CABG group. The 30-day rate of stroke was higher in the CABG group than in the PCI group (1.9% vs. 0.8%), but there was no difference in the long-term adjusted risk of stroke between the PCI and CABG groups. The adjusted risk of hospitalization for heart failure was similar in the PCI and CABG groups.

DISCUSSION

In this nationwide cohort study including all patients with T1D who underwent a first multivessel revascularization in Sweden from 1995 to 2013, we found a benefit favoring CABG over PCI, with lower rates and risks of coronary heart disease mortality, myocardial infarction, and repeat revascularization, with no such differences found for all-cause mortality, stroke, and heart failure.

Earlier studies have provided evidence of a benefit for CABG compared with PCI in terms of prognosis in patients with diabetes in need of multivessel

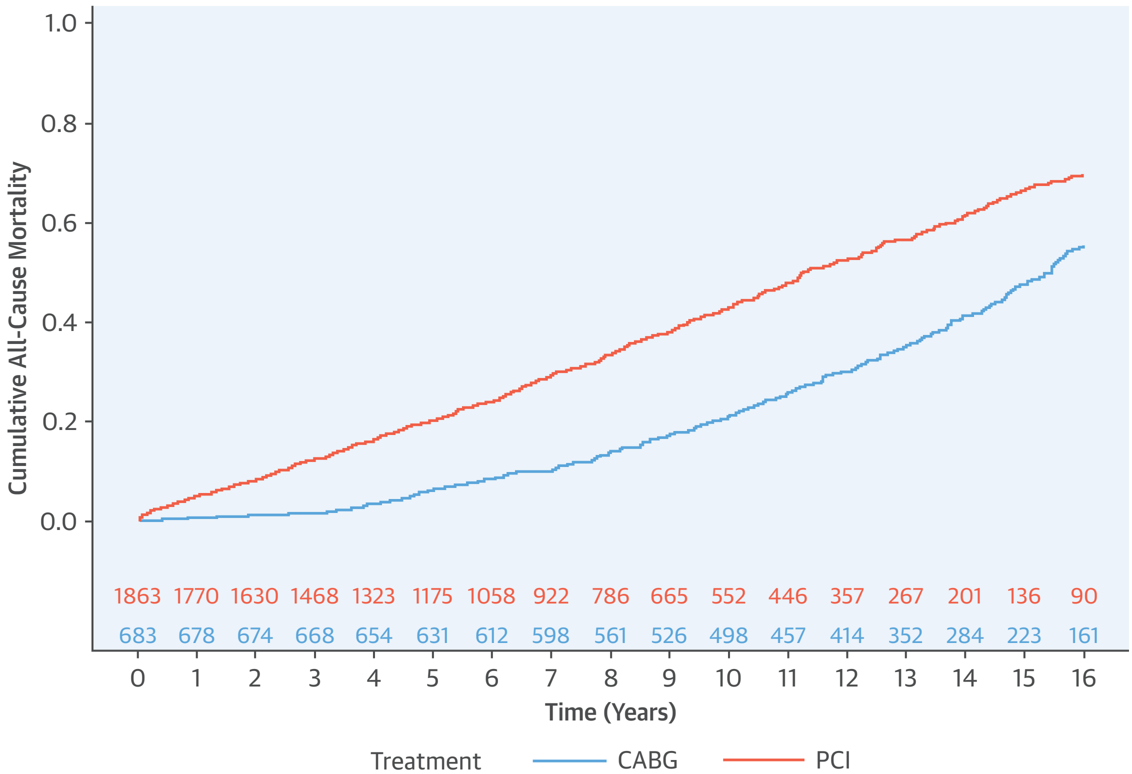
TABLE 3 Absolute Risks of Death From Any Cause, MI, HF, Stroke, Repeat Revascularization, and Death From CHD in Patients With T1D Who Underwent PCI or CABG From 1995-2013 in Sweden

	1-Yr Rate		2-Yr Rate		5-Yr Rate	
Outcome	CABG	PCI	CABG	PCI	CABG	PCI
Death	5 (0.7)	93 (5.0)	8 (1.2)	155 (8.3)	44 (6.4)	347 (18.6)
MI*	7 (1.0)	135 (7.2)	15 (2.2)	189 (10.1)	48 (7.0)	302 (16.2)
HF*	31 (4.5)	155 (8.3)	42 (6.1)	215 (11.5)	75 (11.0)	341 (18.3)
Stroke	16 (2.3)	64 (3.4)	22 (3.2)	105 (5.6)	47 (6.9)	158 (8.5)
Repeat revascularization†	20 (2.9)	673 (36)	32 (4.7)	737 (39.6)	61 (8.9)	816 (43.8)
Death from CHD	3 (0.4)	68 (3.7)	6 (0.9)	103 (5.5)	25 (3.7)	199 (10.7)

Values are number of events (%). *Follow-up started 31 days after revascularization for MI and HF failure hospitalization. †Follow-up started 8 days after the index revascularization.

Abbreviations as in Tables 1 and 2.

CENTRAL ILLUSTRATION **Revascularization in Patients With Type 1 Diabetes: All-Cause Mortality**



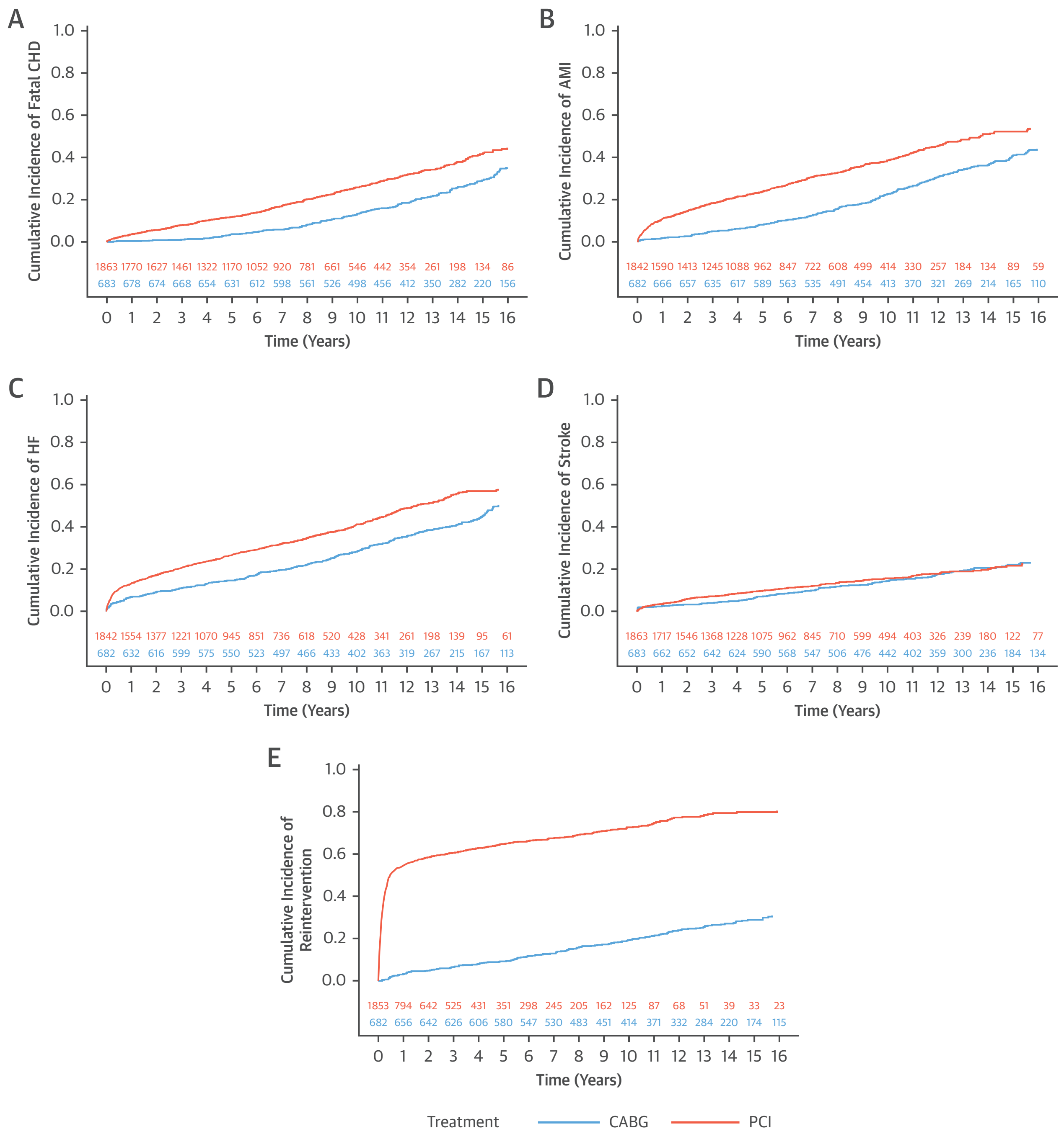
Nyström, T. et al. J Am Coll Cardiol. 2017;■(■):■–■.

This figure shows the cumulative all-cause mortality, estimated with the Kaplan-Meier method, in type 1 diabetes patients with multivessel disease who underwent revascularization by coronary artery bypass grafting (CABG) (n = 683) or percutaneous coronary intervention (PCI) (n = 1,863) from 1995 to 2013 in Sweden.

revascularization (1–3,11). The strongest evidence for using CABG over PCI as the preferred strategy for multivessel revascularization in patients with diabetes comes from the FREEDOM study (2); however, none of the previously mentioned studies reported the proportion of included T1D compared with T2D patients. Because 85% to 90% of all patients with diabetes have T2D (12), it is likely that the proportion of T1D patients included was very small. To the best of our knowledge, only 1 previous study that compared PCI with CABG for multivessel revascularization in patients with diabetes sorted patients into T1D and T2D subgroups (13). This study was prematurely stopped due to slow enrollment, comprising a total of 510 diabetes patients, of whom only 5% had T1D. Due to the small number of T1D patients involved, no interpretation could be drawn from this group. As patients with T1D have a significantly increased long-term risk of death after CABG compared with patients with T2D (6), and patients without diabetes and with T2D have a similar long-term risk of death after CABG (2,6), there is a knowledge gap regarding strategies for multivessel revascularization in patients with T1D.

In the present study, we found increased coronary heart disease mortality in the PCI group. This finding was first reported in the BARI study, which enrolled patients between 1988 and 1991 (1). Similarly, patients treated with PCI in the FREEDOM study (2), which was conducted more than 10 years after the BARI study (1), had increased all-cause mortality. Similar to the findings in our study, in the subgroup analyses of patients with diabetes in the SYNTAX study, there was a trend towards an increased all-cause mortality, and a significantly increased cardiac-specific mortality in patients who underwent PCI compared to those who underwent CABG (2). We found the largest differences in risk between

FIGURE 2 Outcomes in Relation to Revascularization Strategy



This figure shows the cumulative incidence, estimated with the Kaplan-Meier method, of **(A)** coronary heart disease (CHD) mortality, **(B)** acute myocardial infarction (AMI), **(C)** heart failure (HF), **(D)** stroke, and **(E)** repeat revascularization during follow-up in T1D patients treated with PCI or CABG. Follow-up started at the time of revascularization for death and stroke, at 31 days after the intervention for myocardial infarction and heart failure, and 8 days after the intervention for repeat revascularization. Abbreviations as in Figure 1.

CABG- and PCI-treated patients for myocardial infarction and repeat revascularization. In the FREEDOM study, a similar association was found, with more than double the rate of myocardial infarction in the PCI group 5 years after randomization (2).

The FREEDOM study, which included patients between 2005 and 2010, reported 5-year event rates similar to those in our study for all outcomes, except for a higher rate of death. This may partly be related to an older study population included in the FREEDOM study (2). In the current study, the 30-day risk of stroke was higher in the CABG group, with event rates similar to those in the FREEDOM study, but the absolute risk was small, and the difference between patients treated with PCI and those treated with CABG had disappeared after 2 years of follow-up. Furthermore, in the BARI 2D study, patients with T2D were randomized to medical treatment or revascularization in 2 groups: one where patients were treated with PCI, and the other where they were treated with CABG (14). Revascularization was not associated with reduced mortality in either group, but patients who underwent CABG had a significantly reduced risk of major cardiovascular events compared with patients who were treated only with medical therapy during follow-up. There was no difference in major cardiovascular events in patients treated with PCI compared with those treated medically.

Patients with diabetes have an accelerated atherothrombosis (15) with an early onset of atherosclerosis, suggested to be more diffuse, more extensively involved, and with more distal coronary lesions compared with patients without diabetes (16). Therefore, the target vessel for a bypass graft in patients with diabetes is often in an inferior condition compared with the target vessel from patients without diabetes. Despite this, cardiovascular complications differ between T1D and T2D, not only in that T1D presents at younger age, but also in that women are affected to the same degree and at the same age as men (7). Also, poor glycemic control before CABG is associated with increased risk of death in patients with T1D (17), an association that is not as pronounced in patients with T2D (18). Previous studies have demonstrated that both glycemic control and insulin treatment are predictors of long-term outcomes after CABG (19-21). Recently, it was demonstrated, in a substudy of the FREEDOM study, that the clinical event rate was higher in patients with diabetes treated with insulin compared to those without insulin treatment; however, no interaction was demonstrated between groups, suggesting that insulin treatment in itself is not a risk factor for the prognosis in patients with diabetes undergoing PCI or CABG (22). In the current study, patients who underwent PCI were older, were more often female, had a longer duration of diabetes, lower GFR, and were more likely to have heart failure, active cancer, end-stage renal disease, and prior stroke compared with patients who underwent CABG. After adjustment for these and a number of other differences, there was still an excess risk and rate of coronary heart disease mortality, myocardial infarction, and repeat revascularization in patients with T1D who underwent PCI compared with those who underwent CABG.

Based on data from the BARI study, the National Heart, Lung, and Blood Institute released a clinical alert in 1995 recommending CABG as the preferred method for multivessel revascularization in patients with diabetes. However, this alert had no measurable effect on the choice of revascularization method for patients with diabetes in the United States (23). Thereafter, results from both the FREEDOM and SYNTAX studies confirmed the early findings from the BARI study, leading to strong recommendations, in both Europe and the United States, to use CABG over PCI for multivessel revascularization in patients with diabetes (4,5). In the present study, more patients with T1D underwent CABG than PCI each year from 1995 to 1999. Thereafter, there was a steady decline in number of CABGs performed. From 2008 to 2013, the preferred strategy for multivessel revascularization was CABG in only 24 patients compared with PCI in 655 patients. The reason why guideline recommendations were not followed, and PCI was chosen over CABG to such a large extent in our observational study, remains elusive.

STUDY LIMITATIONS. The main limitation was the large differences in risks of outcomes during the first year of follow-up. This indicates that there was significant confounding by indication present, meaning that some patients who underwent PCI did so because they were too sick to undergo CABG. Indeed, there were major differences in patient characteristics between the 2 groups, with more patients with prior stroke, heart failure, active cancer, and end-stage renal disease, all strong predictors of early and late outcomes after cardiac revascularization, in the PCI group. Moreover, there was also most likely unmeasured confounders present that we had no information about, such as frailty, which might have been a reason to choose PCI over CABG. In addition, the vast majority of patients who underwent CABG had their procedures performed within the first few years of the study period. This may explain some of the differences in patient characteristics, between groups. However, by using inverse probability of treatment weighting based on propensity scores, we adjusted for these differences, but cannot exclude that there was residual confounding present, even after adjustment. We had no information about cardiovascular medications aimed at secondary prevention. This most likely diluted the finding of an increased risk associated with PCI treatment compared with CABG treatment because secondary prevention became more aggressive during the study period, specifically in diabetes patients. Moreover, we had no information on the types of stents used, which varied between bare-metal stents and different types of drug-eluting stents due to the long study period. However, in previous studies, the benefit of CABG over PCI in patients with diabetes has been independent of whether bare-metal stents (1), or drug-eluting stents (2,3) have been used. Another limitation was that we were not able to adjust for changes in the epidemiology of coronary heart disease, with a significantly reduced incidence of myocardial infarction and reduced long-term mortality following myocardial infarction during the study period (24). As CABG was the preferred method for multivessel revascularization during the early years of the study period, with higher risks associated with coronary heart disease, we believe that this may have, if anything, diluted our findings. The largest differences in risk were found for repeat revascularization, and myocardial infarction, which is related to the completeness of revascularization among PCI patients (25). These differences may have been attenuated if we would have been able to adjust for complete or incomplete revascularization in the PCI group (25). As our study was an observational cohort study, the results may not be completely comparable to the findings in the BARI, FREEDOM, or SYNTAX studies, where patients with diabetes were randomized to treatment with either PCI or CABG (1–3).

The main strength of our study was the size of this unique study population of T1D patients and the large number of events, with 1,195 deaths, and 726 myocardial infarctions during a mean follow-up of more than 10 years. This allowed us to report risks for each outcome separately, and with high precision in our estimates. We used high-quality national health care registers to obtain information, all of which were previously evaluated and found to have high validity (8–10). The Patient and the Cause-of-Death register used to retrieve outcomes has complete coverage of the country, and therefore we had no loss to follow-up.

CONCLUSIONS

Notwithstanding the inclusion of patients who might not have been able to undergo CABG in the PCI group, in this nationwide cohort of T1D patients with multivessel coronary artery disease, we found that CABG was associated with a lower risk of coronary heart disease mortality, myocardial infarction, and repeat revascularization compared with PCI. Even if our findings indicate that CABG should be the preferred strategy for multivessel revascularization in patients with T1D, our findings should be interpreted with some caution because of the observational nature of the study, and maybe more importantly, the large differences in risks in the first year of follow-up, indicating that there were large inherent differences in risk at baseline between the PCI and CABG groups.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE: Patients with T1D and multivessel coronary artery disease in need of revascularization benefit more from CABG compared with PCI.

TRANSLATIONAL OUTLOOK: More work is needed to improve clinical implementation of recommendations favoring surgical over percutaneous revascularization in patients with T1D as well as T2D.

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APPENDIX For expanded Methods and References sections as well as supplemental figures and tables, please see the online version of this article.