Case Fatality of Patients With Type 1 Diabetes After Myocardial Infarction

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OBJECTIVE

Type 1 diabetes is a risk factor for myocardial infarction (MI). We aimed to evaluate the case fatality in patients with type 1 diabetes after MI.

RESEARCH DESIGN AND METHODS

Consecutive patients experiencing MI with type 1 diabetes (*n* = 1,935; 41% female; mean age 62.5 years) and without diabetes (*n* = 74,671) admitted to 20 hospitals in Finland from 2005 to 2018 were studied using national registries. The outcome of interest was death within 1 year after MI. Differences between groups were balanced by multivariable adjustments and propensity score matching.

RESULTS

Case fatality was higher in patients with type 1 diabetes than in propensity score–matched controls without diabetes at 30 days (12.8% vs. 8.5%) and at 1 year (24.3% vs. 16.8%) after MI (hazard ratio 1.55; 95% CI 1.32–1.81; $P < 0.0001$). Patients with type 1 diabetes had poorer prognosis in subgroups of men and women and of those with and without ST-elevation MI, with and without revascularization, with and without atrial fibrillation, and with and without heart failure. The relative fatality risk in type 1 diabetes was highest in younger patients. Older age, heart failure, peripheral vascular disease, renal failure, and no revascularization were associated with worse prognosis after MI. The case fatality among patients with type 1 diabetes decreased during the study period, but outcome differences compared with patients without diabetes remained similar.

CONCLUSIONS

Patients with type 1 diabetes are at higher risk of death after MI than patients without diabetes. Our findings call for attention to vigorous cardiovascular disease prevention in patients with type 1 diabetes.

Cardiovascular disease (CVD) is a long-term complication of diabetes and accounts for a majority of premature deaths among this vulnerable patient population. The risk of CVD is especially high among patients with type 1 diabetes, among whom CVD events occur on average 10 to 15 years earlier than among individuals without diabetes (1). The risk of myocardial infarction (MI) and death resulting from coronary heart disease among patients with type 1 diabetes is, in addition to traditional CVD risk factors, associated with duration of diabetes, reduced glycemic control, and renal complications (2,3).

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Emerging data show that, in addition to the increased risk of MI in patients with diabetes, the risk of death following MI is higher in patients with diabetes than in individuals without diabetes (4–8). However, these data derive from cohorts of patients with diabetes without distinction of the type of diabetes or from cohorts exclusively of patients with type 2 diabetes with a lack of data regarding type 1 diabetes. In addition to longer disease duration in type 1 diabetes compared with type 2 diabetes, important differences exist in the underlying pathophysiology of CVD in the diabetes subtypes, including different risk factor profiles and more diffuse and more concentric coronary atherosclerosis in type 1 compared with type 2 diabetes (3), which may affect the prognosis of MI.

Poor glycemic control among patients with type 1 diabetes is the strongest modifiable risk factor for first and subsequent CVD events (9). Recent advances in type 1 diabetes care, including continuous glucose monitoring and more precise insulin delivery devices, have improved glucose control for many individuals with type 1 diabetes. Meticulous glycemic control reduces the risk of CVD in type 1 diabetes (10), and rates of mortality and some type 1 diabetes complications have declined in successive type 1 diabetes cohorts (11). Furthermore, the management of other CVD risk factors among patients with diabetes has been intensified. It remains unknown whether these health care advances have translated into improved prognosis of MI among patients with type 1 diabetes.

Therefore, the main aim of this study was to investigate the case fatality of MI and its temporal trends among patients with type 1 diabetes compared with individuals without diabetes between 2005 and 2018 by using nationwide registry data and propensity score matching. In addition, we explored the associations of baseline characteristics of patients with type 1 diabetes with MI case fatality.

RESEARCH DESIGN AND METHODS

Patients and Design

The data for all consecutive patients experiencing MI admitted to participating hospitals in Finland between 1 January 2005 and 31 December 2018 were retrospectively collected from the Care Register for Health Care in Finland (CRHC). All Finnish hospitals that treat patients experiencing MI and are equipped with a coronary catherization laboratory (n = 20, including five university hospitals with emergency coronary surgery available) were included. First-time MI admissions during the study period to medical (including cardiology), surgical (including cardiac surgery), and intensive care wards were included. The index MI was identified with ICD-10 code I21 as the primary discharge diagnosis. Patients treated with valvular or aortic surgery and patients lost to follow-up (0.5%) were excluded (Supplementary Fig. 1). Ward and hospital transfers after MI admission were combined as a single admission.

Patients with type 1 diabetes were identified from a combination of national registry databases. Those who fulfilled all of the following conditions were identified as patients with type 1 diabetes:

1. ICD-10 code E10 for insulin-dependent diabetes in the CRHC.
2. Entitlement to special reimbursement for antidiabetic medications.
3. Insulin purchase within 1 year prior to MI.
4. No oral antidiabetic medication purchase within 1 year prior to MI.

Of these conditions, the first and last were used to distinguish between patients with type 1 and type 2 diabetes. Of note, two patients were excluded because they used sodium glucose cotransporter-2 inhibitors and no other oral antidiabetic medications, which could theoretically have been prescribed off label for patients with type 1 diabetes during our study period.

All prescription medication purchases in Finland are collected in a national drug purchase database. Insulin and oral antidiabetics are available only with a prescription from a pharmacy, and thus, all purchases are recorded in the database. All patients in Finland with appropriately diagnosed diabetes are entitled to special reimbursement for their antidiabetic medications. A treating physician writes a medical certificate describing the rationale for the diagnosis of diabetes, and the certificate is then delivered to the Social Insurance Institution of Finland for approval of special reimbursement entitlement. Patients who experienced MI with no diabetes diagnosis in the CRHC (ICD-10 code E10, E11, E12, E13, or E14), no entitlement to special reimbursement for antidiabetic medications, and no purchases of antidiabetic medications within 1 year prior to MI served as nondiabetic controls.

The primary outcome of interest was death within 365 days after MI admission among patients with type 1 diabetes compared with patients without diabetes. Secondly, we studied the association of baseline features of patients with type 1 diabetes with case fatality after MI. Comorbidities (recognized before or during index MI admission), revascularization (during index MI admission), and index MI type were detected as previously described (12,13). Diabetic hypoglycemic coma was detected with ICD-10 code E10.0, diabetic ketoacidosis with code E10.1, diabetic retinopathy or glaucoma with code E10.3, and diabetic neuropathy with code E10.4 (recognized before or during index MI admission).

Data Sources

The CRHC registry data, including the data for all hospital admissions and major interventional procedures, prescription medication purchase data and special reimbursement entitlement data, and cancer data in the Finnish Cancer Registry, were obtained from the National Institute for Health and Welfare of Finland (permission no. THL/164/14.02.00/2021). Fatality data were obtained from Statistics Finland (TK-53-484-20). The included registries are mandated by law and cover the entire Finnish population (Supplementary Material).

Because of the study design, ethical board review and informed consent were waived, and the participants were not contacted. The legal bases for the processing of personal data were public interest and scientific research (European Union General Data Protection Regulation 2016/679, Article 6[1]I and Article 9[2][j]; Data Protection Act Sections 4 and 6).

Statistical Analysis

Differences between study groups were analyzed with t and χ^2 tests (nonmatched groups) or with paired t and McNemar tests (matched groups). The effect sizes in the baseline characteristics between groups were evaluated by standardized mean differences. Case fatality

was studied using the Kaplan-Meier method and Cox regression.

The follow-up time was 1 year and included a complete follow-up of all included studied patients. Schoenfeld residuals were used for confirmation of proportional hazards assumptions. Covariable adjustment was performed with multivariable regression and with propensity score matching. Propensity score, including age, sex, alcohol abuse, atrial fibrillation, cerebrovascular disease, chronic pulmonary disease, dementia, heart failure, hypertension, liver disease, malignancy, paralysis, peripheral vascular disease, prior coronary artery bypass grafting surgery (CABG), prior MI, psychotic disorder, rheumatic disease, renal failure, valvular disease, revascularization by percutaneous coronary intervention (PCI) or CABG, ST elevation, year of MI (categorized as 2005–2009, 2010–2014, or 2015–2018), and treating hospital (university vs. nonuniversity), was created with logistic regression. Variables were selected based on previous knowledge and clinical judgment. Patients with type 1 diabetes were matched 1:1 with controls without any type of diabetes using the optimal matching method without replacement with a caliper set at 0.2 times the SD of the estimated propensity score. Hospital surviving patients with type 1 diabetes were further matched with hospital surviving controls (Supplementary Material). Sensitivity analyses were performed using 1:1 nearest neighbor matching that included all patients with type 1 diabetes (Supplementary Material). Multivariable regression models included the same variables used for propensity score.

The *E* value for estimating unmeasured confounding was calculated as previously described (14). Subgroup analyses were performed for men and women, patients age <60 years, 60–79 years, and ≥80 years, patients with and without ST-elevation MI (STEMI), patients with and without atrial fibrillation, patients with and without heart failure, patients with and without revascularization, and patients experiencing MI in 2005 to 2009, 2010 to 2014, and 2015 to 2018, with interaction analyses in univariable and multivariable models. The results are given as mean, median, percentage, hazard ratio (HR) with 95% CI, interquartile range (IQR), or ± SD. Statistical significance was defined as a P value <0.05. Analyses were performed with SAS software (version 9.4; SAS Institute, Inc., Cary, NC).

RESULTS

Our study population included 1,935 patients with type 1 diabetes and 74,671 patients without diabetes. Patients with type 1 diabetes tended to be younger, were more often women, and had a higher frequency of alcohol abuse, cerebrovascular and peripheral vascular disease, heart failure, hypertension, liver disease, prior CABG, prior MI, and renal failure than patients without diabetes who experienced MI in the nonadjusted cohort (Table 1). MI presented without ST elevation more often in patients with type 1 diabetes. Patients with type 1 diabetes less frequently underwent revascularization by PCI but had CABG more often compared with patients without diabetes (Table 1). Propensity score matching resulted in 1,787 pairs of patients with type 1 diabetes and without diabetes but with comparable baseline features (Table 1). The duration of hospital stay after MI was longer in patients with type 1 diabetes (median 7 days; IQR 4–14 days; range 0–718 days) than in the matched controls (median 5 days; IQR 3–10 days; range 0–295 days; $P < 0.0001$).

During the 1-year follow-up after MI, 12,647 patients died (486 in the type 1 diabetes group). Nonadjusted in-hospital case fatality was 13.2% in the type 1 diabetes group versus 9.7% in the group without diabetes ($P < 0.0001$), and 30-day case fatality was 12.7% versus 9.5%, respectively ($P < 0.0001$). Thirty-day case fatality was 12.8% in the matched type 1 diabetes group and 8.5% in the matched control group ($P < 0.0001$). At 1-year follow-up, the nonadjusted case fatality was 25.1% in patients with type 1 diabetes versus 16.3% in patients without diabetes (HR 1.60; 95% CI 1.47–1.75; $P < 0.0001$) (Fig. 1). Multivariable adjusted HR for death at 1 year after MI among patients with type 1 diabetes compared with patients without diabetes was 2.06 (95% CI 1.86–2.28; $P < 0.0001$). The 1-year case fatality in the matched cohort was 24.3% in the type 1 diabetes group versus 16.8% in the matched control group (HR 1.55; 95% CI 1.32–1.81; $P < 0.0001$) (Fig. 1). The *E* value for 1-year case fatality in the matched cohort was 2.5 (95% CI 2.0–3.0). Results of nearest neighbor–matched cohort were equal (Supplementary Material). In matched hospital surviving patients, the 1-year case fatality was 12.8% in the type 1 diabetes group versus 8.8% in the control group (HR 1.49; 95% CI 1.19–1.87; $P = 0.001$).

Increasing age, baseline alcohol abuse, heart failure, liver disease, peripheral vascular disease, renal failure, and presence of ST elevation were associated with 1-year case fatality in multivariable analysis of patients with type 1 diabetes (Table 2). Revascularization was associated with a significantly better prognosis. The 1-year outcome of patients with type 1 diabetes improved significantly over the study period in absolute terms (case fatality 28.5% in 2005–2009, 24.8% in 2010–2014, and 22.7% in 2015–2018) and after adjusting for covariates (Table 2).

Patients with type 1 diabetes had a poorer adjusted prognosis after MI than controls in subgroups of men and women, patients with and without STEMI, patients with and without atrial fibrillation, patients with and without heart failure, and patients with and without revascularization (Table 3). Excess relative case fatality risk in patients with type 1 diabetes was attenuated by increasing age (Table 3). HR for 1-year death in patients with type 1 diabetes versus patients without diabetes after MI did not change during the study period (Table 3).

CONCLUSIONS

In this nationwide registry study between 2005 and 2018, we showed that case fatality after MI is 1.6-fold among patients with type 1 diabetes compared with patients without diabetes but with otherwise similar baseline features. A plethora of partly outdated population- and hospital-based data has shown that patients with type 2 diabetes or an unspecified type of diabetes have worse short- and long-term prognoses after MI than those without diabetes (4–8). However, these results cannot be readily extrapolated to individuals with type 1 diabetes; therefore, our study provides new insight into the deleterious effect of type 1 diabetes on the short-term prognosis of MI. Our findings were consistent in various subgroups, including men and women, patients with and without STEMI,

Table 1—Baseline features of MI patients with type 1 diabetes and patients without diabetes

	All patients				Matched patients			
Variable	Type 1 diabetes (*n* = 1,935)	No diabetes (*n* = 74,671)	*P*	|SMD|	Type 1 diabetes (*n* = 1,787)	No diabetes (*n* = 1,787)	*P*	|SMD|
Age (SD), years	62.5 (12.6)	70.3 (13.2)	<0.0001	0.602	63.2 (12.6)	63.6 (14.0)	0.241	0.030
Women, %	40.6	36.4	0.0001	0.087	40.2	40.0	0.902	0.003
Comorbidities, %								
Alcohol abuse	5.0	3.2	<0.0001	0.091	4.9	5.3	0.641	0.015
Atrial fibrillation	12.1	15.0	0.0004	0.085	12.4	12.4	1.000	<0.001
Cerebrovascular disease	19.5	11.2	<0.0001	0.231	18.2	18.5	0.816	0.007
Chronic pulmonary disease	12.4	13.1	0.350	0.022	12.8	12.2	0.581	0.017
Dementia	4.1	6.0	0.0004	0.088	4.4	4.3	0.933	0.003
Heart failure	37.3	19.6	<0.0001	0.398	34.6	35.2	0.638	0.013
Diabetic retinopathy or glaucoma	40.9	—	—	—	38.6	—	—	—
Diabetic hypoglycemic coma	11.8	—	—	—	11.3	—	—	—
Diabetic neuropathy	10.8	—	—	—	10.6		—	—
Diabetic ketoacidosis	8.4	—	—	—	7.7		—	—
Hypertension	73.8	45.2	<0.0001	0.609	71.8	70.1	0.109	0.037
Liver disease	3.3	1.0	<0.0001	0.161	2.8	2.9	0.842	0.007
Malignancy	11.5	13.0	0.050	0.046	11.7	12.8	0.250	0.034
Paralysis	1.0	0.4	<0.0001	0.070	1.0	0.8	0.590	0.018
Peripheral vascular disease	29.9	6.4	<0.0001	0.642	25.6	25.8	0.893	0.004
Prior CABG	7.8	2.7	<0.0001	0.232	6.5	7.6	0.197	0.042
Prior MI	22.2	13.3	<0.0001	0.235	20.3	20.5	0.857	0.006
Psychotic disorder	3.4	3.1	0.403	0.019	3.5	3.5	1.000	<0.001
Rheumatic disease	7.1	6.5	0.336	0.022	7.0	8.0	0.245	0.038
Renal failure	27.0	2.6	<0.0001	0.733	21.3	21.6	0.773	0.007
Valvular disease	5.9	5.8	0.812	0.005	6.0	5.2	0.289	0.034
Revascularization, %	54.0	57.4	0.003	0.068	55.2	55.6	0.763	0.008
PCI	43.9	51.2	<0.0001	0.154	45.0	45.2	0.863	0.004
CABG	11.1	6.4	<0.0001	0.163	11.1	11.3	0.852	0.005
STEMI, %	30.4	39.4	<0.0001	0.189	31.5	32.3	0.494	0.018
Anterior MI*	52.7	50.0	0.110	0.054	51.7	49.9	0.356	0.039
University hospital, %	53.9	49.7	0.0002	0.085	53.6	55.3	0.185	0.036
Year of MI			<0.0001	0.172			0.988	0.026

Features of all patients and propensity score–matched patients. SMD, standardized mean difference. *Among patients with STEMI.

patients with and without revascularization, and patients with and without heart failure. The relative risk of case fatality was especially high in patients age <60 years.

Acute treatment of MI, revascularization, and secondary CVD prevention strategies have been developed and enhanced during the last few decades, resulting in improved MI outcomes in the general population. Furthermore, more aggressive treatment of type 1 diabetes itself, including the adoption of intensive insulin therapy and increased use of glucose-monitoring systems, as well as improved management of CVD risk factors, has affected the development of atherosclerosis and resulted in reductions in all-cause and CVD mortality among type 1 diabetes populations over time (11,15,16). According to a Swedish nationwide registry study from 1998 to 2014, although the rate of CVD outcomes remained significantly higher among patients with type 1 diabetes compared with controls during the study period, the risk of nonfatal CVD outcomes was reduced to a greater extent among patients with type 1 diabetes compared with those without type 1 diabetes (16). Therefore, it may be asked whether the abovementioned improvements in care have translated into a reduction in the survival gap after MI between patients with type 1 diabetes and controls. We assessed recent trends in the case fatality of MI and found that, although MI case fatality among patients with type 1 diabetes declined between 2005 and 2018, the multivariable-adjusted HR for 1-year death after MI compared with that among controls remained similar (∼2) during the study period.

Similar findings of little or no secular improvement in survival disadvantage of patients with diabetes in somewhat earlier MI cohorts from Finland, Sweden, Australia, and the Netherlands have been reported in patients with unspecified diabetes and type 2 diabetes (17–21) but not in those with type 1 diabetes. An earlier Finnish registry study from 1988 to 2002 concluded that, although case fatality rates after first acute coronary syndrome improved similarly in patients with type 2 diabetes and controls, twice as high case fatality rates during the first year after MI persisted in those with type 2 diabetes compared with those without diabetes (20).

Lack of improvement in the survival disparity over time between patients with and without diabetes who experience MI also seems to extend to long-

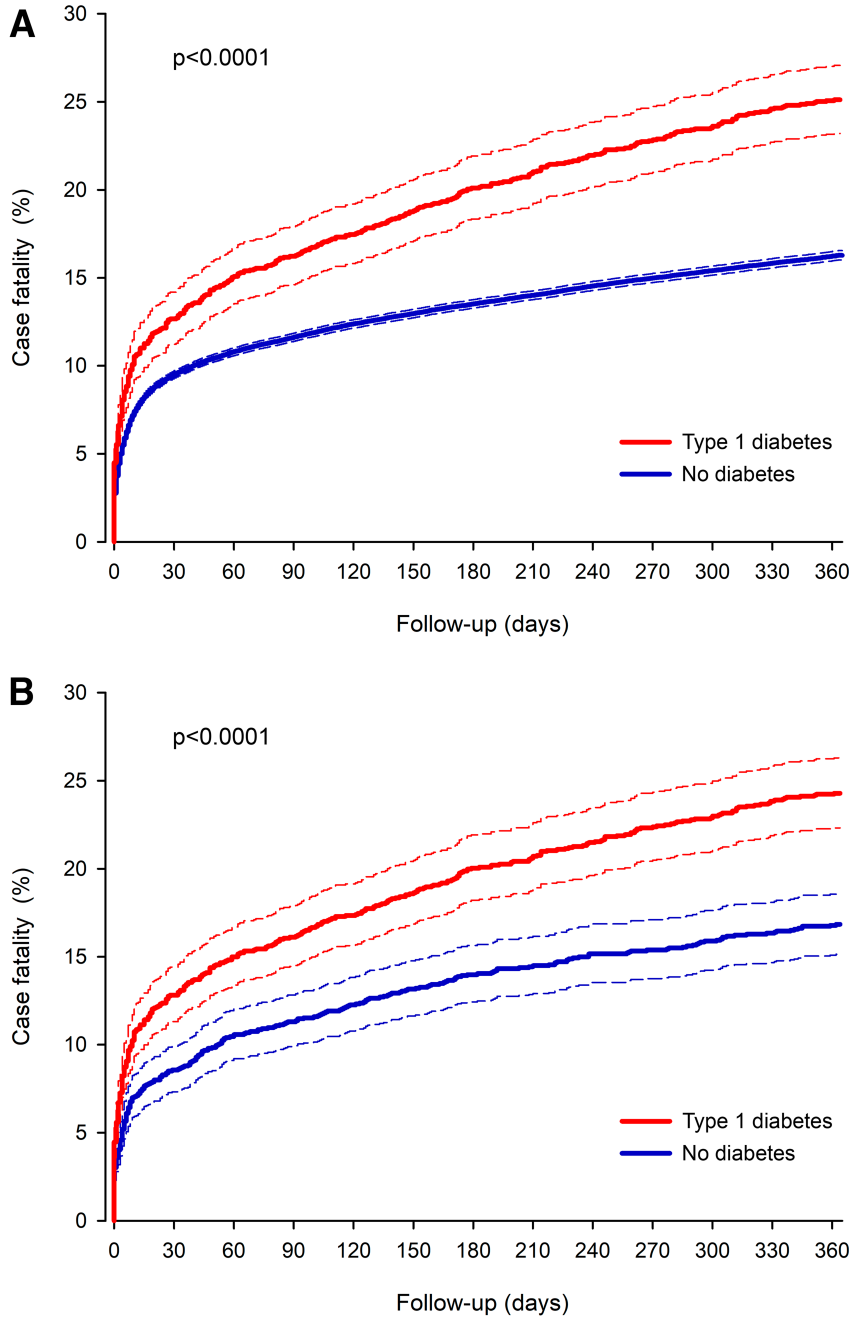

Figure 1—Case fatality in patients with type 1 diabetes and patients without diabetes after MI in all nonadjusted (*A*) and propensity score–matched (*B*) cohorts. Dashed lines represent 95% CIs.

term mortality after MI. The Northern Sweden MONICA study, involving 6,776 patients, showed that the difference in mortality in patients with and without diabetes after first MI did not change between 1989 and 2006 (median follow-up 6.8 years), with an age-adjusted HR for mortality of 1.56 (95% CI 1.39–1.79) for men with diabetes compared with those without diabetes and 1.97 (95% CI 1.62–2.39) for women with diabetes compared with women without diabetes (18).

The risks of all-cause mortality and CVD mortality in type 1 diabetes may be up to three- to fivefold compared with the general population (22), with up to a 30-fold increased risk of serious CVD outcomes in young patients with early-onset type 1 diabetes (23). Relative to this background, our observed HRs for 1-year mortality after MI in type 1 diabetes may seem modest (multivariable-adjusted HR 2.06; 95% CI 1.86–2.28 and propensity score–matched cohorts HR 1.55; 95% CI 1.32–1.81). However, these relative risk estimates are comparable to or slightly higher than those reported in previous studies that assessed mortality after MI in unspecified diabetes or type 2 diabetes cohorts (mortality risk elevated by a factor of 1.3 to 2) (6,8,18–20). It should be noted that the patients with type 1 diabetes experiencing MI and their controls were older (mean age 64 years) in our analyses than in several other type 1 diabetes mortality studies and had a high prevalence of comorbidities that may have affected the outcome of MI (heart failure in 36% and cerebrovascular disease, prior MI, and renal failure in almost 20%). These factors may explain why the relative impact of type 1 diabetes on survival may be of less significance among patients experiencing MI compared with unspecified type 1 diabetes cohorts.

The natural history and pathophysiology of MI may differ between patients with type 1 diabetes compared with patients with type 2 diabetes or without diabetes (3) and contribute to the observed higher MI case fatality among those with type 1 diabetes. Coronary atherosclerosis in type 1 diabetes may be more severe and extensive and of the distal type compared with in patients without diabetes (24). Factors such as diabetic cardiomyopathy and hypoglycemia may also expose patients with type 1 diabetes to worse outcomes compared with patients without diabetes (25,26). Some researchers have suggested that a post-MI autoimmune syndrome, characterized by cardiac autoantibodies and myocardial inflammation, could explain worse MI outcomes in type 1 diabetes (27). Despite these differences, traditional CVD risk factors are key determinants of CVD outcomes in both the general population and in those with type 1 diabetes; the strongest predictors of CVD and death among patients with type 1 diabetes include age, renal function, duration of type 1 diabetes, glycemic control as measured by HbA_{1c}, LDL cholesterol, and systolic blood pressure, with the latter three having almost linear associations with CVD outcome (28).

Treatment differences have been suggested to contribute to the observed survival gap between patients with diabetes and controls after MI (19,29). In the 1990s, patients with diabetes experiencing MI may have received less active

Table 2—Associations of baseline features with 1-year case fatality after MI in patients with type 1 diabetes

Variable	Univariable		Multivariable	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Age, years		<0.0001		<0.0001
<60	Reference		Reference	
60–79	2.42 (1.95–3.01)	<0.0001	2.25 (1.78–2.84)	<0.0001
≥80	4.13 (3.09–5.53)	<0.0001	3.62 (2.59–5.05)	<0.0001
Women	0.90 (0.75–1.08)	0.271	0.91 (0.74–1.10)	0.325
Comorbidities				
Alcohol abuse	1.52 (1.08–2.13)	0.017	1.50 (1.04–2.17)	0.030
Atrial fibrillation	1.82 (1.46–2.27)	<0.0001	1.10 (0.87–1.40)	0.435
Cerebrovascular disease	1.67 (1.37–2.04)	<0.0001	1.16 (0.94–1.43)	0.158
Chronic pulmonary disease	1.53 (1.22–1.93)	0.0003	1.25 (0.98–1.60)	0.073
Diabetic retinopathy or glaucoma	0.76 (0.63–0.92)	0.003	0.95 (0.77–1.17)	0.625
Diabetic hypoglycemic coma	1.16 (0.90–1.50)	0.256	1.18 (0.91–1.86)	0.069
Diabetic neuropathy	1.00 (0.75–1.33)	0.988	1.11 (0.82–1.49)	0.495
Diabetic ketoacidosis	1.07 (0.78–1.46)	0.688	1.35 (0.98–1.86)	0.069
Dementia	2.09 (1.46–2.98)	<0.0001	1.33 (0.91–1.93)	0.140
Heart failure	2.55 (2.13–3.05)	<0.0001	1.76 (1.44–2.16)	<0.0001
Hypertension	1.60 (1.27–2.01)	<0.0001	1.05 (0.82–1.36)	0.684
Liver disease	2.39 (1.68–3.41)	<0.0001	2.10 (1.47–2.99)	<0.0001
Malignancy	1.38 (1.08–1.78)	0.011	0.99 (0.76–1.29)	0.924
Paralysis	1.01 (0.44–2.34)	0.982	1.19 (0.51–2.77)	0.684
Peripheral vascular disease	1.99 (1.67–2.38)	<0.0001	1.53 (1.25–1.86)	<0.0001
Prior CABG	0.95 (0.68–1.32)	0.754	0.70 (0.50–0.98)	0.040
Prior MI	1.52 (1.25–1.85)	<0.0001	1.11 (0.90–1.36)	0.344
Psychotic disorder	0.80 (0.45–1.42)	0.441	0.74 (0.39–1.41)	0.361
Rheumatic disease	1.30 (0.96–1.77)	0.092	1.15 (0.83–1.58)	0.406
Renal failure	2.06 (1.72–2.46)	<0.0001	1.70 (1.38–2.08)	<0.0001
Valvular disease	1.55 (1.14–2.12)	0.006	1.06 (0.77–1.46)	0.712
Revascularization	0.39 (0.32–0.47)	<0.0001	0.59 (0.48–0.73)	<0.0001
PCI	0.42 (0.35–0.52)	<0.0001	0.57 (0.45–0.70)	<0.0001
CABG	0.65 (0.47–0.91)	0.012	0.78 (0.55–1.11)	0.172
STEMI	0.99 (0.82–1.21)	0.932	1.80 (1.46–2.22)	<0.0001
University hospital	0.65 (0.54–0.78)	<0.0001	0.69 (0.57–0.84)	0.0001
Year of MI		0.048		0.003
2005–2009	Reference		Reference	
2010–2014	0.85 (0.68–1.05)	0.127	0.77 (0.62–0.96)	0.021
2015–2018	0.76 (0.61–0.95)	0.015	0.66 (0.52–0.84)	0.001

evidence-based treatment, including lipid-lowering therapy, reperfusion therapy, and revascularization, than patients without diabetes, which may partly explain the excess mortality after MI among patients with diabetes during earlier decades (29,30). However, this gap in quality of MI care seems to have closed during the 2000s (30). Nonetheless, patients with diabetes have longer prehospital delays during MI than patients without diabetes (31), which contributes to worse prognosis. Optimal revascularization strategy differs between patients with type 1 diabetes and patients without diabetes. Because of the more favorable outcomes in patients with diabetes in need of multivessel revascularization, CABG is preferred over PCI. Specifically, observational data on patients with type 1 diabetes support this finding (32).

In our multivariable-adjusted analysis, the excess case fatality among patients with type 1 diabetes persisted in both the revascularization and nonrevascularization subgroups. When comparing patients with type 1 diabetes and the matched controls, propensity score matching balanced differences in revascularization strategy between study groups (45% underwent PCI and 11% CABG). Therefore, our findings are not explained by differences in revascularization rates. As expected, among the type 1 diabetes cohort, revascularization with either PCI or CABG was associated with improved survival compared with no revascularization.

Outcomes after PCI (not necessarily in the context of MI) have been studied extensively in type 2 diabetes and have been shown to be impaired in patients with type 2 diabetes compared with individuals without diabetes in a meta-analysis of both randomized controlled trials and observational studies (33). Moreover, insulin-treated compared with non–insulin-treated patients with type 2 diabetes tend to fare worse with regard to both short- and long-term outcomes after PCI (34), as well as in the settings of STEMI and primary PCI (35). According to a recent U.S.-based observational study from 2015 to 2018, patients with type 1

Table 3—HRs for 1-year case fatality after MI in patients with type 1 diabetes versus patients without diabetes by subgroups

	Univariable		Multivariable	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Sex		<0.0001*		0.966*
Male	2.02 (1.80–2.26)	<0.0001	2.07 (1.82–2.35)	<0.0001
Female	1.15 (0.99–1.32)	0.064	2.06 (1.76–2.41)	<0.0001
Age, years		<0.0001*		<0.0001*
<60	5.60 (4.55–6.90)	<0.0001	3.50 (2.83–4.33)	<0.0001
60–79	3.14 (2.79–3.52)	<0.0001	2.20 (1.95–2.49)	<0.0001
≥80	1.33 (1.07–1.65)	0.011	1.23 (0.98–1.54)	0.071
STEMI		0.009*		0.007*
Yes	1.89 (1.60–2.24)	<0.0001	2.56 (2.13–3.09)	<0.0001
No	1.45 (1.31–1.62)	<0.0001	1.90 (1.69–2.14)	<0.0001
Atrial fibrillation		0.009*		0.126*
Yes	1.31 (1.07–1.59)	0.008	1.79 (1.45–2.20)	<0.0001
No	1.76 (1.59–1.94)	<0.0001	2.14 (1.91–2.40)	<0.0001
Heart failure		<0.0001*		0.090*
Yes	1.01 (0.90–1.13)	0.892	1.92 (1.69–2.19)	<0.0001
No	1.59 (1.39–1.83)	<0.0001	2.28 (1.96–2.66)	<0.0001
Revascularization		<0.0001*		<0.0001*
Yes	2.80 (2.40–3.27)	<0.0001	3.35 (2.87–3.91)	<0.0001
No	1.22 (1.09–1.36)	0.001	1.72 (1.52–1.93)	<0.0001
Year of MI		0.298*		0.967*
2005–2009	1.53 (1.30–1.79)	<0.0001	2.09 (1.76–2.48)	<0.0001
2010–2014	1.63 (1.41–1.89)	<0.0001	2.06 (1.75–2.41)	<0.0001
2015–2018	1.83 (1.56–2.15)	<0.0001	2.05 (1.71–2.45)	<0.0001

*Interaction *P* value.

diabetes were at particularly high risk for adverse in-hospital outcomes after PCI compared with patients with type 2 diabetes and individuals without diabetes (36). In addition to revascularization status, higher age, presence of ST elevation, and many prior comorbidities (e.g., liver or renal disease, peripheral vascular disease, alcohol abuse, and heart failure) were predictors of higher case fatality after MI in the type 1 diabetes cohort of our study. These findings are congruent with previous reports of patients experiencing MI with or without diabetes (37).

In our study, the disparity in survival after MI between patients with type 1 diabetes and controls was similar in both sexes. Furthermore, perhaps because of lack of power, we found no association between sex and MI case fatality in type 1 diabetes. In the general population, female sex has been associated with higher early mortality rates after MI (38), although this association may be negated or even reversed with more comprehensive adjustments and when assessing long-term prognosis of MI (12,13). In addition, some but not all reports in diabetes of unspecified type or type 2 diabetes have disclosed higher relative risks of death after MI in women compared with men with diabetes (6,18,20).

Although we were not able to assess the effect of glycemic control on case fatality after MI, it may be hypothesized that such an association exists. Poor glycemic control in type 1 diabetes is associated with higher CVD mortality and risk of CVD events (2,22). A Swedish nationwide cohort study of patients with type 1 diabetes with manifest severe coronary heart disease who underwent primary isolated nonemergency CABG between 1997 and 2012 showed that, during a median follow-up of 4.7 years, the HR for death or major adverse cardiovascular event for a 1% increase in HbA_{1c} was 1.18 (95% CI 1.06–1.32) (39). Another hospital-based study from the U.S. including >3,000 patients with diabetes undergoing PCI showed that higher HbA_{1c} was associated with greater long-term mortality, but this study did not distinguish between type 1 and type 2 diabetes (40). In our study, a history of ketoacidosis as well as diabetic hypoglycemic coma seemed to be linked to higher case fatality after MI, but these associations did not reach statistical significance. Furthermore, the presence of diabetic retinopathy or neuropathy, which may reflect poor diabetes control, was not associated with MI case fatality.

Strengths of the current study include the population-based/nationwide design with nearly all patients with MI in Finland included during a 14-year period as well as the use of propensity score–matched controls, comprehensively accounting for factors that may have influenced mortality rates. We lacked data on some relevant risk factors, such as coronary angiography findings, laboratory and blood pressure measurements, BMI, and smoking. Because our study was observational, residual confounding could not be excluded, but based on the analysis of *E* value (14), unmeasured confounders would have had to have a minimum strength of association of 2.5 on the risk ratio scale with both the exposure and the outcome to explain away our main finding. Our case identification of patients with type 1 diabetes relied on four complementary requirements: purchases of

insulin but not of oral antidiabetic medications during the year preceding the index MI, ICD-10 code E10 for insulin-dependent diabetes in CRHC, and entitlement to special reimbursement for antidiabetic medications. Nevertheless, we had no information on islet autoantibodies or C-peptide levels, and because of the uncertainty in diagnosis or erroneous recording of ICD-10 codes, it is possible that individual patients with type 2 diabetes treated solely with insulin were included, but this is unlikely to have influenced the study results.

In conclusion, despite treatment advances, 1-year case fatality after MI among patients with type 1 diabetes remains markedly increased compared with individuals without diabetes. Although we observed a decrease in case fatality rates among patients with type 1 diabetes over time, the relative risk of 1-year mortality remained roughly double among successive type 1 diabetes cohorts compared with individuals without diabetes between 2005 and 2018. Our results underscore the need for vigorous acute treatment of MI as well as for effective CVD prevention strategies, including optimal glycemic control, for both men and women with type 1 diabetes.

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