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Prevalence of diabetes before and after first diagnosis of coronary artery disease

ORIGINAL ARTICLE

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BACKGROUND

Diabetes is associated with coronary artery disease, and cardiovascular disease is the main cause of death in persons with the disease. In this study we have investigated the prevalence of known and undiagnosed diabetes in patients with initial myocardial

infarction, percutaneous coronary intervention or coronary artery bypass graft as well as the incidence of subsequent cardiovascular events for a period of up to five years afterwards.

MATERIAL AND METHOD

All patients < 80 years of age with no previously known coronary artery disease who were hospitalised at Sørlandet Hospital Arendal in connection with initial myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft in the period 2007–16 were added consecutively to the study and followed for up to five years (median follow-up time three years).

RESULTS

Of the 1 259 patients included, 178 (14 %) had known diabetes at the time of hospitalisation and 49 (4 %) had undiagnosed diabetes. A further 102 patients (8 %) developed diabetes during the follow-up period. Approximately half of those with diabetes had an HbA_{1c} value of ≤ 7 %. The risk of subsequent cardiovascular events developing was higher in patients with diabetes than in patients without diabetes (age- and gender-adjusted hazard ratio 1.5; 95 % confidence interval: 1.1–2.1, p = 0.005).

INTERPRETATION

The study shows a high prevalence of diabetes in patients with a first diagnosis of coronary artery disease and a high risk of subsequent cardiovascular events in patients with diabetes. Regular monitoring for the development of diabetes and good prophylactic treatment of patients with diabetes and coronary artery disease are essential.

MAIN MESSAGE

Every fifth patient with a first diagnosis of coronary artery disease had diabetes

Almost half of the patients with diabetes and coronary artery disease did *not* achieve their treatment goal for blood glucose level during the follow-up period

Patients with a first diagnosis of coronary artery disease and diabetes had a greater risk of subsequent cardiovascular events than non-diabetic patients

The prevalence of diabetes in Norway is estimated at 4.7 % (1). It is thought that more than 60 % of all patients with type 2 diabetes will develop cardiovascular disease, and this is the main cause of death in persons with diabetes (2–5). In 2013, a known diabetes diagnosis was recorded in as many as 19 % of all myocardial infarctions in Norway (6).

Type 2 diabetes may be asymptomatic in adults, and in around half of the cases the disease is undiagnosed (7). Persons with diabetes or reduced glucose tolerance may therefore go untreated for several years, entailing a significant risk of developing complications.

Undiagnosed diabetes and reduced glucose tolerance are both important risk factors for the development of coronary artery disease (8, 9). Early diagnosis and proper blood glucose treatment is assumed to affect the risk of developing this disease, although it is not established with certainty that this affects the cardiovascular prognosis (2).

In this study we have investigated the prevalence of known and undiagnosed diabetes, the intensity of blood glucose level treatment and the development of cardiovascular events within five years in patients < 80 years of age with no previously known coronary artery disease, hospitalised at Sørlandet Hospital Arendal for acute myocardial infarction (AMI), percutaneous coronary intervention (PCI) or following coronary artery bypass graft (CABG) in the period 2007–16.

Material and method

Patients < 80 years with no previously known coronary artery disease, hospitalised at Sørlandet Hospital Arendal in connection with acute myocardial infarction or percutaneous coronary intervention/coronary artery bypass graft and followed up by the hospital's preventive cardiac outpatient clinic in the period 2007–16 were added consecutively to the study. They were followed for up to five years after the index event (until death, completion of the study on 6 June 2017 or the point at which follow-up ceased).

During this period, the hospital's preventive cardiac outpatient clinic was organised as a programme run by nurses and offering individual patient consultations. At each consultation, height, weight and blood pressure were measured, smoking and dietary habits were recorded and various blood values checked (including HbA_{1c} value, fasting blood sugar, LDL cholesterol level and creatinine level).

The treatment consisted of a lifestyle intervention (dietary advice, smoking cessation follow-up and provision of organised training) and drug therapy for hypertension, hyperlipidaemia and diabetes according to applicable guidelines. A cardiologist was available for consultation as needed. All the patients were offered follow-up at the outpatient clinic 2–3 weeks after an acute myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft, after which they were generally offered annual follow-up.

Sørlandet Hospital Arendal is the regional centre for invasive cardiology, covering Vest-Agder, Aust-Agder and Telemark counties. Patients from Vest-Agder and Telemark counties were offered follow-up at their own local hospitals and were not included in this study.

All the patients were registered in a local electronic study register. The register contained information on sex, age, previous diseases, the coronary event that resulted in inclusion, treatment, various biochemical values including HbA_{1c} value, and any subsequent cardiovascular events (death, acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft and cerebral insult). An index myocardial infarction was classed as a separate category, but percutaneous coronary intervention and hospitalisation following coronary artery bypass graft were registered in one combined category. All registered data were quality assured for logical errors, including checking abnormally low or abnormally high values against the patient records.

In accordance with the Directorate of Health's recommendation of 2016 in the *Nasjonal faglig retningslinje for diabetes* [National clinical guidelines for diabetes] (10), we have used an HbA_{1c} value ≥ 6.5 % as the primary diagnostic criterion for diabetes in this study. Values over the diagnostic threshold were confirmed by a further test before the diabetes diagnosis was made. The guidelines recommend an HbA_{1c} value of around 7.0 % as the treatment goal for most patients with diabetes, but there is also room for individual adaptation.

Continuous variables are presented as means with standard deviations or medians (lower, upper quartile). The total incidence of subsequent cardiovascular events is presented using Kaplan-Meier curves. Differences between the groups were analysed with the aid of Cox regression analysis and are presented as age- and sex-adjusted hazard ratios (HR) with a 95 % confidence interval (CI). A p-value < 0.05 was regarded as statistically significant. Data were analysed using the Stata statistics program (version 14).

The study was approved by the Regional Committee for Medical and Health Research Ethics and all the patients gave written consent to participation in the study.

Results

PREVALENCE OF DIABETES

In the period 2007–16, altogether 2 050 patients < 80 years of age from the local hospital district of Sørlandet Hospital Arendal were offered follow-up and treatment at the preventive cardiac outpatient clinic following hospitalisation in connection with initial acute myocardial infarction, percutaneous coronary intervention or after coronary artery bypass graft.

A total of 1 259 patients (61 %) availed themselves of this service. Of these, 178 (14 %) had known diabetes and 49 (4 %) undiagnosed diabetes at the time of hospitalisation. Table 1 shows the patients' clinical characteristics when hospitalised. The percentage that developed diabetes at different points during the follow-up period is presented in Figure 1. In the course of the entire follow-up period, we registered a total of 329 patients (26 %) with diabetes.

Table 1

Clinical characteristics of patients without diabetes, with known diabetes and with undiagnosed diabetes at time of first myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft. Sørlandet Hospital Arendal 2007–16

	Patients without diabetes		**Patients with known diabetes**		**Patients with undiagnosed diabetes**	
	n = 1 032		**n = 178**		**n = 49**	
Average age (years) (± SD)	62	10	63	9	61	10
Women	248	24 %	49	28 %	10	20 %
Cardiovascular index event						
Myocardial infarction	588	57 %	64	36 %	21	43 %
Percutaneous coronary intervention/ coronary artery bypass graft[1]	444	43 %	114	64 %	28	57 %
Median body mass index (kg/m^2) (lower, upper quartile)	27	(25, 30)	29	(26, 33)	29	(26, 34)
Fasting plasma glucose (mmol/l) (lower, upper quartile)	5.8	(5.3, 6.4)	8.0	(6.5, 9.9)	6.7	(6.2, 8.0)
HbA_{1c} (%) (lower, upper quartile)	5.7	(5.5, 5.9)	7.2	(6.5, 8.2)	6.8	(6.6, 7.0)
Statin treatment	348	34 %	97	54 %	23	47 %
Daily smoking	298	29 %	40	22 %	19	39 %
Hypertension treatment	419	41 %	112	63 %	19	39 %

[1]Percutaneous coronary intervention/coronary artery bypass graft were registered as one category

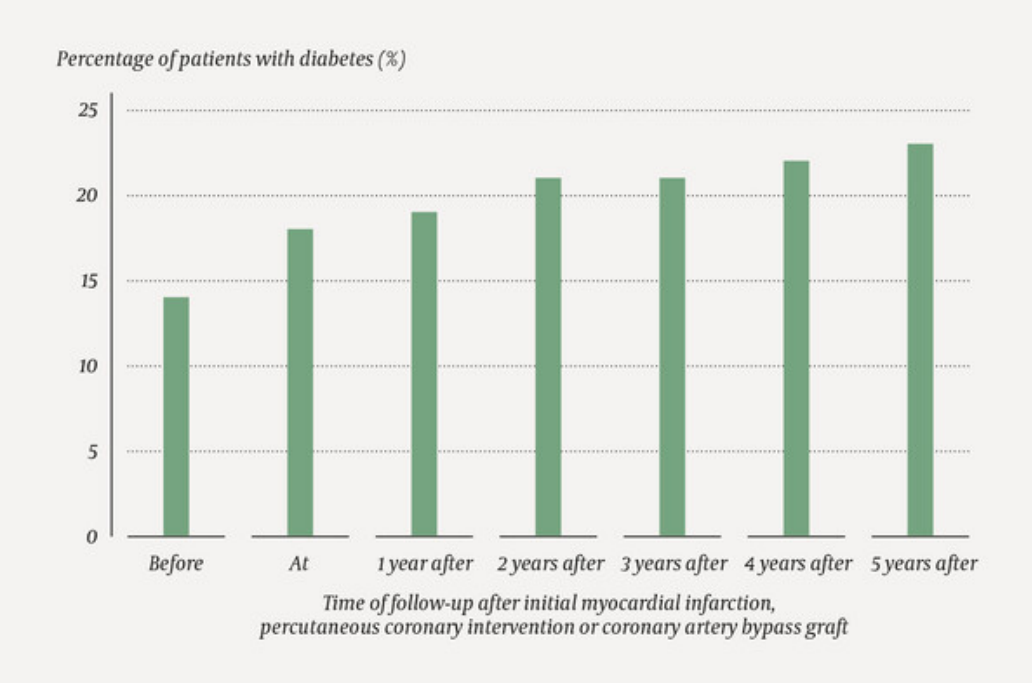

Figure 1 Percentage of patients at Sørlandet Hospital Arendal in the period 2007–16 with diagnosed diabetes before, at discharge and at various follow-up times after initial myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft. The percentages are calculated on the basis of the section of the study population that reached each follow-up time

INTENSITY OF BLOOD GLUCOSE TREATMENT

HbA_{1c} value at time of the index event is presented in Table 1. Change in HbA_{1c} value in the follow-up period for those who had known or previously undiagnosed diabetes at the time of the index event is presented in Figure 2.

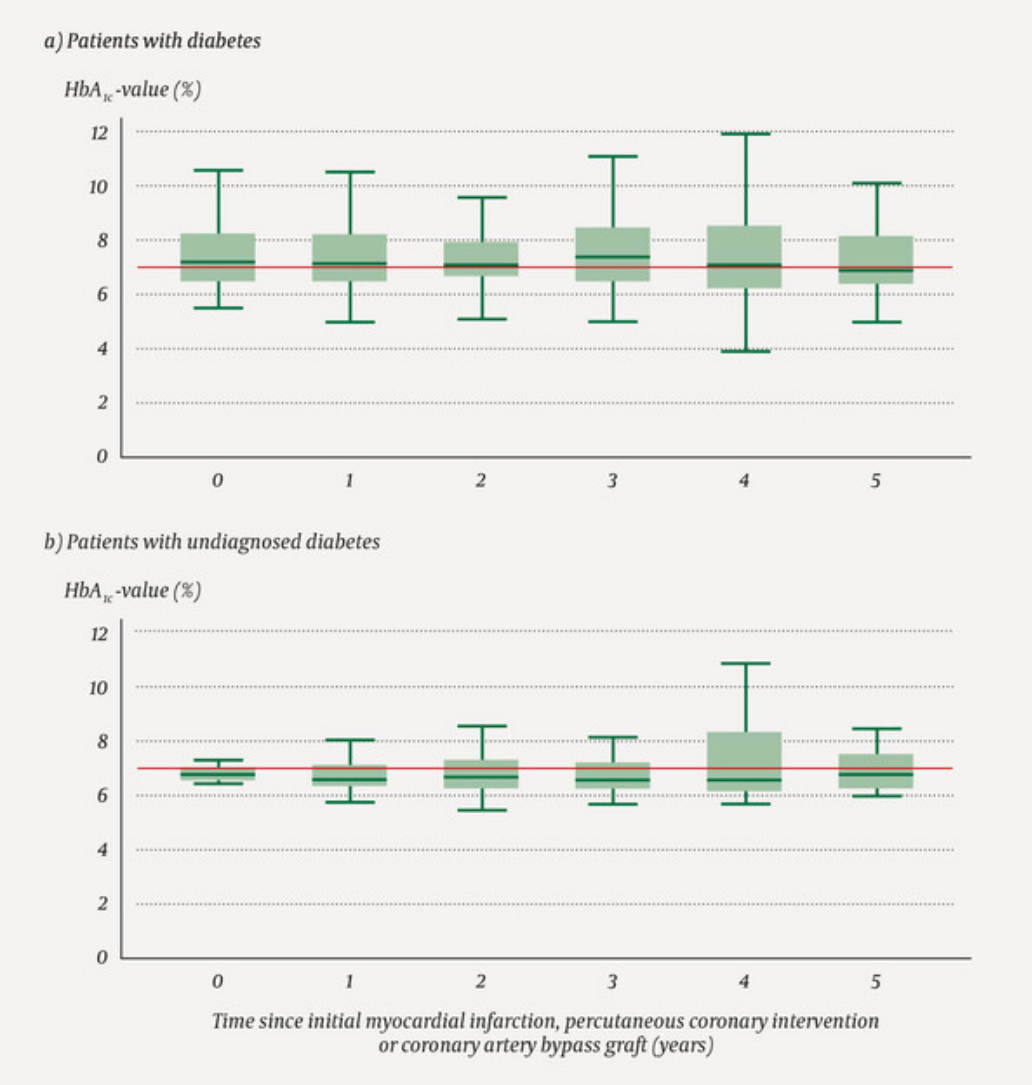

Figure 2 Development of HbA1c- value after first myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft in patients who at time of index event had a) known diabetes or b) undiagnosed diabetes. Sørlandet Hospital Arendal 2007–16. Reference line (red) indicates treatment goal for HbA1c (≤ 7.0 %)

A total of 75 patients with known diabetes (42 %) had an HbA_{1c} value ≤ 7 % at the time of inclusion. At the final follow-up visit, 96 of those with known diabetes (54 %) had a similar value. Of the 49 patients with undiagnosed diabetes at the time of the index event, 34 (69 %) had an HbA_{1c} value ≤ 7 % at their final follow-up visit.

SUBSEQUENT CARDIOVASCULAR EVENTS

The patients were followed for up to five years – median follow-up time was 3.0 years (lower quartile 2.0 years, upper quartile 5.0 years). Altogether 226 patients (18 %) withdrew from the study during the follow-up period, most of them (74 %) because they did not want further follow-up at the hospital.

The total number of deaths, new myocardial infarctions, coronary artery bypass grafts or cerebral insults is presented in Table 2. Patients with known diabetes at the time of initial coronary artery disease had significantly more subsequent cardiovascular events than non-diabetic patients (adjusted for age and sex HR 1.5; 95 % CI: 1.1–2.1, p = 0.005) (Figure 3). We found no difference in subsequent cardiovascular events between non-diabetic patients and patients with undiagnosed diabetes.

Table 2

Subsequent cardiovascular events in non-diabetic patients, patients with known and patients with undiagnosed diabetes treated at Sørlandet Hospital Arendal after initial myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft in the period 2007–16. Median follow-up time 3 years (lower quartile 2 years, upper quartile 5 years)

	Non-diabetic patients		Patients with known diabetes		Age and sex-adjusted HR (95 % CI)[1]	Patients with undiagnosed diabetes		Age and sex-adjusted HR (95 % CI)[1]
	n = 1 032		n = 178			n = 49		
Death	19	2 %	3	2 %	0.9 (0.3–2.9)	1	2 %	1.1 (0.1–8.0)
Myocardial infarction	30	3 %	7	4 %	1.4 (0.6–3.2)	2	4 %	1.2 (0.3–5.2)
Percutaneous coronary intervention	163	16 %	37	21 %	1.4 (1.0–2.0)	6	12 %	0.7 (0.3–1.7)
Coronary artery bypass graft	16	2 %	1	1 %	0.3 (0.0–2.2)	0	0 %	
Cerebral insult	19	2 %	9	5 %	2.7 (1.2–6.0)	1	2 %	1.0 (0.1–7.4)

[1]Reference: Non-diabetic patients

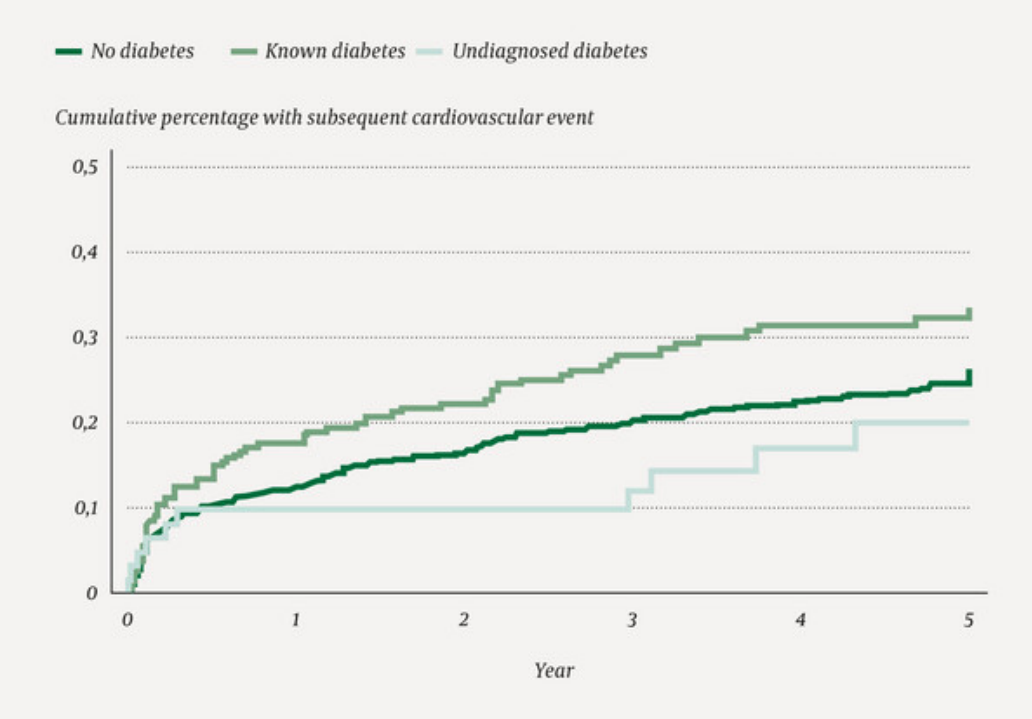

Figure 3 Subsequent cardiovascular event (death, myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft or cerebral insult) in non-diabetic patients, patients with known and patients with undiagnosed diabetes after initial myocardial infarction, percutaneous coronary intervention or coronary artery bypass graft. Sørlandet Hospital Arendal 2007–16

Discussion

This study shows a high prevalence of diabetes (18 %) when coronary artery disease was first diagnosed (acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft), and that several patients (8 %) developed diabetes in the period following such an event. The median HbA_{1c} values in those with known diabetes were 7.2 % and 6.9 % at the time of first diagnosis of coronary artery disease and after five years, respectively. Patients with known diabetes at the time of first diagnosis of coronary artery disease had significantly more subsequent cardiovascular events than patients without diabetes in the course of the follow-up period.

Increased prevalence of diabetes in patients with coronary artery disease is well established from older studies such as the Framingham Heart Study (11) and the Multiple Risk Factor Intervention Trial (MRFIT) (12). The percentage of patients with diabetes in this study (14–26 %) also corresponds well with the percentage of patients with diabetes registered in the Norwegian Myocardial Infarction Registry. (19 %) (6).

Many patients treated for coronary artery disease have undiagnosed diabetes. The percentage was far lower in our study (4 %) than in several earlier studies (13–15). There may be many reasons for this, including the fact that in this study we only investigated patients with a first diagnosis of coronary artery disease. Moreover, a number did not wish to participate.

Our findings nevertheless underscore the importance of routine examination of all patients who have undergone coronary events for diabetes. The HbA_{1c} value should be registered in the Norwegian Myocardial Infarction Registry, which may lead to the detection of more patients with diabetes in connection with acute myocardial infarction. The oral glucose tolerance test has been shown in some studies to have a prognostic value and may be considered after an acute coronary event but is not recommended as a normal procedure (13, 14, 16)(16–18).

Many of the patients developed diabetes in the years following treatment of coronary artery disease. Regular follow-up of the development of the disease in the period following a coronary event is therefore also essential.

The association between control of blood glucose and the development of microvascular complications is well established (19–21), but the importance of good blood glucose control for the development of macrovascular disease and long-term cardiovascular prognosis has not been documented in randomised studies. However, epidemiological studies demonstrate a strong correlation between blood glucose level and cardiovascular events (22).

Poor achievement of treatment goals in diabetes have been documented in many European countries (23). The patients in this study were treated relatively effectively, with HbA_{1c} values close to the treatment goal both at the time of the index event and throughout the study period. If an HbA_{1c} value ≤ 7 % is used as the treatment goal, however, only around half of the patients achieved this.

Intensive blood glucose control requires a significant effort on the part of the patients. They must have a reflective approach to physical activity and diet, perform frequent blood glucose measurements and accept constant adjustments to their treatment. Intensive blood glucose control is also associated with an elevated risk of symptomatic hypoglycaemia and other adverse effects. Diabetes treatment also requires effort on the part of the doctor – the treatment may be perceived as complex, with many different drugs available and several different regimens.

We believe that the results of this study provide support for placing greater emphasis on the achievement of treatment goals for blood glucose level in patients with diabetes and coronary artery disease. Recently published recommendations for the treatment of diabetes from the Norwegian Directorate of Health, containing clear advice on treatment options, may help in this regard (10).

Cardiac disease, particularly coronary artery disease, is the main cause of morbidity and death in patients with diabetes (3-5). They are at increased risk of myocardial infarction and frequently have more extensive coronary artery disease, with more vascular segments involved than those who do not have diabetes (8, 24, 25). In this study we also found more cardiovascular events, in patients with known diabetes than in non-diabetic patients. The difference between the groups primarily consisted of more PCI procedures and more cerebral insults in those with diabetes.

In cases of stable coronary artery disease, multivascular disease and low surgical risk, coronary artery bypass graft is recommended in preference to percutaneous coronary intervention in patients with diabetes (26), and the choice of revascularisation therapy prior to inclusion in this study may have had a bearing on the incidence of subsequent cardiovascular events.

We found an elevated risk in the patients with undiagnosed diabetes; however, the small number of patients, shorter period with diabetes, lower HbA_{1c} level and short follow-up time may be possible explanations for these findings. The high percentage of patients with diabetes who experienced a subsequent cardiovascular event within five years underscores the need for better follow-up and treatment – also in other respects than good control of blood glucose. Many of these patients also had other risk factors for coronary artery disease, such as being overweight, smoking, and having an unfavourable lipid profile and hypertension. It is therefore our opinion that a multifactorial intervention with emphasis on total risk reduction is crucial.

Smoking cessation is the most effective single intervention, also in patients with diabetes (27). Weight reduction, aggressive lipid reduction and good blood pressure control are interventions that are at least as important in those with diabetes as in non-diabetic patients.

This study included a high number of patients and had a long follow-up time, but nevertheless contains a number of weaknesses. The study's descriptive design made it impossible for us to demonstrate causal associations between diabetes and subsequent cardiovascular events or between the intensity of diabetes treatment and new events.

The study included patients at only one hospital, and treatment traditions and procedures at this hospital may have had a bearing on the results and incidence of subsequent cardiovascular events. It was also based on voluntary participation, and we had no information on the patients who did not wish to participate for various reasons.

Because the follow-up was undertaken at a hospital outpatient clinic, a skewed distribution with regard to geography and age could be assumed. Our experience is that patients who live some distance from the hospital prefer to receive follow-up from their GP, and the same applies to the oldest patients. Many participants also withdrew during the study period.

Treatment of other cardiovascular risk factors such as being overweight, hyperlipidaemia, hypertension and smoking was not analysed, but several of these are associated with diabetes and should not be interpreted as independent risk factors. Nor did we have a detailed overview of the drugs used for regulation of blood glucose or for other prophylactic treatment.

In summary, this study from a regional Norwegian hospital shows a continued high prevalence of diabetes in patients with a first diagnosis of coronary artery disease, and still more subsequent cardiovascular events in diabetic than in non-diabetic patients. We therefore believe that regular testing for diabetes in patients with coronary artery disease, and a continued emphasis on improved treatment of patients with coronary artery disease are necessary.

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