



UNIVERSITY OF GOTHENBURG

Cardiovascular Risk Factors and Complications in Type 1 and Type 2 Diabetes

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av

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Avhandlingen baseras på följande delarbeten:

I Eeg-Olofsson K, Cederholm J, Nilsson PM, Gudbjornsdottir S, Eliasson B. Glycemic and risk factor control in type 1 diabetes: results from 13,612 patients in a national diabetes register. *Diabetes Care*. 2007;30(3):496-502.

II Eeg-Olofsson K, Cederholm J, Nilsson PM, Zethelius B, Svensson AM, Gudbjornsdottir S, Eliasson B. Glycemic control and cardiovascular disease in 7,454 patients with type 1 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *Diabetes Care*. 2010;33(7):1640-1646.

III Eeg-Olofsson K, Cederholm J, Nilsson PM, Zethelius B, Nunez L, Gudbjornsdottir S, Eliasson B. Risk of cardiovascular disease and mortality in overweight and obese patients with type 2 diabetes: an observational study in 13,087 patients. *Diabetologia*. 2009;52(1):65-73.

IV Eeg-Olofsson K, Cederholm J, Nilsson PM, Zethelius B, Svensson AM, Gudbjornsdottir S, Eliasson B. New aspects of HbA1c as a risk factor for cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register (NDR). *J Intern Med*. 2010. Article first published online: 21 July 2010.

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ABSTRACT

Patients with diabetes have increased risk of cardiovascular disease (CVD) and mortality compared to the general population. The aim of this work was to describe the clinical characteristics and risk factors in patients with type 1 diabetes, and also to investigate the association between glycaemic control and CVD in type 1 and type 2 diabetes, and to analyse the association between BMI, overweight and obesity, and CVD in type 2 diabetes.

These observational studies comprise patients from the Swedish National Diabetes Register (NDR). Clinical characteristics and risk factor control in type 1 diabetes were analysed in two cross-sectional samples, in 1997 and 2004. 7454 patients with type 1 diabetes were followed from 2002/03 to 2007, and 13,087 patients (Study III) and 18,336 (Study IV) with type 2 diabetes were followed from 1997/98 to 2003, regarding fatal/non-fatal CVD events. Cox proportional hazard models were used to estimate adjusted hazard ratios with 95% confidence intervals and to estimate 5- and 6-year event rates for the outcomes.

In patients with type 1 diabetes slight but significant improvements were seen in glycaemic control, blood pressure and lipid levels from 1997 to 2004. Hazard ratios for coronary heart disease (CHD) and CVD per 1%-unit increase in baseline HbA1c were 1.31 and 1.26 ($p < 0.001$), respectively, when adjusted for age, sex, duration of diabetes and cardiovascular risk factors. Adjusted 5-year event rates of CHD and CVD increased progressively with higher HbA1c levels. Patients with HbA1c levels of 5-7.9% (mean 7.2%) at baseline had about 40% lower risk for CHD and CVD, compared with patients with HbA1c 8-11.9% (mean 9.0%). In type 2 diabetes adjusted hazard ratios for a 5-unit increase in BMI were 1.15 for first-incident CHD and 1.13 for CVD. Obesity was associated with a 44% increase in risk of CVD, and overweight with a 24% increase in risk, compared with normal weight. Adjusted hazard ratios for a 1%-unit increase in HbA1c were 1.11 for CHD and 1.10 for CVD ($p < 0.001$), and the corresponding adjusted 6-year event rates for these outcomes increased progressively with higher baseline and updated mean HbA1c values, also when sub-grouping the data by duration, previous CVD or hypoglycaemic treatment. A group of patients with a mean baseline HbA1c of 6.5% showed a 20% lower risk of CHD and a 16% lower risk of CVD, than a group with a mean HbA1c of 7.5%.

These large observational studies on patients with diabetes in everyday clinical practice show a slow improvement in glycaemic control and risk factors in type 1 diabetes. Higher HbA1c level was found to be independently associated with increased risk of CHD and CVD, emphasizing the role of HbA1c as a strong independent risk factor in type 1 diabetes. In type 2 diabetes, increasing risks of CHD and CVD were seen in patients with higher HbA1c levels, while no risk increase was seen in those with low HbA1c levels. HbA1c levels lower than 7% were associated with a lower risk of CVD, providing support for current treatment guidelines. Higher BMI, overweight and obesity independently increased the risk of CHD and CVD in patients with type 2 diabetes, providing additional evidence that overweight and obesity should be counteracted in type 2 diabetes.