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Association of serum adiponectin with diabetes, its relation to established risk factors, and the prognostic value for the manifestation of cardiovascular diseases: results of an epidemiologic study in elderly subjects

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Adipose tissue, in addition to its function as the major storage depot for lipids, seems to play an active role in normal metabolic homeostasis and in the development of several diseases, such as type 2 diabetes, artherosclerosis and cardiovascular diseases. These roles are mediated by factors known as adipocytokines, which are secreted from adipose tissue. Adiponectin is an adipocytokine with a wide range of biological activities. Adiponectin's role in stimulating ß-oxidation in muscle and decreasing insulin resistance in the liver indicates its possible involvement in the development of type 2 diabetes. Moreover the association of decreased plasma adiponectin levels with the presence of coronary artery disease indicated the pathophysiological role of adiponectin in the development of coronary artery disease. However, epidemiological evidence investigating the association between adiponectin serum levels and future cardiovascular events is limited and inconsistent in results.

We made use of a large population based cohort study (Esther-1) to answer our research questions. Firstly, in a sample of the Esther-1 study consisting of patients diagnosed with type 2 diabetes, and sex and aged-matched controls, we explored in a case-control design the determinants of adiponectin serum levels in diabetic patients and in control subjects as well as the association between adiponectin serum levels with type 2 diabetes with special attention to the potential effects of age and chronic kidney disease on adiponectin levels. Secondly, we employed in a prospective cohort study design including all these subjects from the sample of the Esther-1 study who participated in a follow-up 2 years after baseline recruitment, to

investigate the role of baseline adiponectin serum levels on the risk for subsequent cardiovascular disease events, in order to clarify and extend current knowledge regarding this association.

A total of 1308 clinically diagnosed type 2 diabetes mellitus patients were identified at baseline, in addition 1308 age and sex matched controls were selected. Recruitment time started at July 2000 and ended at December 2002. In case of participation, patients were requested for permission to pass on the results of the "Gesundheits check-up", an anamnesis to establish existing and past illnesses as well as current medication intake. Additionally patients were asked to fill out a questionnaire with information on possible risk factors and other health related information. To complete the information about study participants, a blood, urine and stool samples were extracted.

Adiponectin serum levels were considerably lower in persons with type 2 diabetes than in nondiabetic persons, even after controlling for obesity-related measurements, lipid values and renal function. These variables explained 68% of the difference in cross-sectional adiponectin levels between type 2 diabetic and nondiabetic persons. Baseline adiponectin was independently associated with type 2 diabetes in our population with an OR of 0.25 (95% CI 0.15-0.43) when the fifth quintile was compared to the first one. In the prospective study part however, baseline levels of adiponectin were not predictive for future cardiovascular disease events (n=72 events during follow-up), nor in patients with diabetes nor in others. The hazard ratio from the highest quintile was of 0.94 (95% CI 0.30 to 2.92) when compared to the lowest.

Our results support the hypothesis that adiponectin may play an important role in the pathogenesis of abnormal glucose metabolism and that adiponectin could be used as an indicator of risk in addition to the established risk parameters such as obesity and physical activity. We did not find any association between adiponectin serum levels and future cardiovascular events after 2 years of follow-up. These findings further support a stronger association of adiponectin with diabetes than vascular disease. Further studies with on larger populations are needed, as well as plausible explanations of adiponectin's pathophysiology.