

# **Epidemiological aspects on renal impairment in patients with type 2 diabetes**

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## **Avhandlingen baseras på följande delarbeten:**

1. Afghahi H, Cederholm J, Eliasson B, Zethelius B, Gudbjörnsdottir S, Hadimeri H, Svensson MK. Risk factors for the development of albuminuria and renal impairment in type 2 diabetes- the Swedish National Diabetes. *Nephrol Dial Transplant*. 2011 Apr;26(4):1236-43.
2. Afghahi H, Miftaraj M, Svensson AM, Hadimeri H, Gudbjörnsdottir S, Eliasson B, Svensson MK. Ongoing treatment with RAAS-blockade does not predict normoalbuminuric renal impairment in a general type 2 diabetes population. *Journal of Diabetes and its Complications*. 2013 May-Jun;27(3):229-34.
3. Afghahi H, Svensson MK, Pirouzifard M, Eliasson B, Svensson AM. Optimal blood pressure levels and major cardiovascular events in patients with type 2 diabetes and renal impairment. *Diabetologia*. 2015 Jun;58(6):1203-11.
4. Svensson MK, Afghahi H, Franzén S, Björck S, Gudbjörnsdottir S, Svensson AM, Eliasson B. Decreased in systolic blood pressure during follow up is associated with an increased risk of all-cause mortality in patients with type 2-diabetes and renal impairment-a nationwide longitudinal observational study of 27,732 patients based on the Swedish National Diabetes Register (NDR). Submitted

**SAHLGRENSKA AKADEMIN  
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# Epidemiological aspects on renal impairment in patients with type 2 diabetes

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## Abstract

Diabetes is a leading cause of renal impairment (RI) and indication of the need for renal replacement therapy in many parts of the world. Albuminuria and RI are the two main forms of diabetic kidney disease. The overall aims of this thesis were to explore risk factors and consequences associated with albuminuria and RI in patients with type 2 diabetes (T2D), as well as to assess the relationship between blood pressure variables, cardiovascular events and all-cause mortality. The studies were based on data from the Swedish National Diabetes Register (NDR).

Study I followed 3,367 patients with T2D who did not exhibit signs of albuminuria or RI from 2002 to 2007 in order to evaluate the risk of developing them. A total of 20% of patients developed albuminuria and 11% developed RI. Among those with one of the two conditions, 62% had normoalbuminuric RI. Development of albuminuria or RI was independently associated with advanced older age, high systolic blood pressure and elevated triglycerides. The independent risk factors were obesity, poor glycemic control, smoking, low HDL-cholesterol and male gender for developing albuminuria, as opposed to elevated plasma creatinine at baseline and female gender for developing RI. Different sets of risk factors were associated with development of RI and albuminuria. High body mass index (BMI) was an independent risk factor for RI when renal function was calculated with the MDRD equation, while low BMI was a risk factor with when the Cockcroft-Gault equation was used. In other words, the equation chosen to estimate renal function is important in when interpreting data. Thus, patients with T2D face have distinct risk factors for albuminuria and RI.

Study II included 94,446 patients with T2D, including 19,330 with RI. The majority with T2D and RI were normoalbuminuric. Normoalbuminuric RI may be partly due to treatment with RAAS blockade. Given, however, that only 25% of the patients with normoalbuminuric renal impairment had received RAAS blockade, the possibility that other underlying pathophysiological mechanisms play a role should be further evaluated.

Study III followed 33,356, and Study IV 27,732, patients with T2D and RI in 2005-2011 in order to evaluate correlations associations between systolic blood pressure (SBP) and all-cause mortality. We observed U-shaped relationships between various aspects of SBP and the risk of all-cause mortality. The greatest risks for cardiovascular events (CVEs) and all-cause mortality were at the highest and lowest blood pressure intervals. SBP of 135-139 and diastolic blood pressure (DBP) of 72-74 mmHg showed the lowest risks of CVEs and all-cause mortality.

Adjusting for presence of albuminuria or chronic heart failure did not significantly alter the results. A reduction in SBP during follow-up is was associated with a greater risk of all-cause mortality.

In summary, this thesis shows that obesity and other traditional cardiovascular risk factors are associated with development of albuminuria and RI in patients with T2D. We also found that normoalbuminuric RI is common in patients associated with T2D. Finally, both the highest and lowest blood pressure intervals are associated with greater risks of cardiovascular events and all-cause mortality.

**Keywords:** Type 2 diabetes, renal impairment, albuminuria, risk factors, blood pressure, cardiovascular disease

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