

Mortality and morbidity in patients with Addison's disease

Akademisk avhandling

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av

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Avhandlingen baseras på följande arbeten:

- Paper I. Bergthorsdottir R, Leonsson-Zachrisson M, Oden A, Johannsson G.
Premature mortality in patients with Addison's disease: a population-based study. *J Clin Endocrinol Metab* 2006; 91(12):4849-53
- Paper II. Bergthorsdottir R, Ragnarsson O, Skrtic S, Ross IL, Leonsson-Zachrisson M, Johannsson G.
Visceral fat mass and cardiovascular risk factors in patients with Addison's disease: a case-control study. *Manuscript.*
- Paper III. Bergthorsdottir R, Chantzichristos D, Skrtic S, Ragnarsson O, Johannsson G.
Patients with Addison's disease have decreased bone mineral density and increased prevalence of osteoporosis: a case-control study. *Manuscript.*
- Paper IV. Bergthorsdottir R, Pappakokkinou E, Skrtic S, Ragnarsson O, Johannsson G.
Health-related quality-of-life (HR-QoL) is compromised in patients with Addison's disease: a case-control study. *Manuscript.*



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MORTALITY AND MORBIDITY IN PATIENTS WITH ADDISON'S DISEASE

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ABSTRACT

Addison's disease (AD) or primary adrenal insufficiency is a rare disease with an estimated prevalence of 100-140 per million inhabitants and deadly unless treated with glucocorticoids (GCs). Very limited information is available on the morbidity and mortality in this patient group. A few old studies report near normal mortality and several studies indicate impaired bone health and reduced health-related quality of life (HR-QoL). It has been suggested that GC treatment, with both too high GC doses and a replacement regime which cannot replicate the physiological cortisol rhythm, may partly explain the impaired outcome in AD patients.

This thesis is based on studies with the main objective of studying mortality and morbidity in patients with AD receiving long-term GC replacement therapy. In a large nation-wide register-based study patients with AD had a more than two-fold higher mortality rate than the general population which was mainly explained by excess mortality from cardiovascular diseases, cancer and infectious diseases. The mortality was further increased among patients with AD who also had diabetes mellitus (DM).

In a case-control study, comparing AD patients to healthy controls matched for age, gender, BMI and smoking habits; cardiometabolic risk factors, visceral abdominal adipose tissue (VAT), bone health and HR-QoL were studied. The patients did not have increased VAT measured using computerized tomography, but a greater proportion of patients had the metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM). The patients had reduced bone mineral density (BMD) and an increased frequency of osteoporosis and osteopenia and patients using higher GC doses for replacement had increased risk of osteoporosis and osteopenia. Finally, using four different validated questionnaires we could demonstrate that the patients experienced more fatigue and had impaired HR-QoL.

In conclusion, patients with AD in Sweden have increased mortality, which is mainly explained by cardiovascular diseases. Despite compatible VAT between the AD patients and controls, the patients have an increased prevalence of MetS and T2DM, both of which are known to be related to increased cardiovascular risk. Patients with AD also have impaired bone health and reduced HR-QoL. The thesis strongly suggests that there is a need for improvement in the overall management of patients with AD.

Key words: Addison's disease, mortality, glucocorticoid(s), glucocorticoid replacement therapy, cardiovascular diseases, bone mineral density, osteoporosis, quality of life

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