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# Cardiovascular events linked to levels of cortisol production

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Adrenal incidentalomas—also known as 'silent' adrenal tumours—are being increasingly identified as a result of the greater frequency with which abdominal CT scans are now carried out. A long-term follow-up study, published in *The Lancet Diabetes & Endocrinology*, is the first to examine the natural progression of nonsecreting adrenal incidentalomas and subclinical Cushing syndrome. The researchers report that cardiovascular disease occurs more frequently in patients with stable mild hypercortisolism than in patients with stable normal cortisol secretion and, furthermore, that the incidence of cardiovascular disease is highest in those patients whose production of cortisol increases over time.

In light of the known association between overt hypercortisolism and cardiovascular disease, "we wanted to address whether even subtle hypersecretion of cortisol (persistent over time) could lead to impairment of the cardiovascular system," explain Guido Di Dalmazi and Renato Pasquali, the lead and senior authors of the study. In total, 198 patients with adrenal incidentalomas were recruited (129 patients had nonsecreting adrenal incidentalomas, 59 had intermediate phenotypes and 10 had subclinical Cushing syndrome). Participants were assessed every 18–30 months for the first 5 years with an average follow-up of 7.5 years. Cortisol levels after the 1 mg dexamethasone suppression test were used to define nonsecreting adrenal incidentalomas (<50 nmol/l), intermediate phenotypes (50–138 nmol/l), and subclinical Cushing syndrome (>138 nmol/l without symptoms of glucocorticoid excess).

At the end of follow-up, patients were assigned to one of three groups for analysis; patients with stable nonsecreting tumours, stable intermediate or subclinical Cushing syndrome secreting patterns, and worsened secretion levels (patients who moved from nonsecreting to intermediate phenotype, or from intermediate phenotype to subclinical Cushing syndrome). Patients with stable intermediate phenotypes and subclinical Cushing syndrome (16%, $P = 0.04$), and patients with worsening secretion levels (28%, $P = 0.02$), had a higher incidence of cardiovascular disease than patients with stable nonsecreting adrenal incidentalomas (6%). "The incidence of cardiovascular events and mortality are related to cortisol secretion independently of the other potential risk factors," say Di Dalmazi and Pasquali.

Importantly, this study provides guidance for the appropriate management of patients with adrenal incidentalomas, and for identifying those patients who should be monitored for cardiovascular problems who are more likely to need medical intervention. The authors propose that even patients with nonsecreting adrenal masses should be periodically assessed to monitor any progression towards the overproduction of cortisol. "Future studies should address whether the surgical treatment (for monolateral diseases) or the medical treatment (for bilateral diseases) could be beneficial for these patients in a long-term follow-up," conclude Di Dalmazi and Pasquali.

***Bryony Jones***

**Original article** Di Dalmazi, G. *et al.* Cardiovascular events and mortality in patients with adrenal incidentalomas that are either non-secreting or associated with intermediate phenotype or subclinical Cushing's syndrome: a 15-year retrospective study. *Lancet Diabetes Endocrinol.* doi:10.1016/S2213-8587(13)70211-0