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ORIGINAL ARTICLE

The size of adrenal incidentalomas correlates with insulin resistance. Is there a cause-effect relationship?

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Summary

Context Adrenal incidentalomas (AI) have often been associated with a high prevalence of insulin resistance (IR) and cardiovascular risk factors, although direct measurement of insulin sensitivity (IS) has never been carried out.

Objective We aimed to investigate whether the morphological and hormonal features of AI correlate with the presence and severity of IR, using the hyperinsulinaemic euglycaemic clamp (HEC).

Design and Measurements Forty patients with AI (22 women) with a mean age of 58·5 ± 11·1 years underwent hormonal and morphological evaluation. Nineteen patients with AI without known history of diabetes mellitus (DM) or impaired glucose tolerance (IGT) and 17 matched controls underwent oral glucose tolerance test (OGTT) and hyperinsulinaemic euglycaemic clamp (HEC).

Results Diabetes mellitus was observed in 13 patients (33%), while three (8%) had IGT. Thirty-one of the AI were nonfunctioning (82·5%), whereas two (5%) secreted cortisol (Cushing's syndrome) and seven (12·5%) showed subclinical secretion of cortisol. The 19 patients with nonfunctioning AI were more insulin resistant than controls (glucose up-take: 4·58 ± 1·80 *vs* 5·85 ± 2·48 mg/kg/min respectively; $P = 0{\cdot}01$); IS was inversely related to the mass size ($r = -0{\cdot}57$; $P = 0{\cdot}04$), free urinary cortisol ($r = -0{\cdot}68$; $P = 0{\cdot}01$), serum cortisol after 1-mg dexamethasone suppression (−0·65; $P = 0{\cdot}02$) and percentage of trunk fat mass (−0·77; $P = 0{\cdot}02$) and directly related to serum adreno cortico tropic hormone (ACTH) ($r = 0{\cdot}62$; $P = 0{\cdot}03$). After performing multivariate regression, the mass size was found to be the most powerful predictor of IR.

Conclusion Our study showed a high prevalence of insulin resistance in patients with nonfunctioning AI and suggests its possible involvement in AI growth.

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Introduction

The adrenal mass occasionally detected during radiological examinations, the so-called 'adrenal incidentaloma' (AI), has become quite frequent, because of the widespread use of imaging techniques.[1,2] Its management is still controversial, mostly because the associated morbidity is unknown.

By definition, patients with AI do not display any physical sign of adrenal hormonal excess because no clinical suspicion has led to the detection of the adrenal masses. However, AIs, although considered hormonally inactive, have often been associated with a high prevalence of hypertension, dyslipidaemia, glucose intolerance and obesity,[3–5] all parameters closely linked to insulin resistance.

Careful endocrine evaluation has led some authors to find abnormal cortisol responses to hypothalamo-pituitary-adrenal axis testing (subclinical Cushing syndrome) in patients with AIs, despite the absence of clinical features, suggesting subclinical hypersecretion as responsible for the onset of the metabolic syndrome.[6,7] Further, Terzolo *et al.*[3] reported that patients with nonsecreting adrenal masses undergoing surgery for tumour size or growth experienced an improvement in blood pressure and fasting glucose even in the absence of any (causative) hormonal change. Several studies examining the relationship between insulin resistance and adrenal masses have provided controversial results,[8] probably due to variability of method used. In fact, it is recognized that indirect indices of insulin resistance derived from fasting values of insulin and glucose mostly reflect hepatic insulin sensitivity, while post-OGTT indices do not take into account all variables influencing the results, including insulin secretion.[6,7] Thus, the present study was designed to examine insulin sensitivity in patients with AIs, as evaluated by HEC, therefore supplying a direct measure of insulin sensitivity independently from insulin secretion, to find a relationship between glucose metabolism and AI features and, finally, to possibly identify the earliest hormonal and morphological changes responsible for insulin resistance in patients with nonsecreting adrenal masses.