



Adrenal tumours associated with increased risk of bone fractures

New research shows that male patients with benign tumours of the adrenal gland suffer more bone fractures. Published in the latest edition of *Clinical Endocrinology*, the study found men with a certain type of adrenal tumour have reduced bone mass and more vertebral bone fractures compared to controls. This study highlights the importance of screening men with adrenal tumours for bone strength and fractures, even in the absence of clinical symptoms.

Tumours that are discovered by coincidence, usually during a scan for an unrelated condition, are called incidentalomas. Adrenal incidentalomas (AIs) are benign growths of the adrenal gland. AIs are being diagnosed with increased frequency due to an increase in the use of abdominal scanning; the current diagnosis is up to 3% of the general population⁽¹⁾. Generally, adrenal incidentalomas are considered benign and do not show any clinical symptoms. However, approximately 20% of patients with AIs show a slight excess of the hormone cortisol, which is defined as 'subclinical hypercortisolism' (SH). SH can cause a negative effect on bone⁽²⁾ however, the association between SH and vertebral bone fractures has not yet been studied in male AI patients.

Researchers led by Dr Iacopo Chiodini at the University of Milan, assessed the bone mass of AI patients with and without SH and in matched controls. Patients with adrenal incidentalomas and SH were identified by measuring three parameters of cortisol secretion (SH+, n=22), and compared with patients with AI but cortisol levels in the normal range (SH-, n=66) and with control patients that were matched for age and BMI.

Patients with cortisol-secreting tumours (SH+) had significantly lower bone mass in their spines compared to SH- and control patients. More patients had osteoporosis in the SH+ group (40.9%) compared to the SH- group (18.2%) and control group (16.7%). There were also significantly more patients with vertebral fractures in the SH+ group (72.7%) compared to the SH- group (21.2%) and controls (20.0%). In addition, there was a significantly higher prevalence of type 2 diabetes and high blood pressure in the SH+ patients compared to SH- patients. This association has been previously reported with overt cortisol excess and confirms the idea that subtle cortisol excess, despite being 'subclinical' may cause the same consequences as overt cortisol excess.

This finding that bone mass is reduced and vertebral fractures increased in adrenal incidentaloma patients with SH may help to address the future treatment choice in these patients. The results highlight the importance of screening patients with adrenal

incidentalomas and SH for bone mass and fractures, in order to reduce the risk of further bone fractures.

Researcher Dr Iacopo Chiodini said:

“This work helps us to understand the relationship between these adrenal tumours and bone structure. The men that took part in the study had adrenal tumours that had been discovered coincidentally whilst they were undergoing abdominal scans. Approximately 20% of patients with adrenal incidentalomas show subtle degrees of cortisol excess, which we describe as subclinical hypercortisolism. The link between overt cortisol excess and bone fractures is well documented, but the relationship between subclinical hypercortisolism in patients with adrenal incidentalomas and bone fractures has not been extensively studied. This study shows that subtly raised cortisol levels can cause the same clinical outcome as overtly raised levels of cortisol. Our research is the first to show a clear link between adrenal incidentalomas with SH and bone fractures in men, and represents an important step towards understanding the causal role of cortisol on bone loss and risk of fractures. There is a clear need for screening of adrenal incidentaloma patients with SH for bone fractures despite the absence of clinical symptoms in these patients.”

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Notes for editors

- (1) Kloos et al. (1995) Incidentally discovered adrenal masses. *Endocrine Reviews*, **16**: 460-484.
- (2) Mazziotti et al. (2006) Glucocorticoid-induced osteoporosis: an update. *Trends in Endocrinology and Metabolism*, **17**: 144-149.

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ABSTRACT

Eugonadal male patients with adrenal incidentalomas and subclinical hypercortisolism have increased rate of vertebral fractures

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Objective

Subclinical hypercortisolism (SH) is suggested to exert a deleterious effect on bone. This effect and the role of gonadal status in male subjects are not fully elucidated. We evaluated bone mineral density (BMD) and prevalence of vertebral fractures in eugonadal male subjects with adrenal incidentalomas (AI) and without SH.

Design

This 12-month observational multicentre study was performed between January and December 2006 on inpatient basis in three referral Italian centres.

Patients

Eighty-eight consecutive eugonadal male patients with AI and 90 matched control subjects were studied.

Measurements

All subjects underwent the determination of BMD by dual-energy X-ray absorptiometry at lumbar spine (LS) and femoral neck (FN), and spinal radiograph. In AI patients SH was diagnosed in the presence of two of the following: urinary free cortisol > 193.1 nmol/l, cortisol after 1 mg dexamethasone suppression test > 82.8 nmol/l, ACTH levels < 2.2 pmol/l.

Results

As compared to patients without SH (SH-, $n = 66$) and controls, patients with SH (SH+, $n = 22$) had lower BMD at LS (Z-score: SH+, -1.04 ± 1.84 ; SH-, 0.19 ± 1.34 , Controls 0.20 ± 1.28 , $P = 0.001$ and FN (Z-score: SH+, -0.63 ± 1.01 ; SH-, 0.01 ± 1.01 , Controls 0.26 ± 1.06 , $P = 0.002$) and higher prevalence of fractures (SH+, 72.7%; SH-, 21.2%, Controls 20.0%, $P = 0.0001$). Multivariable analyses showed that SH was associated to BMD at LS ($\beta = -0.378$, $P = 0.0001$) and vertebral fractures (OR = 7.81, 95% CI 1.96–31.17, $P = 0.004$).

Conclusion

In eugonadal male patients with AI, SH is associated with low BMD and high prevalence of vertebral fractures.