

## BONE

## Treatment for Addison disease reduces BMD

Glucocorticoid replacement therapy reduces BMD in the femoral neck and lumbar spine in patients with Addison disease, which potentially increases the risk of developing osteoporosis. “For patients with increased background risk for osteoporosis, the excess risk may be clinically significant,” says lead researcher Kristian Løvås of the Haukeland University Hospital, Norway.

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Previous studies demonstrated that conventional doses of glucocorticoid replacement for the treatment of Addison disease exceed the normal endogenous production of cortisol. Research shows that glucocorticoids cause adverse effects on bone. Accordingly, concern exists that patients

with Addison disease are at risk of developing osteoporosis. Small studies that investigate this theory have yielded inconsistent results. Løvås *et al.* sought to determine the effects of glucocorticoid replacement therapy on bone in a large cohort of patients with Addison disease. “We ... aimed to identify genetic polymorphisms that might increase the susceptibility to glucocorticoid-induced osteoporosis in these patients,” Løvås adds.

The researchers studied two separate cohorts of patients with verified primary adrenal insufficiency from Norway ( $n=187$ ) and from the UK and New Zealand ( $n=105$ ). Measurements of BMD taken at different study centers were standardized and compared with a reference population. Genetic polymorphisms (common, single-nucleotide polymorphisms in genes associated with glucocorticoid sensitivity) were studied in the Norwegian cohort.

Compared with the reference population, both study cohorts had reduced BMD in

the lumbar spine and the femoral neck. The investigators observed a notable association between BMD and a polymorphism in *ABCB1*, the gene encoding P-glycoprotein, an efflux transporter of glucocorticoids from cells. “Variable efficacy of P-glycoprotein may explain some of the variation in susceptibility to glucocorticoid-induced osteoporosis in this and in other groups of patients,” Løvås commented.

Mean daily doses of glucocorticoid replacement given to study participants were 26.5 mg hydrocortisone or 32.1 mg of cortisone acetate. Data from the present study suggest that recommendations to lower glucocorticoid replacement doses (15–25 mg hydrocortisone daily) are appropriate.

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