

GENETICS

**FRACTURE RISK
IN ACROMEGALY**

A polymorphism of the growth hormone receptor gene (*GHR*) is associated with an increased risk of vertebral fracture in a new cross-sectional study of patients with acromegaly. Patients with this polymorphism do not have the portion of the receptor that is encoded by exon 3.

Both the prevalence and the incidence of fragility-related vertebral fractures are higher in patients with acromegaly than in the general population. However, “this observation does not correlate with BMD values in our patients,” comments study researcher Marilda Mormando. Previous work has shown that patients with acromegaly in whom the exon 3 of *GHR* is absent have higher serum levels of insulin-like growth factor 1 (IGF-1), even after treatment, than patients with the full-length protein. The researchers investigated whether any differences in susceptibility to vertebral fractures could also be noted in these patients.

The study included 73 patients with controlled acromegaly and 36 patients with active disease. The researchers genotyped patients for *GHR* variants and assessed the prevalence and incidence of vertebral fractures and BMD at the lumbar spine and hip. They also measured serum levels of IGF-1 and markers of bone metabolism.

The risk of vertebral fracture was threefold higher in patients who carried the deleted exon in at least one *GHR* allele than in patients with the full-length protein. “The lack of exon 3 enhances signal transduction by altering the structure of the extracellular domain of the protein,” explains Mormando. “Consequently, this polymorphism determines an increased susceptibility to growth hormone stimulation in patients with acromegaly, thus resulting in increased bone turnover and bone fragility.”

The new findings contrast with previous studies in which no relationship between prevalence of vertebral fractures and absence of the exon 3 of *GHR* in patients with acromegaly was observed, although these studies only included patients with controlled disease.

As BMD values in patients with acromegaly do not correlate with the actual risk of developing a fragility fracture, “genetic testing may represent an additional tool for stratification of fracture risk in these patients,” says Mormando.

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Original article Mormando, M. *et al.* Growth hormone receptor isoforms and skeletal fragility in acromegaly. *Eur. J. Endocrinol.* doi:10.1530/EJE-14-0205