

Genes linked to osteoporosis, bone breaks

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Researchers at The Institute for Aging Research at Hebrew SeniorLife, an affiliate of Harvard Medical School, have co-authored the largest meta-analysis of genome-wide association studies of osteoporosis as part of an international consortium and have identified dozens of genetic variants found to be linked to an increased risk of developing osteoporosis and of suffering broken bones.

The paper, published today in <u>Nature Genetics</u>, identifies 56 genetic variants that have been found to influence Bone Mineral Density (BMD), which is the hallmark of osteoporosis or thinning bones.

Fourteen of the genetic variants were specifically linked to an increased risk of bone fracture, the first time such a large number of genetic variants has been found to be strongly associated with fracture risk.

The issue is important because osteoporosis accounts for about 1.5 million new fractures each year. In addition, half of all those over age 80 who fracture a hip die within a year of the accident and women over age 65 are at greater risk of death after hip fracture than after getting breast cancer.

"This is the largest osteoporosis genetic study ever done," said senior author Douglas P. Kiel, M.D. M.P.H., Director of the Musculoskeletal Research Center and Senior Scientist at the Institute for Aging Research at Hebrew SeniorLife as well as Professor of Medicine at Harvard Medical School.



"The ultimate goal of genetic studies like this is to develop personal, gene-based treatments for osteoporosis as well as to better identify those at high risk for the disease," said Dr. Kiel, the only senior author of the study who is based in the United States. "The findings could lead to new treatments to prevent or treat osteoporosis."

Dr. Kiel and Yi-Hsiang Hsu, also of the Institute for Aging Research and HMS, were among the leaders of the international study that involved hundreds of researchers from all over the world who conducted 17 separate studies on the subject of Bone Mineral Density of the spine and hip. The Consortium infrastructure and some of the genotyping resources were funded by the European Union.

The researchers pooled the data from the 17 studies, which involved 32,961 individuals, then replicated their findings by looking at data from 34 more studies that had involved 50,933 more subjects. The subjects had received bone density scans. They also had genotyping done. The findings from the bone mineral density work were then compared with data culled from 31,016 individuals with a history of fracture and 102,444 control subjects.

Today's study identifies 32 new genetic variants linked to the level of bone mineral density in addition to 24 that had already been so linked. Bone mineral density is the most accurate predictor of fracture risk.

The research adds to a better understanding of the biology of skeletal health and fracture susceptibility. "Our results indicate that hundreds of variants with small effects may contribute to the genetic architecture of BMD and fracture risks," the paper says.

"We also established that, as compared to women carrying the normal range of genetic factors, women with an excess of BMD-decreasing genetic variants had up to a 56 percent higher risk of having osteoporosis



and a 60 percent increased risk for all types of fractures," Dr. Kiel said.

Even more interesting, he said, was the discovery of groups of individuals who had fewer than normal genetic factors linked to BMD issues, something that seems to protect them from developing osteoporosis or sustaining fractures.

Dr. Kiel said the Consortium is already planning a study that will look for genetic variants across the genome that are associated with fracture risk, rather than bone density. He noted that <u>fracture risk</u> may be related to other factors in addition to bone density, such as poor balance, which can lead to falls. In fact, half of those without osteoporosis as diagnosed by bone scan still suffer fractures.

Provided by Hebrew SeniorLife Institute for Aging Research

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