Study summarizes fracture prediction strength of reference bone turnover markers

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A new study by an International Osteoporosis Foundation (IOF) and International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) scientific working group summarizes the clinical performance of serum procollagen type I N propeptide (s-PINP) and serum C-terminal cross-linking telopeptide of type I collagen (s-CTX) in fracture risk prediction in untreated individuals in prospective cohort studies.

The current study follows a position paper published in 2011 by the IOF-IFCC Bone Marker Standards Working Group recommending the use of bone formation marker serum s-PINP and bone resorption marker serum s-CTX as reference markers to be used in future studies of fracture risk assessment.

In the study, ten potentially eligible publications were identified and six included in meta-analysis. The results showed a moderate but significant association between the bone turnover markers (BTMs) studied and the risk of future fractures not adjusted for bone mineral density (BMD). There was a significant association between s-PINP and the risk of fracture. The hazard ratio (HR) per standard deviation (SD) increase in s-PINP was 1.23 (95% CI: 1.09-1.39) for men and women combined unadjusted for bone mineral density. There was also a significant association between s-CTX and risk of fracture, HR per SD 1.18 (95% CI: 1.05-1.34) unadjusted for bone mineral density. For the outcome of hip fracture, the association between s-CTX and risk of fracture was slightly higher 1.23 (95% CI: 1.04-1.47).

"This is the first meta-analysis of BTMs which was made possible by standardising the expression of risk," said Working Group Co-Chair Professor Howard A. Morris, School of Pharmacy and Medical Sciences, University of South Australia. He added, "One strength of the study is that we were able to standardize the metric of predictive power. The metric used was the gradient of risk – namely the increase in fracture hazard ratio between two individuals who differ by 1SD in BTM. This has the advantage of maximizing the use that can be made of publications that used differing indices of risk."

The fracture risk increased by approximately 20%, depending on the analyte and the outcome fracture that was studied. These gradients of risk are substantially lower than those reported for the use of femoral neck BMD in the prediction of fracture.

Professor John A. Kanis, IOF President and report author said, "More studies are required to better evaluate the independent role of BTMs in fracture risk prediction. The use of common reference BTMs in prospective cohort studies with the standardization of their measurements, as recommended by the IOF and the IFCC, will help address these important issues."

More information: Johansson H, Odén A1, Kanis JA, McCloskey EV, Morris HA, Cooper C, Vasikaran S and the IFCC-IOF Joint Working Group on standardisation of biochemical markers of bone turnover. A meta-analysis of reference markers of bone turnover for prediction of fracture. Calcif Tissue Int, DOI: 10.1007/s00223-014-9842-y

Related paper:

Vasikaran S, Eastell R, Bruyere O, Foldes AJ, Garnero P, Griesmacher A, McClung M, Morris HA, Silverman S, Trenti T, Wahl DA, Cooper C, Kanis JA; IOF-IFCC Bone Marker Standards Working Group. Markers

of bone turnover for the prediction of fracture risk and monitoring of osteoporosis treatment: a need for international reference standards. Osteoporos Int 2011;22(2):391-420. link.springer.com/article/10.1 … 07/s00198-010-1501-1