Oxidative stress is significant predictor for hip fracture, research shows

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Oxidative stress is a significant predictor for hip fracture in postmenopausal women, according to new research led by University of Cincinnati (UC) epidemiologists.

The research, appearing online ahead of print in the *Journal of Bone and Mineral Research*, was led by Tianying Wu, MD, PhD, an assistant professor in the UC College of Medicine Department of Environmental Health, and Shuman Yang, a postdoctoral fellow in the department. They collaborated with researchers from the Harvard School of Public Health and Harvard Medical School.

"To our knowledge, this is the first prospective study among postmenopausal women demonstrating that oxidative stress was a significant predictor for hip fracture," says Wu, the study's corresponding author.

Oxidative stress is defined as physiological stress on the body that is caused by the cumulative damage done by free radicals, which are inadequately neutralized by antioxidants. Free radicals are unstable molecules that react with other substances in the human body to damage cells or organs.

Oxidative stress occurs naturally, but environmental factors such as natural and artificial radiation, toxins in air, food and water and miscellaneous sources such as tobacco smoke can add to the overall burden and defeat the body's antioxidant defenses.

The researchers assessed oxidative stress by measuring fluorescent oxidation products (FlOP) in blood plasma. FlOP reflects a mixture of oxidation products from lipids, proteins and DNA and can be measured by a fluorescent spectrophotometer.

Researchers studied participants in the Nurses' Health Study, which began in 1976 with funding from the National Institutes of Health (NIH). Participants are female nurses who periodically respond to questionnaires and submit samples.

The researchers studied 996 women aged 60 or older at baseline blood collection (1989-1990). Plasma FlOPs were measured at three excitation/emission wavelengths: 360/420 nm (nanometers), named as FlOP_360; 320/420 nm, named as FlOP_320; and 400-475 nm, named as FlOP_400.

FlOP_360 represents oxidation products that are generated from oxidized phospholipids or from lipid oxidation products reacting with proteins. FlOP_320 is formed when oxidation products such as lipid hydroperoxides, aldehydes and ketones react with DNA in the presence of metals. FlOP_400 reflects the interaction between malondialdehyde (a specific marker for lipid oxidation), proteins and phospholipids.

Of the three wavelengths, researchers found that baseline levels of FlOP_320 products predicted risk of future hip fracture in the study cohort. (No association was found with FlOP_360 and FlOP_400.) Increased FlOP_320 was associated with greater risk of hip fracture; women in the upper 30 percent of FlOP_320 readings were found to have 2.67 times the risk of hip fractures of those in the bottom 30 percent.

"Because FlOP_320 is generated in the presence of metals, its strong association with hip fractures may reflect the co-existing effect of

reactive oxygen species and heavy metals," says Wu, who notes that the other FlOP products can be generated without metals.

Hip fracture is associated with substantial cost, as well as higher risk of disability, co-morbidities and mortality than any other fractures. Current fracture risk assessment uses traditional risk factors such as age and presence of osteoporosis, but Wu sees FlOP_320 playing an important role in risk assessment.

"If our findings are confirmed in other studies, adding this marker into the existing fracture assessment model could improve the prediction of hip fracture in postmenopausal women," she says.

Provided by University of Cincinnati Academic Health Center