Osteoporosis, controversial fractures and various bone markers

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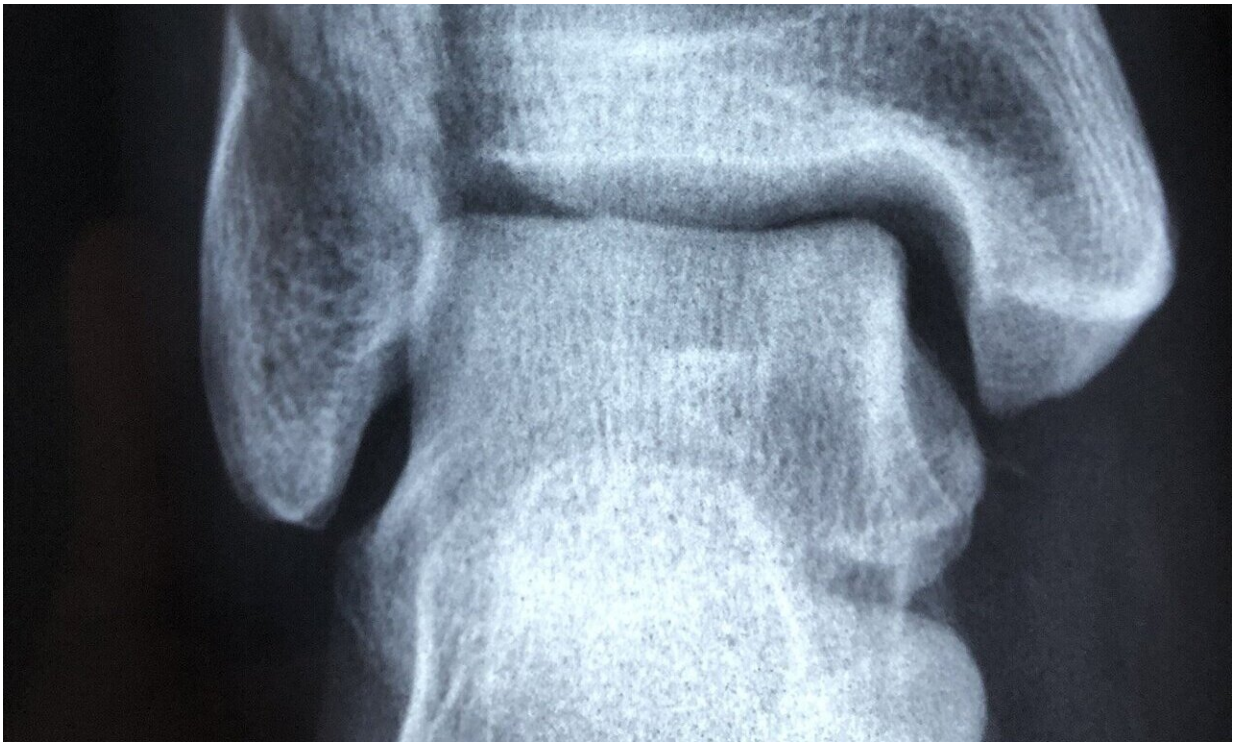

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Aging and lifestyle-related metabolic imbalances, such as hyperglycemia, hyperlipidemia, and oxidative-stress, cause the accumulation of advanced glycation end products (AGEs), including pentosidine (PEN, crosslinked type) and carboxymethyl-lysine (CML, non-crosslinked type). Osteoporosis is a widespread metabolic skeletal

disease characterized by diminished bone mineral density (BMD) or bone strength, which increases the risk of fractures.

To date, the association of PEN and CML with osteoporotic fracture has been reported, and the accumulation of AGEs in bone tissue is thought to contribute to bone vulnerability via the deterioration of bone matrix proteins, especially collagen. However, the precise mechanisms of PEN and CML in fracture occurrence are unclear and remain controversial, while no studies to uncover why CML associates with fractures have been attempted. There have been no reports investigating the implications of both PEN and CML on bone metabolism, BMD, and fractures in the same patients.

Accordingly, a team of doctors from the Department of Orthopaedic Surgery, Shinshu University School of Medicine et al. examined the levels of urinary PEN and serum CML to assess and compare the impacts of those AGEs on bone status and prevalent osteoporotic fractures in a cohort of postmenopausal women.

The group found that PEN as well as CML was significantly associated with prevalent vertebral fracture in postmenopausal women. The mechanism of PEN might be independent of lumbar BMD, while that of CML could be BMD dependent. It would appear that PEN, a crosslinked type of AGE, associated independently with the occurrence of fracture via collagen network deterioration, leading to impaired bone quality without affecting BMD. On the other hand, as a non-crosslinked type of AGE, CML could have contributed to fracture occurrence through lowered BMD. Both AGEs therefore appear to impact bone status and health, although possibly via different mechanisms.

Corresponding author of the study, Associate Professor Yukio Nakamura states, this study assessed the impacts of both PEN and CML on a number of bone turnover-related markers, BMD, and fractures in

the same postmenopausal outpatients who visited a primary care institution and demonstrated possible different mechanisms of those AGEs for the occurrence of fracture. Since this investigation was just a cross-sectional study, the team could not identify a causal relationship of AGEs with osteoporotic fractures.

Therefore, the pathophysiological importance of AGEs in fractures requires confirmation by a longitudinal prospective study design with general population, such as community-dwelling participants. Together with the laboratory experiments, we would like to uncover the epidemiologic and mechanistic associations between AGEs and fractures.

Finally, the team hopes to provide an effective intervention for the AGEs accumulation in bone tissue leading to bone health retention in the elderly.

More information: Masaki Nakano et al, Pentosidine and carboxymethyl-lysine associate differently with prevalent osteoporotic vertebral fracture and various bone markers, *Scientific Reports* (2020). DOI: 10.1038/s41598-020-78993-w

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