

博士論文の要旨及び審査結果の要旨

氏名 PLATONOVA Kseniia
学位 博士 (医学)
学位記番号 新大院博 (医) 第 1033 号
学位授与の日付 令和3年9月21日
学位授与の要件 学位規則第4条第1項該当
博士論文名 Dietary calcium and vitamin K are associated with osteoporotic fracture risk in middle-aged and elderly Japanese women, but not men: the Murakami Cohort Study.
(中高年女性における食事中のカルシウムとビタミンKは骨粗鬆症性骨折と関連するが男性では関連しない: 村上コホート研究)

論文審査委員 主査 教授 赤澤 宏平
副査 特任教授 菖蒲川 由郷
副査 特任教授 今井 教雄

博士論文の要旨

Background and Aims

Dietary nutrients are important factors associated with osteoporosis. Calcium (Ca) is a basic nutrient important for maintaining normal bone metabolism, and its insufficiency is a risk factor for osteoporosis. However, the impact of low Ca intake on osteoporotic fractures in East Asian populations has yet to be fully elucidated, although a global systematic review evaluated many cohort studies and demonstrated no association between Ca intake and fracture risk. Vitamin D and Vitamin K are also nutrients involved in normal bone metabolism. Especially, vitamin K plays a role in osteocalcin carboxylation. Although dietary Ca, vitamin D and vitamin K are nutritional factors associated with osteoporosis, little is known about their effects on incident osteoporotic fractures in East Asian populations. This study aimed to determine if intakes of basic nutrients related to bone health, including Ca, vitamin D and vitamin K, are associated with incident osteoporotic fractures in middle-aged and elderly Japanese.

Methods

We adopted a cohort study design with a 5-year follow-up. Subjects were 12 794 community-dwelling individuals (6301 men and 6493 women) aged 40-74 years. A self-administered questionnaire survey was conducted between 2011 and 2013. The questionnaire elicited information on age, sex, marital status, education, occupation, height, weight, lifestyle and history of osteoporotic fracture. Dietary intakes of Ca, vitamin D and vitamin K were assessed with a validated food frequency questionnaire (FFQ). All incident cases of major osteoporotic limb fractures, including those of the distal forearm, neck of humerus, neck or trochanter of femur and lumbar or thoracic spine

were collected. Only low-energy trauma fractures, that is, fractures due to falls from a standing height or lower, were included. Fractures due to high-energy trauma, such as traffic accidents, were not included. Among the 12 794 study subjects, multivariate analysis was performed in 12 306 (96.2 %) after excluding those with incomplete questionnaire data. Hazard ratios (HR) for energy-adjusted Ca, vitamin D and vitamin K were calculated with the residual method.

Results

Mean age was 58.8 (SD 9.3) years. Lower energy-adjusted intakes of Ca and vitamin K in women were associated with higher adjusted HR of total fractures (P for trend = 0.005 and 0.08, respectively). When vertebral fracture was the outcome, P for trend values for Ca and vitamin K were 0.03 and 0.006, respectively, and HR of the lowest and highest (reference) intake groups were 2.03 (95 % CI 1.08, 3.82) and 2.26 (95 % CI 1.19, 4.26), respectively. In the age stratified analysis (<60 v. ≥60 years), similar associations between energy-adjusted Ca intake and incident total fractures were observed, with a marginal significance in the older subgroup (P for trend = 0.054). Lower energy-adjusted vitamin K intake was associated with a higher incidence of total fractures in the older group, but not in the younger subgroup (P for trend = 0.009 and 0.67, respectively). In men, there were null associations between incident fractures and each of the three nutrient intakes.

Discussion:

The findings regarding Ca can be interpreted as an indication that women with low Ca intake do not consume much milk/dairy products. In this regard, higher intakes of milk and dairy products as well as adequate Ca supplements may be helpful, especially in women with low Ca intake. Previous studies reported that a higher intake of natto (fermented soybeans), high in vitamin K2 (phylloquinone), is associated with higher BMD, and support our results. We did not find a significant association between vitamin D intake and fractures, suggesting dietary vitamin D intake may contribute less to vitamin D status in the body than vitamin D biosynthesis in the skin. Fracture incidence in men was much lower than that in women, and thus, we were unable to identify risk factors for men, due to the smaller sample size. Lifestyle information, including dietary intake, was based on self-report, and thus misclassification bias may have occurred.

Conclusion

Lower intakes of dietary Ca and vitamin K are independent lifestyle-related risk factors associated with osteoporotic fractures in middle-aged and elderly Japanese women. This association was robust for vertebral compression fractures, but not for osteoporotic limb fractures. These associations were not observed in men and thus should be re-examined with a longer follow-up period.

審査結果の要旨

食事中の栄養素は骨粗鬆症に関連する重要な因子である。本研究は、中高年日本人におけるカルシウム (Ca)、ビタミンD、ビタミンKの摂取量と骨粗鬆症性骨折の罹患率の関連を明らかにすることを目的とした。対象は、40～74歳の12,794人の地域住民であった。2011-2013年に自己記入式のアンケート調査を行い、人口統計学的特徴、ライフスタイルおよび骨粗鬆症性骨折の病歴に関する情報を得た。食事栄養摂取量は妥当性の検証された食物摂取頻度調査票で評価された。5年間の追跡により前腕骨遠位部、上腕骨頸

部、大腿骨頸部・転子部骨折、および腰椎・胸椎圧迫骨折の新規発生症例を収集した。Cox 比例ハザードモデルによりハザード比 (HR) を算出した。女性において、Ca とビタミン K の摂取量が少ないほど、全骨折の調整後 HR は高かった。脊椎骨折をイベントとした場合も有意な HR の増加が見られ、最低摂取グループの最高摂取グループ (基準) に対する HR は、それぞれ 2.03 (95%CI 1.08-3.82) および 2.26 (95%CI 1.19-4.26) であった。男性ではこのような関連は見られなかった。結論として、食事中的 Ca とビタミン K の低摂取量は、中高年日本人女性における骨粗鬆症性骨折の独立した危険因子であることがわかった。骨折予防に関連した食事栄養要因を定量的に明らかにした点に博士論文としての価値を認める。